Data-Driven (Machine/Deep learning) Biomedical Image Analysis Research

Yale Image Processing and Analysis Group
Division of Bioimaging Sciences
Department of Biomedical Engineering
Department of Radiology & Biomedical Imaging

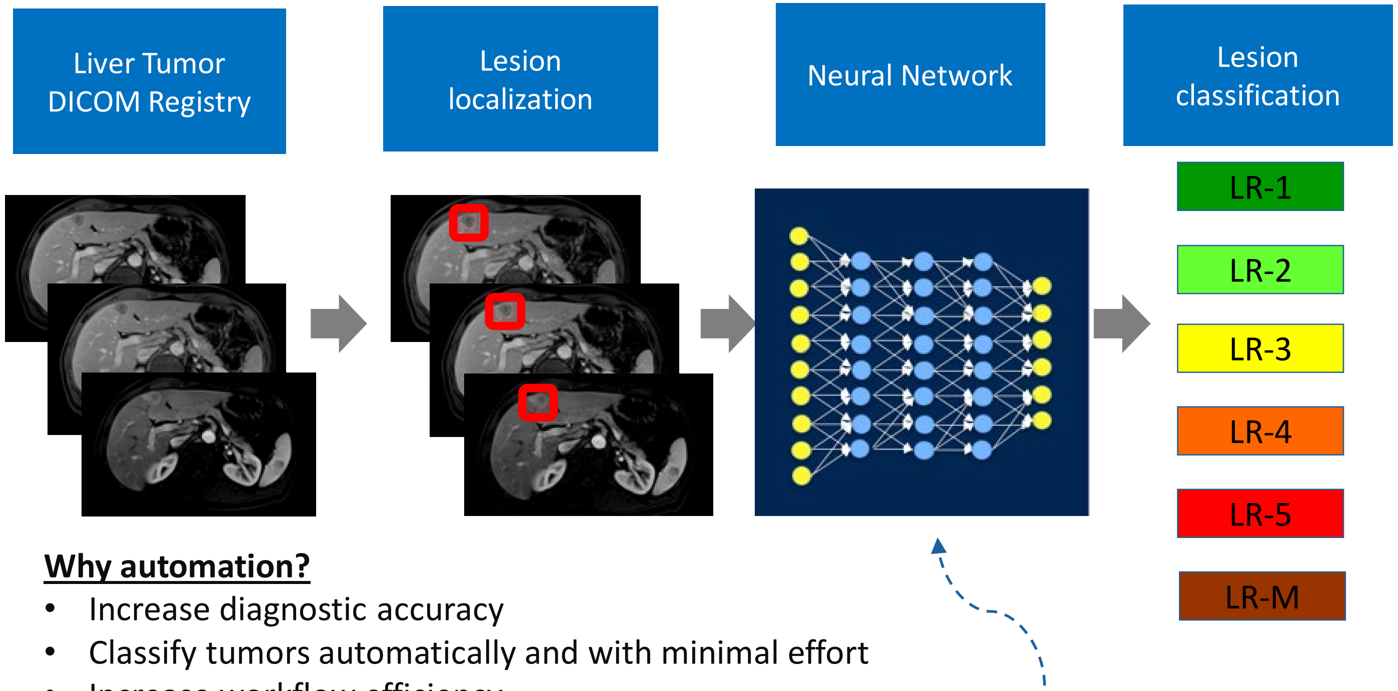
Yale University

Jim Duncan, Ph.D.

LI-RADS – Automation of Diagnosis and Classification of Liver Cancer

Input = multi-phasic contrast enhanced MRI in the arterial, venous, and equilibrium phases;

draw a 3D bounding box around the lesion



Why automation?

- Increase diagnostic accuracy
- Classify tumors automatically and with minimal effort
- Increase workflow efficiency

Supervised CNN:

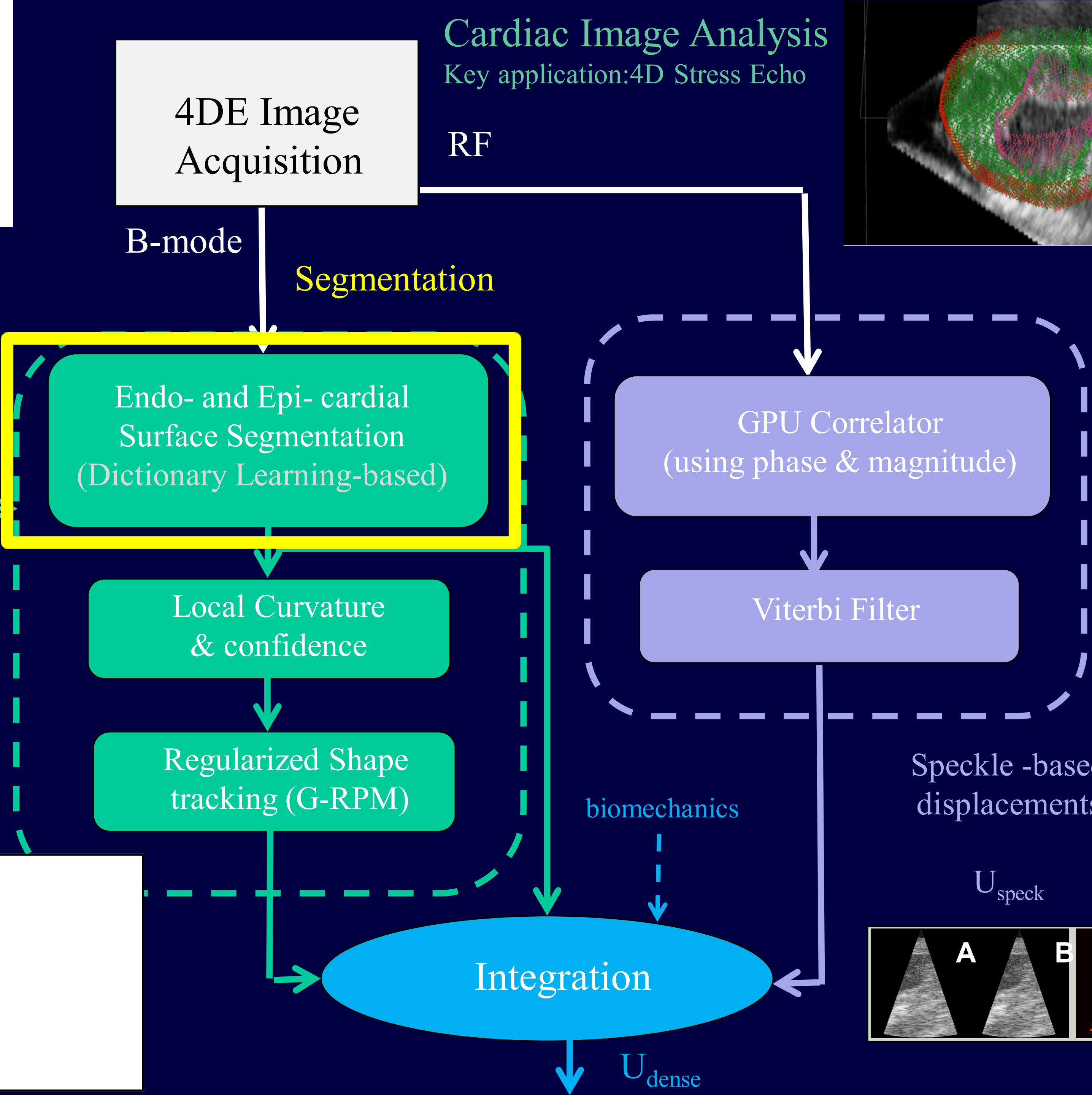
- 3 Convolutional Layers
- 2 Fully Connected Layers

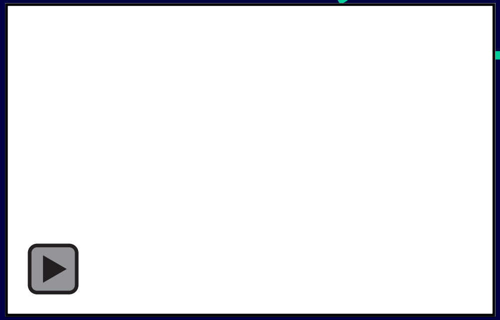
c/o Charlie A. Hamm, Brian Letzen

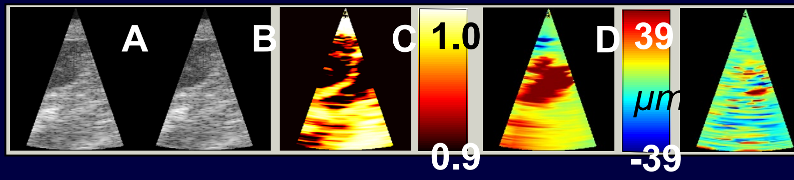
From Hamm, … Schlacter, Weinreb, Duncan, Chapiro,…Et al., *European Radiology*, 2019.

Cardiac Image Analysis

Key application:4D Stress Echo



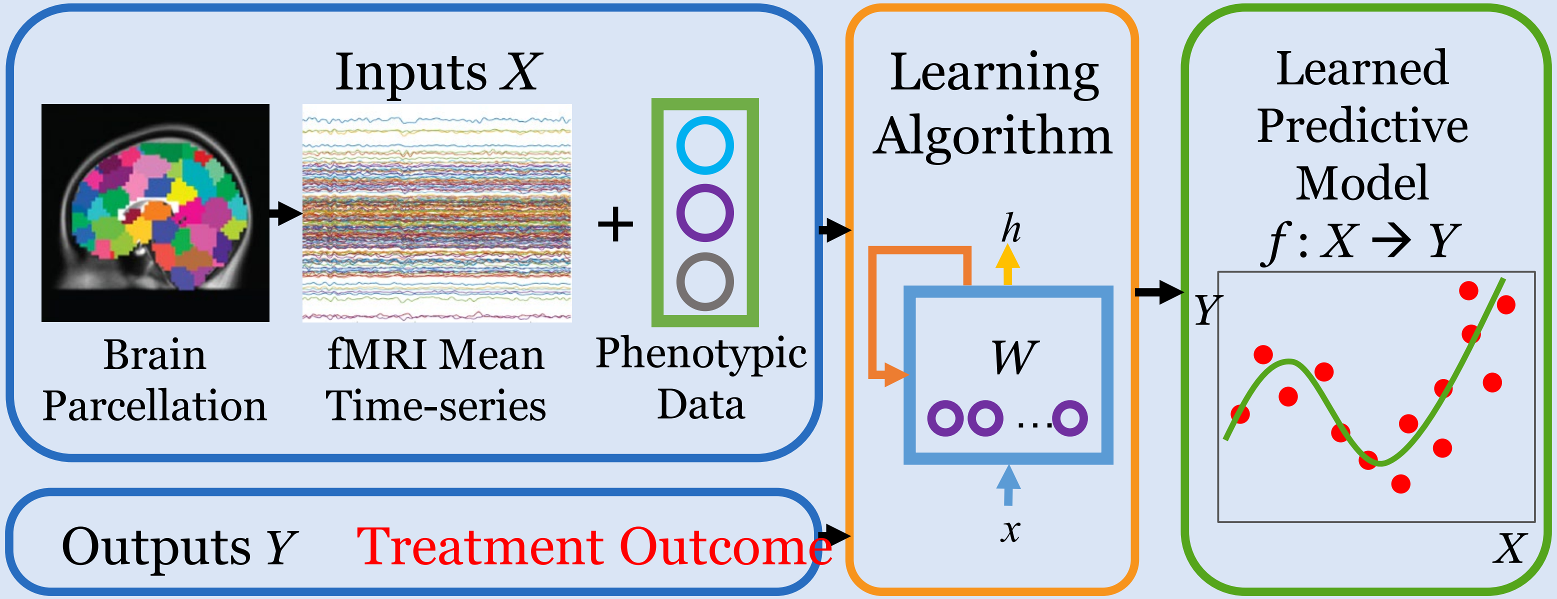




Autism Spectrum Disorder(ASD): Prediction of PRT Treatment Outcome Using LSTMs with fMRI + Phenotypes (MICCAI 2018)

- Pivotal Response Therapy (PRT): Targets social skills development in play-based format
- Large commitment from patients and families
- Early intervention is crucial, yet treatment currently assigned by trial and error

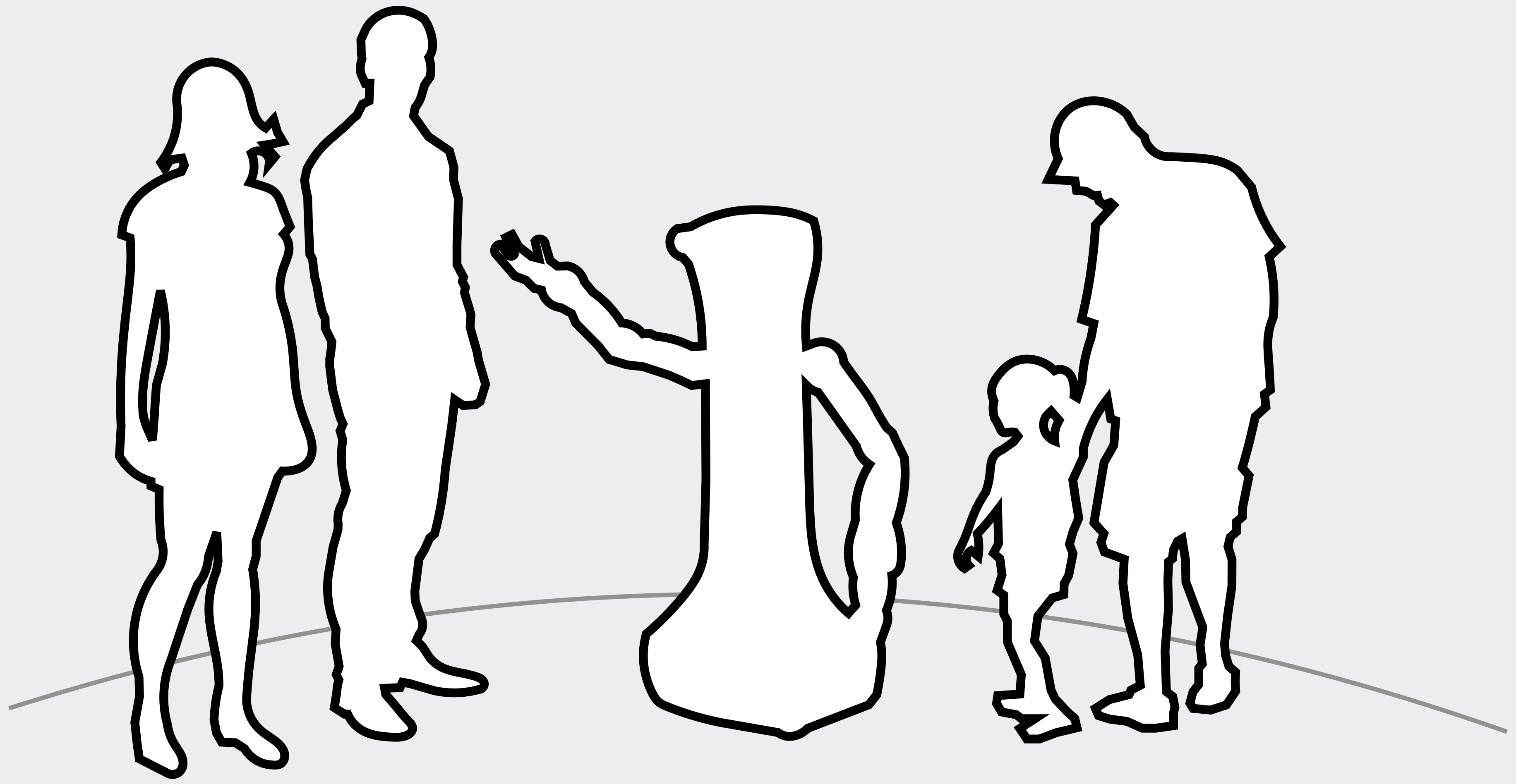
→ Can we predict treatment outcome from baseline measures?



Prediction: Change in Social Responsive Scale (SRS) score

Do you want to help us advance Human-Robot Interaction?

We create social robots for complex human environments.

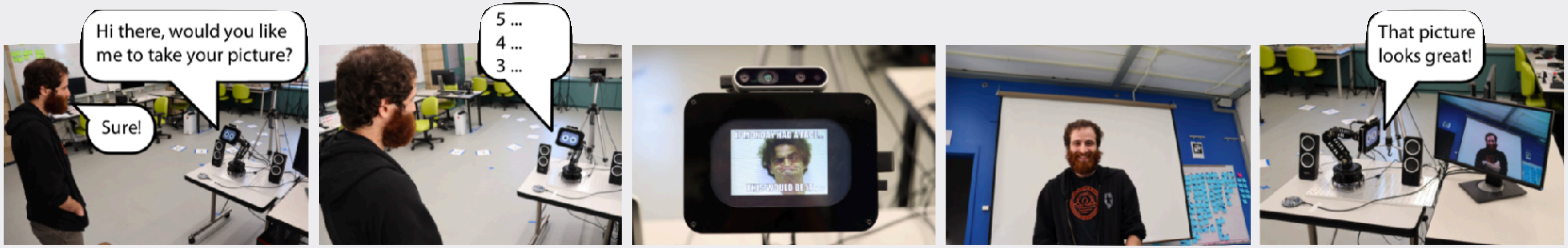


Yale

INTERACTIVE MACHINES GROUP

Marynel Vázquez
Assistant Professor, Yale Computer Science
http://www.marynel.net
marynel.vazquez@yale.edu

Project 1. Shutter, the Robot Photographer



We are building a **social robot photographer**. The robot tells jokes to make people laugh while trying to take portrait pictures of them.

Yale

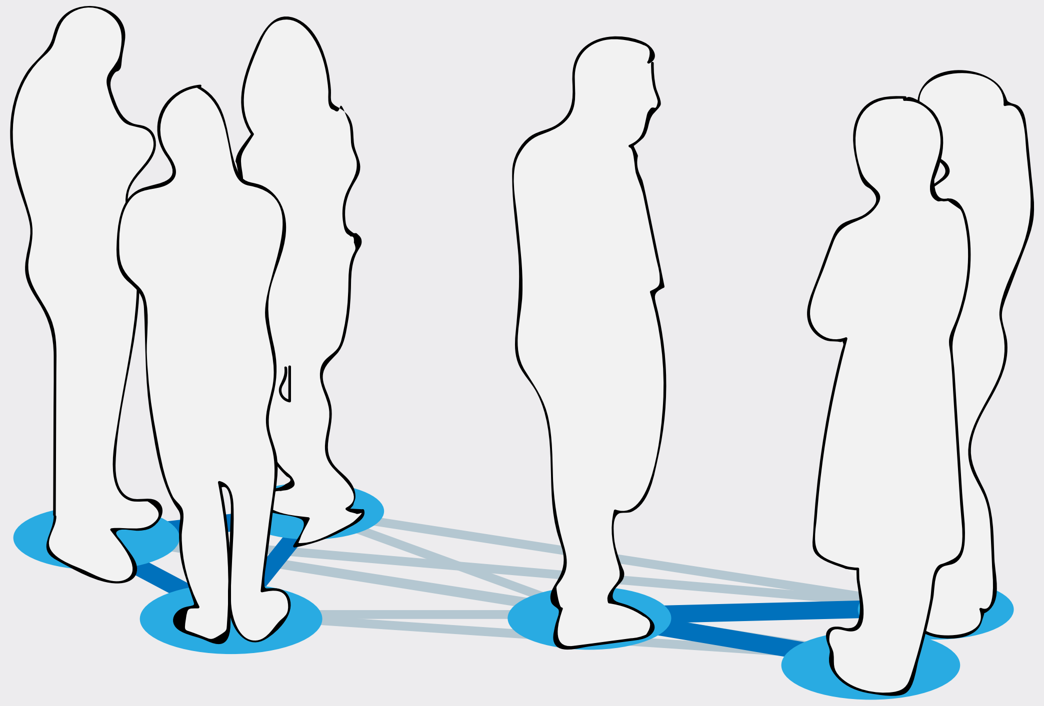
INTERACTIVE MACHINES GROUP

Marynel Vázquez
Assistant Professor, Yale Computer Science
http://www.marynel.net
marynel.vazquez@yale.edu

Project 2. Understanding Spatial Group Behavior

We are creating **models of spatial patterns of behavior** that are typical of social conversations. These models allow robots to predict who is conversing with whom in social settings.

Scene from the Coffee Break dataset



Node for an individual
Edge among two individuals
Edge connecting people in the same group

Yale

INTERACTIVE MACHINES GROUP

Marynel Vázquez
Assistant Professor, Yale Computer Science
http://www.marynel.net
marynel.vazquez@yale.edu

Contact us!

What can you do in the lab? Help us prototype robotic systems, conduct user experiments, and/or implement algorithms.

Mentoring: Direct supervision by Marynel and her graduate students. Weekly meetings.

Students: We are looking for 1-2 students.

Want to learn more? http://interactive-machines.com

Yale

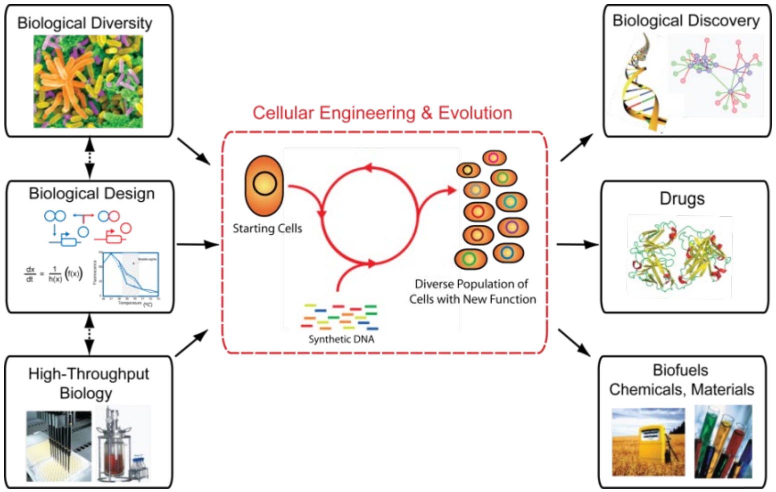
INTERACTIVE MACHINES GROUP

Marynel Vázquez
Assistant Professor, Yale Computer Science
http://www.marynel.net
marynel.vazquez@yale.edu

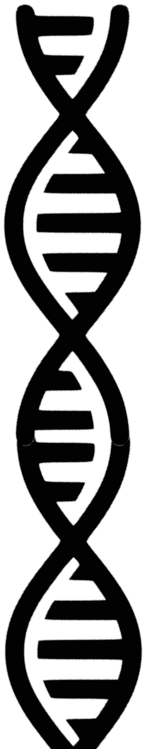
Synthetic Biology @ Yale

Farren Isaacs
Associate Professor & DGS
Molecular, Cellular & Developmental Biology
Biomedical Engineering
Systems Biology Institute
Yale University

Isaacs Lab



- Invent new genome engineering technologies
- Construct organisms with new genetic codes
- Engineer novel proteins & biomaterials
- Develop biological safeguards
- ➢ **Undergrads publish papers!** **Isaacslab.org**



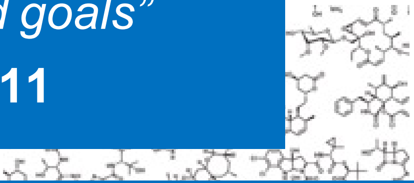
iGEM

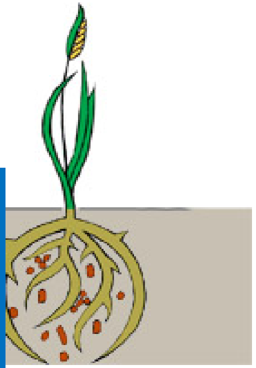
- International genetically engineered machines
- Multidisciplinary teams work together to build, design, and test novel biological systems
- Push the boundaries of science by tackling real-world global problems
- ➢ Compete against 6,000 people from around the world at annual Jamboree @ MIT **igem.org**

Synthetic Biology: a new approach for meeting grand challenges and societal needs

"the quest to hijack living systems and convert them to human-directed goals"

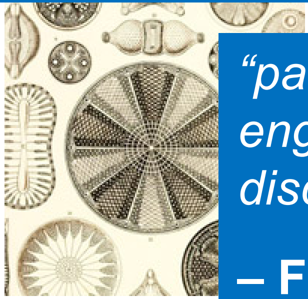
-Nicholas Wade, NY Times 2011





"By combining elements of engineering, chemistry, computer science, and molecular biology, synthetic biology seeks to assemble the biological tools necessary to redesign the living world."
– New Yorker 2009

ricultural



"part of the natural maturation of biotechnology, in which the engineering of biological systems is becoming a formal discipline"

– Farren Isaacs & Lingchong You, Genome Biology 2009

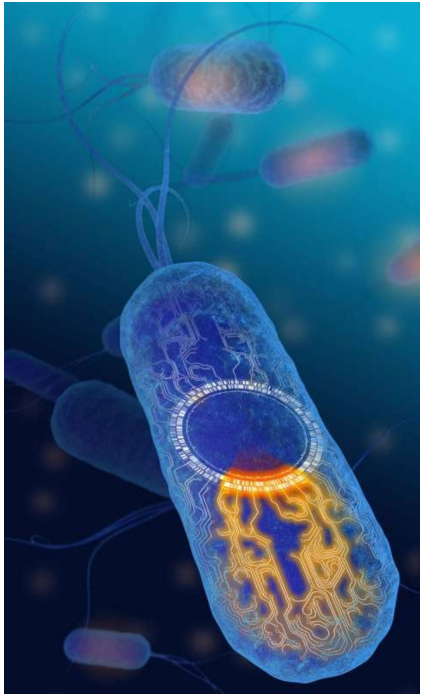
Materials

Energy

Global Health

Synthetic Biology is "Engineering Biology"

- the design and construction of new biological parts, devices, and systems
- the re-design of existing, natural biological systems for useful purposes



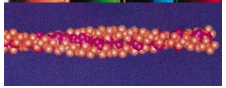
Medicine

Food

Energy

Chemicals

Materials



iGEM at Yale

Team History

Yale iGEM was **founded in 2009** by a group of undergraduates passionate about the **potential of synthetic biology**. Inspired by the iGEM foundation mission, they set out to make their own contributions, completing their first project in 2010.

Nature's Antifreeze: Microbial Expression and Characterization of a Novel Insect Antifreeze Protein for De-Icing Solutions

Developing a Framework for the Genetic Manipulation of Non-Model and Environmentally Significant Microbes

Publications

- Journal of Biological Chemistry (cover)
- Nature, eLife, ACS-Synthetic Biology, Nucleic Acids Research

Team Awards

- Food/Energy Project Grand Prize
- Best Natural Biobrick
- Gold Medal
- Grand Finalist

Individual Awards

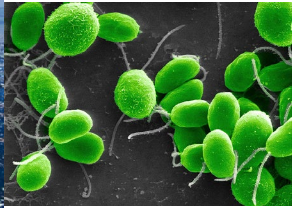
- Gates Fellowship
- Hertz Fellowship
- Goldwater Award
- Beckman Scholar
- Schwartzman Scholarship

iGEM Alumni

- Grad School @ Yale, Duke, Stanford, Harvard, Princeton
- Regeneron
- NIH
- Microsoft
- Promega
- McKinsey & Co., BCG

Recent Project

"its all about plastics"



To mitigate PET microplastic waste build-up, the Yale iGEM team has been working to engineer a strain of *Chlamydomonas reinhardtii,* a freshwater green algae, with the ability to secrete proteins capable of breaking down plastics.

WE WANT YOU!

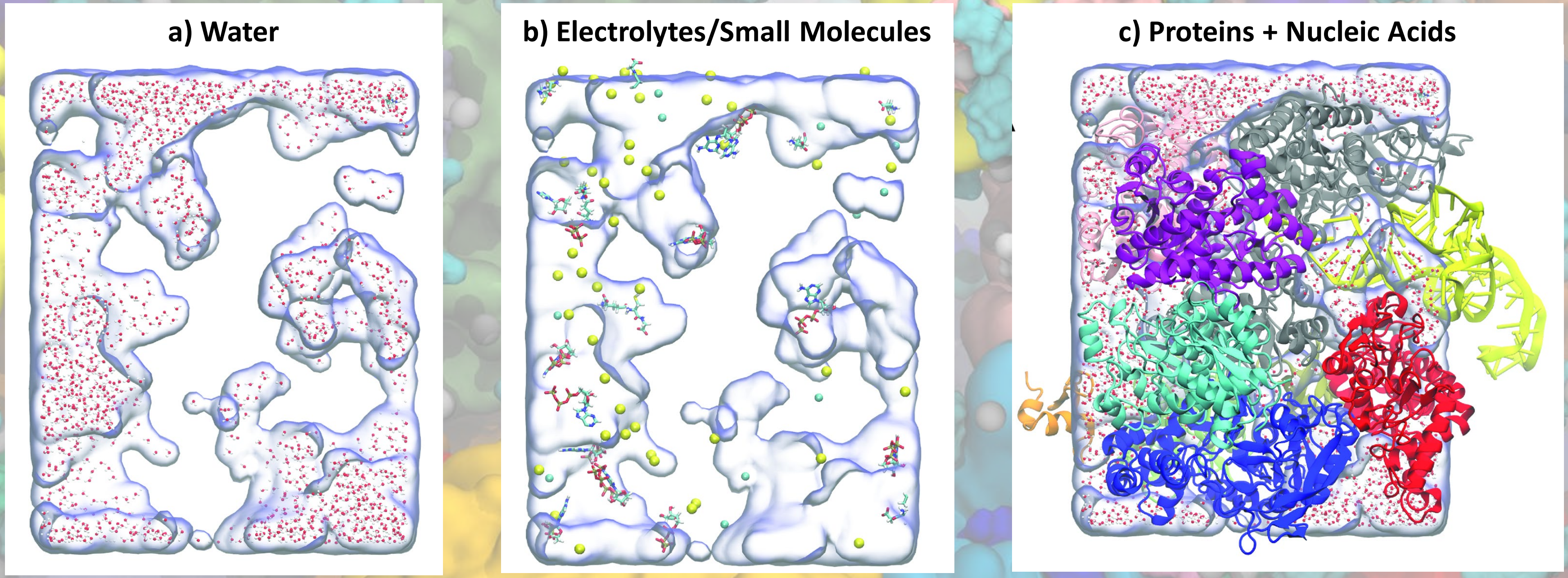
THE iGEM TEAM SEEKS A FEW GOOD **YALIES** …
… TO CHANGE THE WORLD

farren.Isaacs@yale.edu

Caitlin Davis, Department of Chemistry contact: c.davis@yale.edu

Davis Lab Research

- Traditionally chemistry is studied in test tubes, but chemistry happens inside cells
- A test tube is mostly water, but the cell volume includes approximately:
    a) 70% water
    b) 10% electrolytes and small organic molecules
    c) 20% nucleic acids and proteins
- **How does the cellular environment affect protein and RNA interactions?**



C. M. Davis, M. Guebele, and S. Sukenik, *Curr. Opin. Struct. Biol.* **2018,** *48*, 23-29.

Background: Meredith Rickard, Gruebele Lab

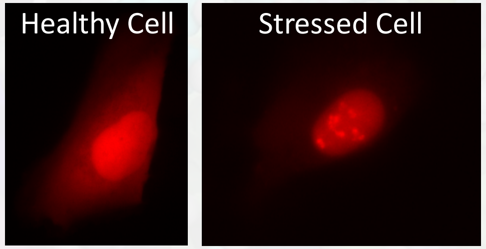
Caitlin Davis, Department of Chemistry

contact: c.davis@yale.edu

Potential Undergraduate Projects

Mapping Huntington's Disease-Associated Protein Phase Transitions

- Cells organize dysfunctional proteins into “droplets” like oil droplets in water



Proteins move from the cytoplasm and nucleus of healthy cells to droplets in the nucleus of stressed cells.

- It is difficult to study droplets inside cells because cells are hard to control, but…
- Physical properties of droplets measured in test tubes differ from inside cells
- We will test how crowding, sticking, pH, temperature, etc. impact droplets
- <u>We will create an assay that reproduces in-cell observations in a test tube</u>

Development of a Microfluidic Mixer for Cell Culture Investigations

- Because cells are difficult to control, we need new ways to trigger and monitor reactions inside ce

A laser quickly heats the sample to induce a “temperature jump,” an microscopy monitors dynamics of protein or R

- A complementary approach uses rapid mixing to quickly change the local environment (pH, salt, temperature, etc)
- <u>We will design and test a microfluidic mixer for our infrared microscope</u>
- This will be the basis for future studies of how cells respond to external stimuli

Background: Meredith Rickard, Gruebele Lab

Student Mentoring and Expectations

Qualifications

Motivated and enthusiastic researchers interested in research at the interface of biology, physics, and chemistry.

Mentoring

Day-to-day supervision by a postdoc mentor. Professor in lab for additional mentoring.

Meetings

Weekly group meeting to discuss research progress. Available for additional meetings informally or on request.

Funding

Looking for two students. Expected to apply for external funding.

Learning Outcomes

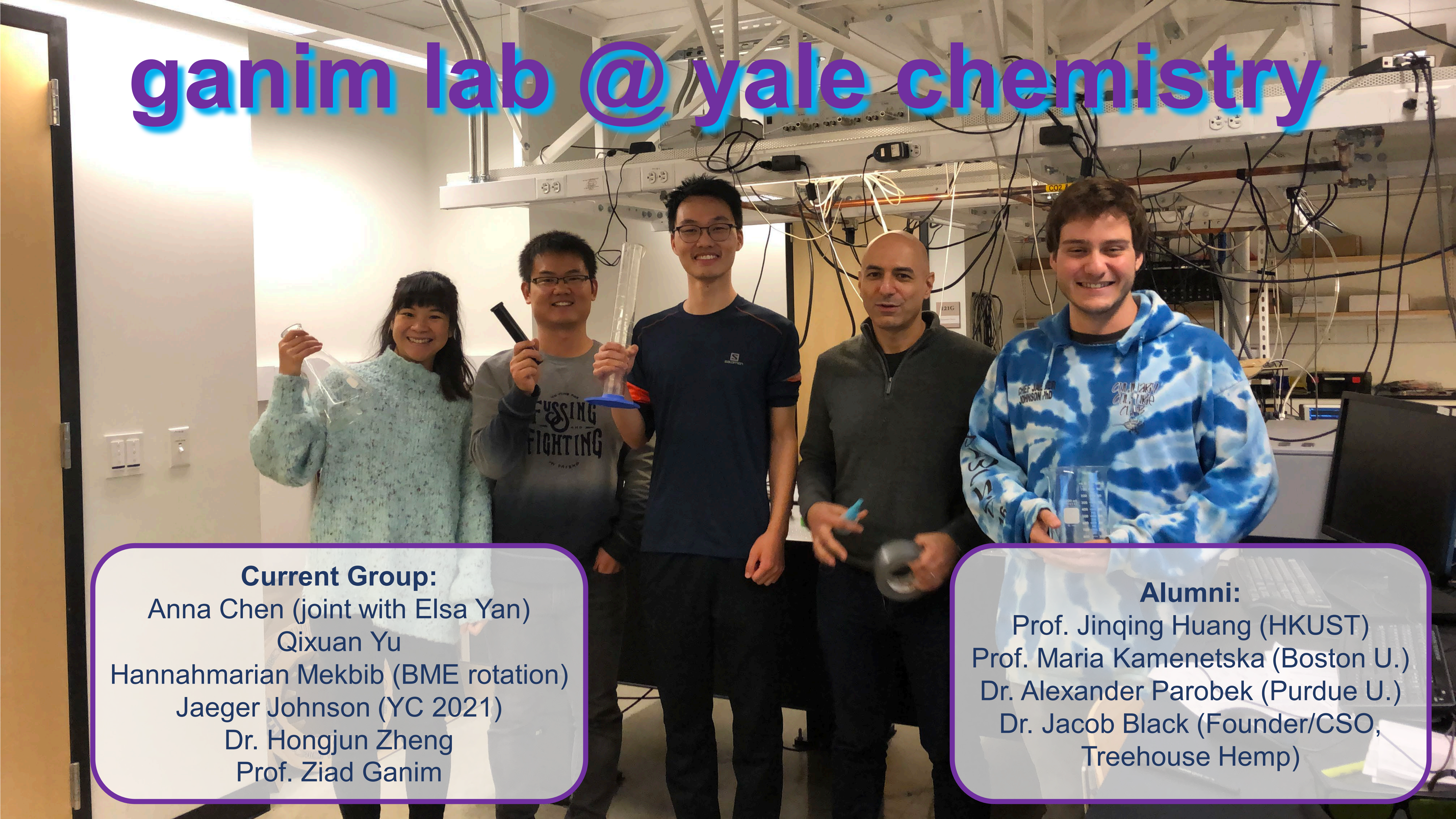
Students will receive training in a combination of protein and RNA biophysics, live cell microscopy, spectroscopy, programming, data analysis, and physical chemistry.

Contact Information

Dr. Caitlin Davis
Assistant Professor
Department of Chemistry
Yale University
c.davis@yale.edu

@thedavislab
www.caitlindavislab.com

Background: Meredith Rickard, Gruebele Lab


ganim lab @ yale chemistry
Current Group:
Anna Chen (joint with Elsa Yan)
Qixuan Yu
Hannahmarian Mekbib (BME rotation)
Jaeger Johnson (YC 2021)
Dr. Hongjun Zheng
Prof. Ziad Ganim
Alumni:
Prof. Jinqing Huang (HKUST)
Prof. Maria Kamenetska (Boston U.)
Dr. Alexander Parobek (Purdue U.)
Dr. Jacob Black (Founder/CSO, Treehouse Hemp)

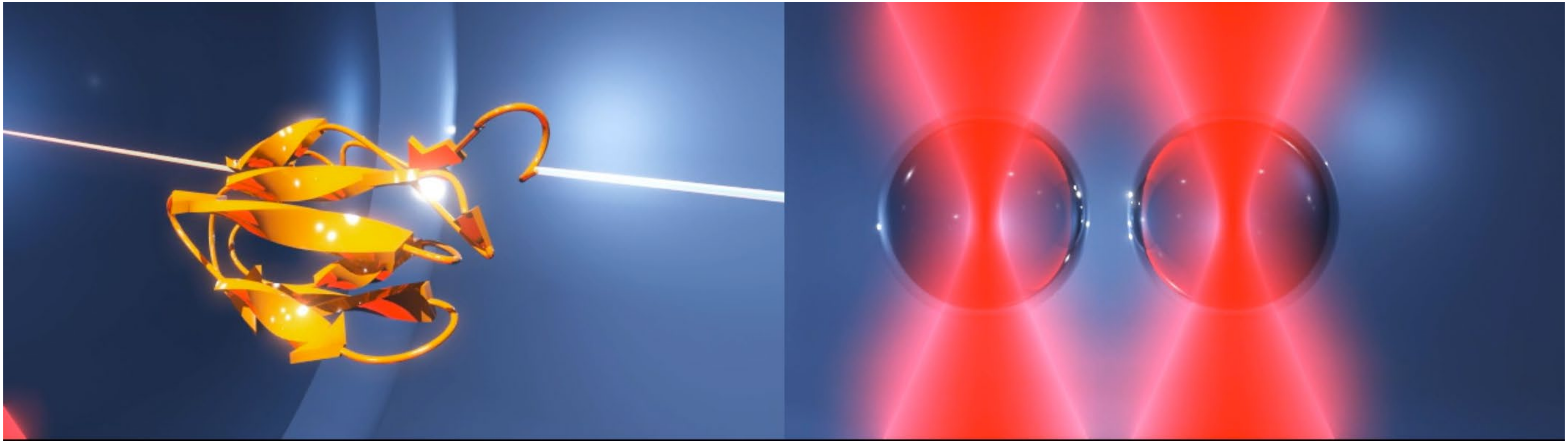
optical tweezers and spectro/microscopy

as a tool to:

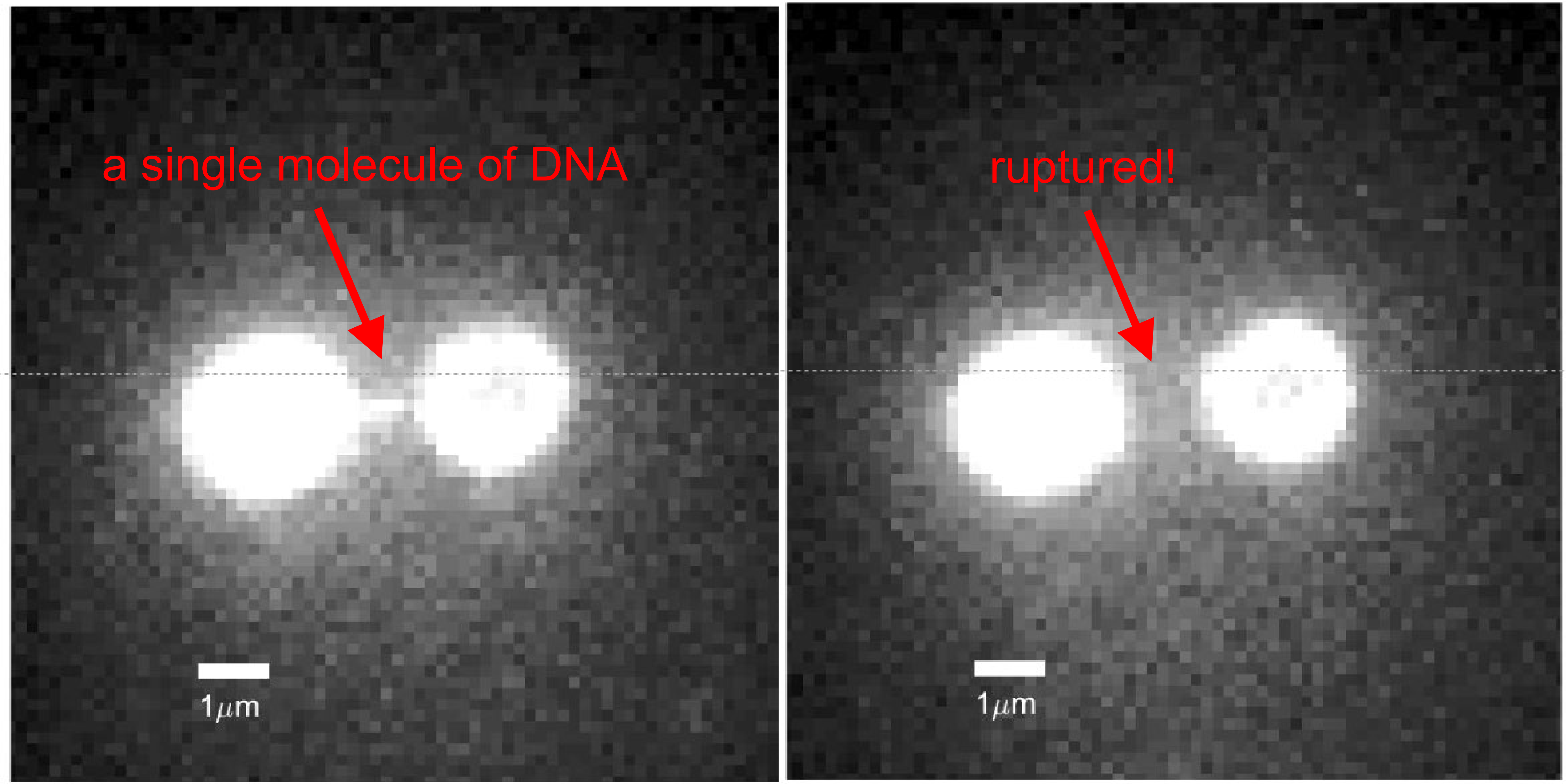
immobilize single molecules in solution

apply and measure force

perform advanced spectroscopies

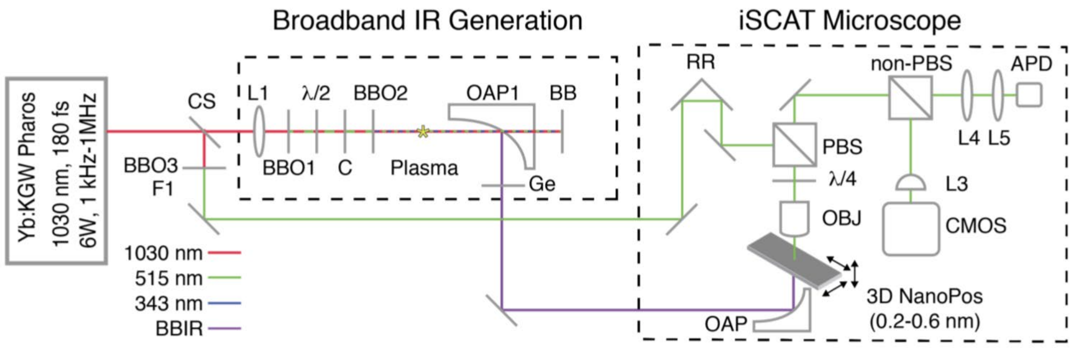


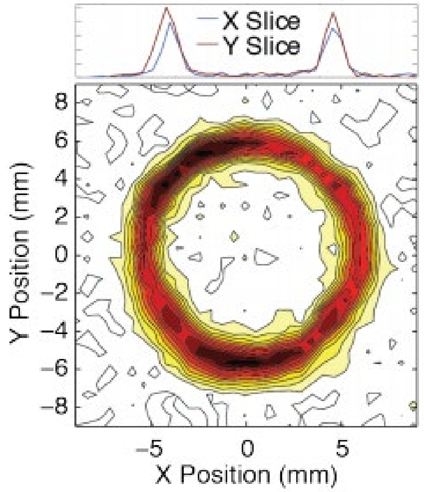
concept graphics: criss hohmann und alexander mehlich

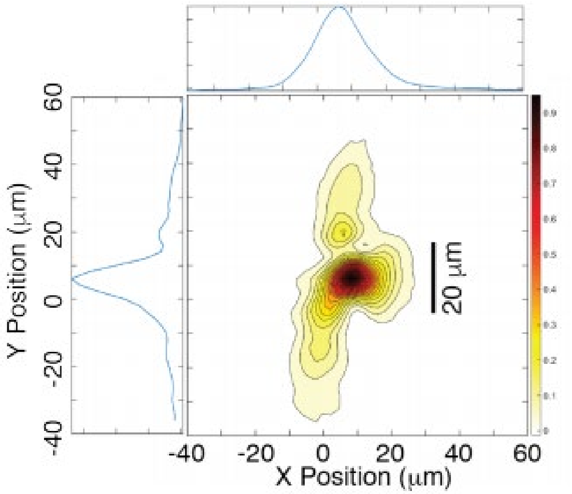

a single molecule of DNA
1μm
ruptured!
1μm

femtosecond broadband infrared microscopy

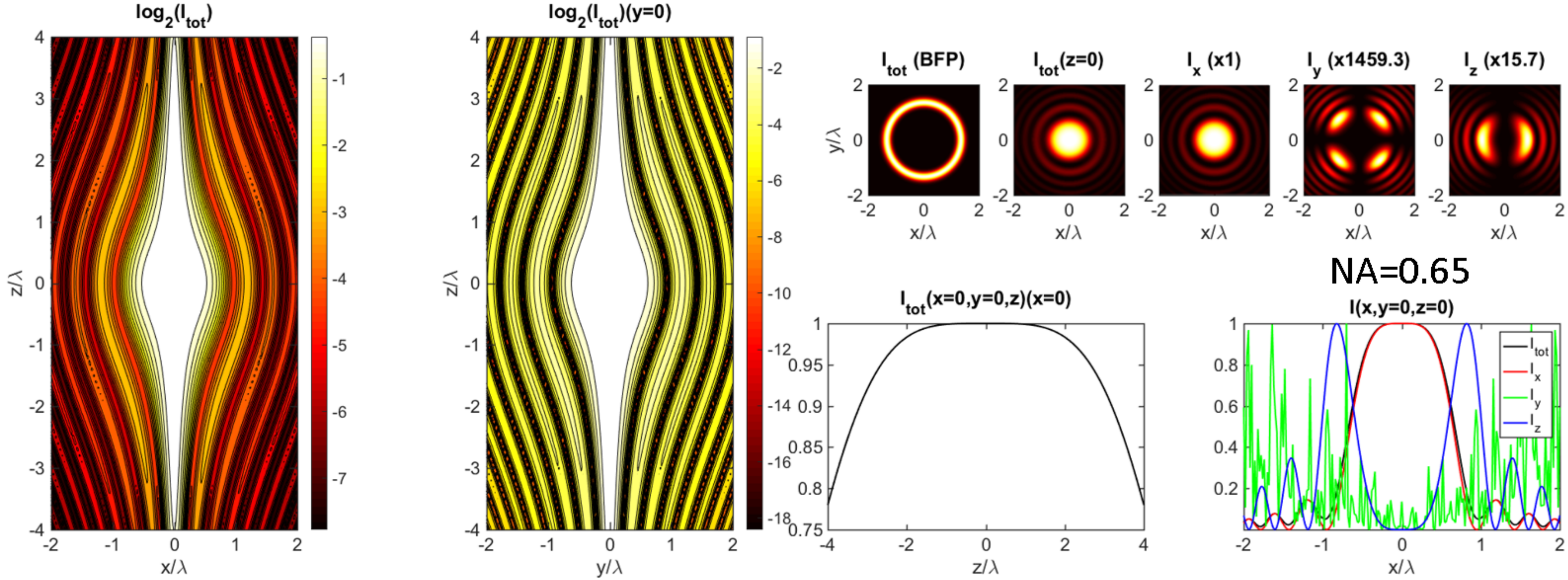
experiments







beam propagation simulations



Laura Newburgh

laura.newburgh@yale.edu

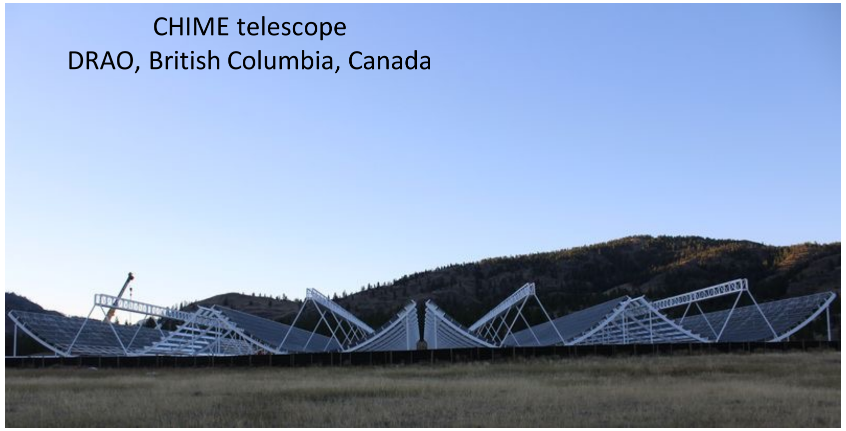
Next-generation Cosmology Instrumentation and Science with Millimeter and Radio Telescopes

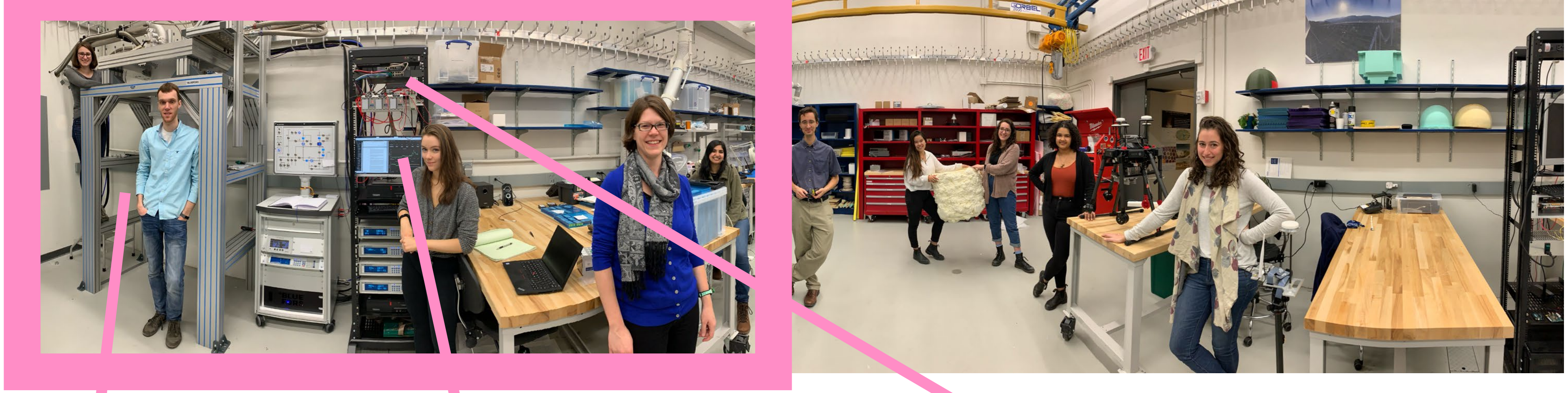
Cosmic Microwave Background Measurements with the Simons Observatory (and CMB-S4)

- Simons Observatory: 4 telescopes in ~2020
- Main science goals using measurements of the power spectrum, maps, and lensing: inflation, neutrino mass sum, light relics, dark energy
- I lead the group on 'data acquisition' focusing on software development: all acquisition and control, software, timing, live monitoring

21cm Measurements of Dark Energy with CHIME and HIRAX

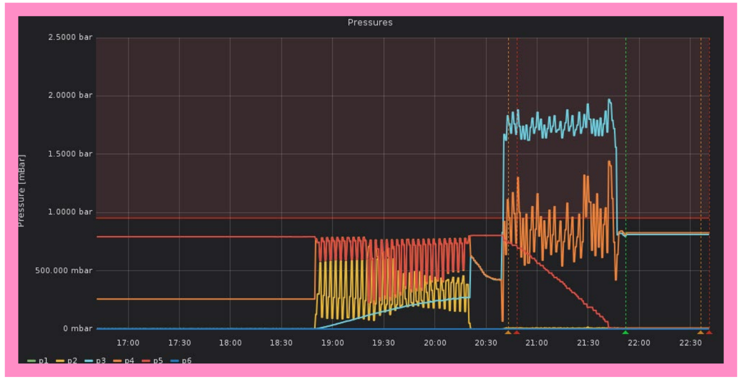
- CHIME is a new radio interferometer in Canada, seeking to use a new technique ('21cm intensity mapping') to expand the reach of galaxy surveys to very high redshift, critical for improving our understanding of Dark Energy
- I work on calibration: measuring the PSF of the instrument using a co-located a steerable dish and quadcopter drone measurements
- I also am a collaborator on HIRAX, a prototype instrument in South Africa which should overlap with other cosmological surveys (like SO)





Simons Observatory work

Sanah (gap year student, now grad student here) working with low temperature thermometry in the Dilution Refrigerator



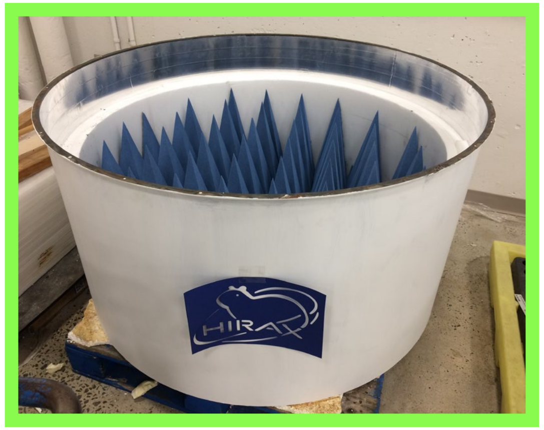
Sam, Sebastian, and Ananya contributed to software for calibrating thermometry in the Dilution Refrigerator. Shown here is our grafana-based live monitor of the state of our Fridge.

Sam (pictured) and Sebastian (not pictured) designed and built power and thermometry boxes for fielding in Chile

This was version #1 —- it got much more 'real'

Receiver noise testbed - led by graduate student Emily Kuhn

Maile constructing the fibreglass insert



One of two receiver noise test-beds done!

Emily and Ben building the foam insert

The picture can't be displayed.

Emily and and Maile shaving down the foam insert (power tools were very helpful!)

Debating

Ry is building a radio dish at Leitner for drone flight testing

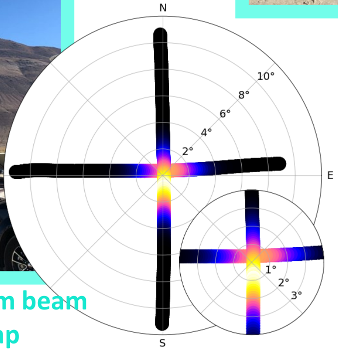
Drone beam mapping

pre-flight testing in New Haven

(Drone test flight at Owens Valley Radio Observatory in Oct 2019)

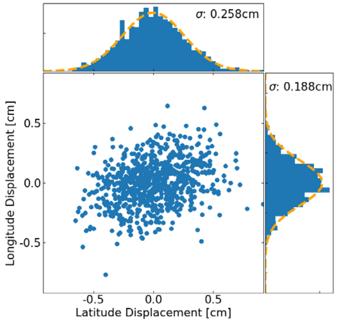
Annie and Maile checking out the drone radio signal chain

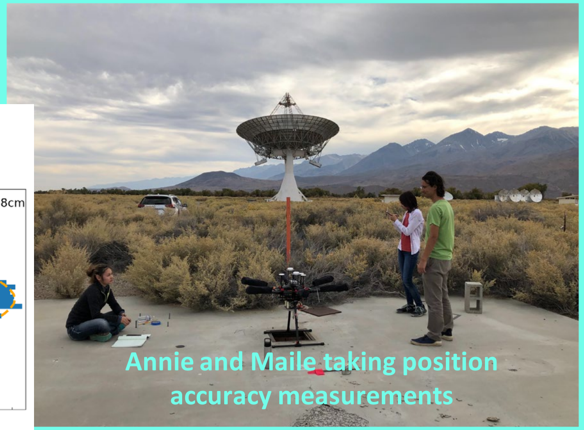
in flight!



data from beam map

Annie analyzed the data — the drone has excellent relative position accuracy

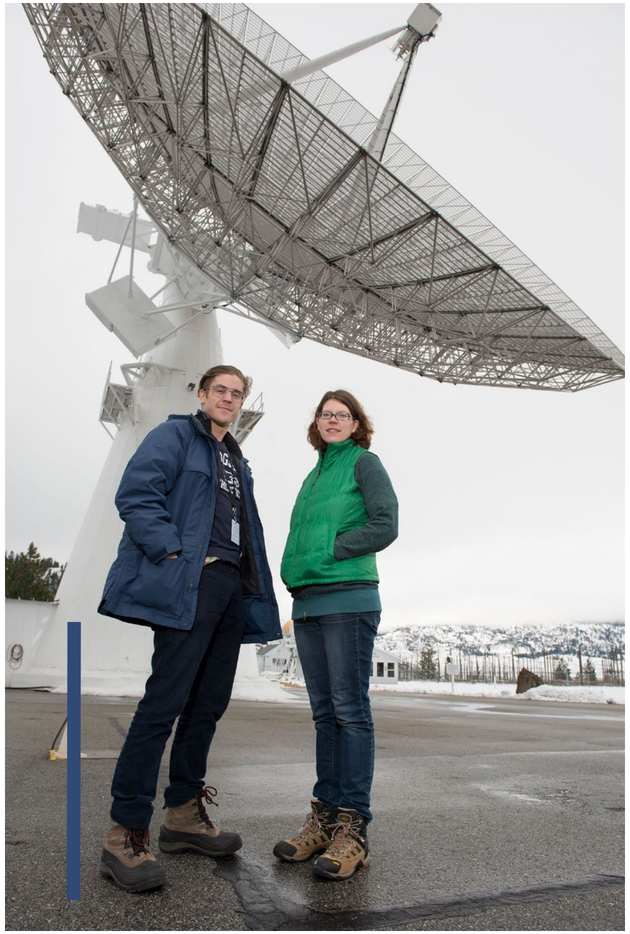


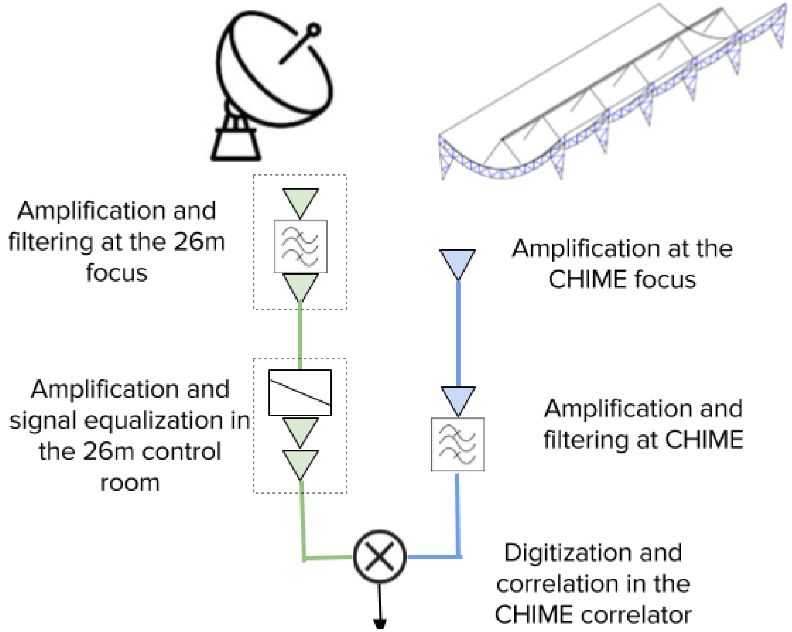


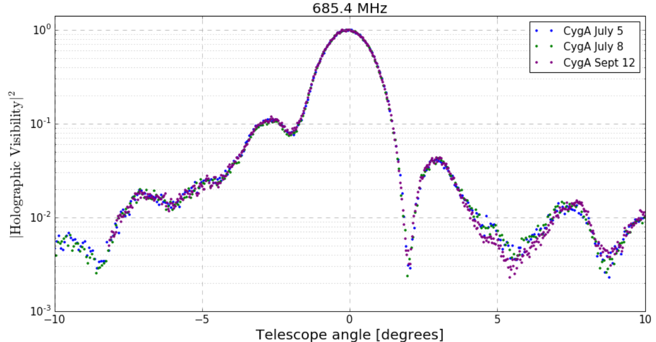
Annie and Maile taking position accuracy measurements

Calibrate with Holography

Tracking dish





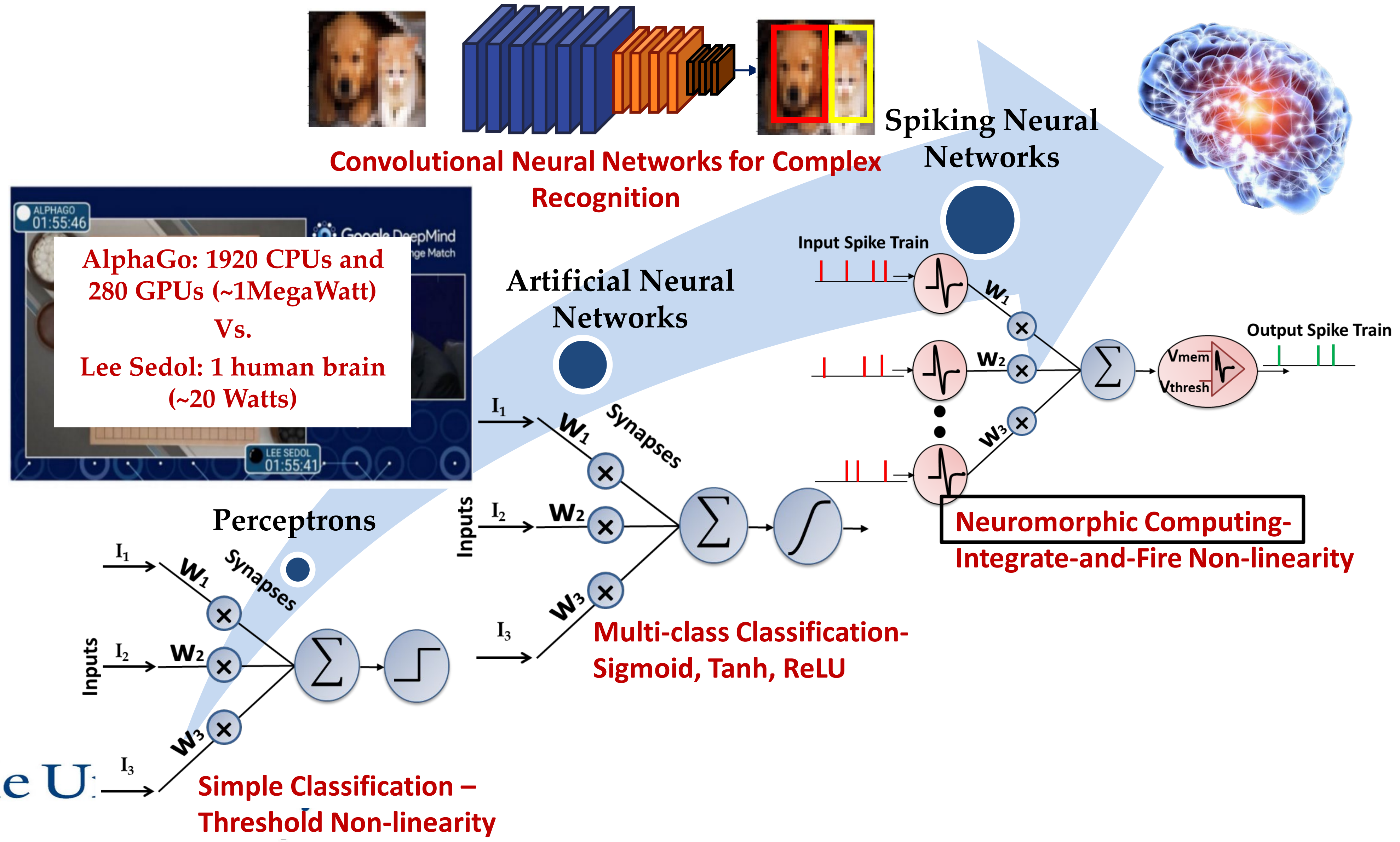


Prof. Priya Panda
Assistant Professor,
Electrical Engineering
priya.panda@yale.edu

INTELLIGENT COMPUTING LAB

https://intelligentcomputinglab.yale.edu/

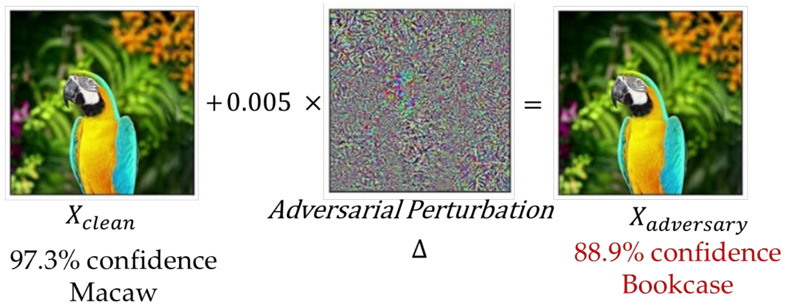
Research Focus: Towards energy-efficient and robust machine intelligence with brain inspired 'spikes' computing

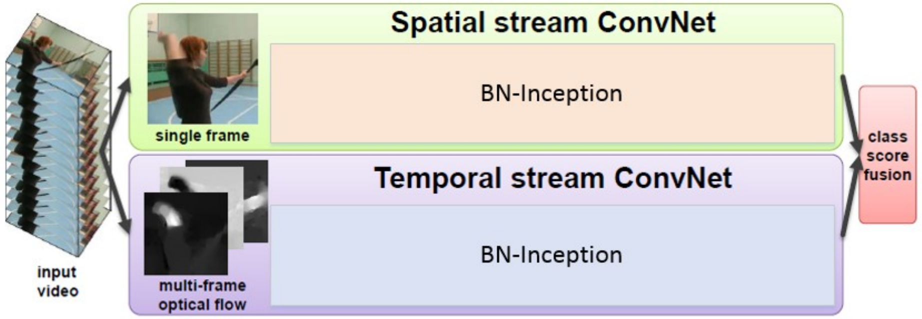


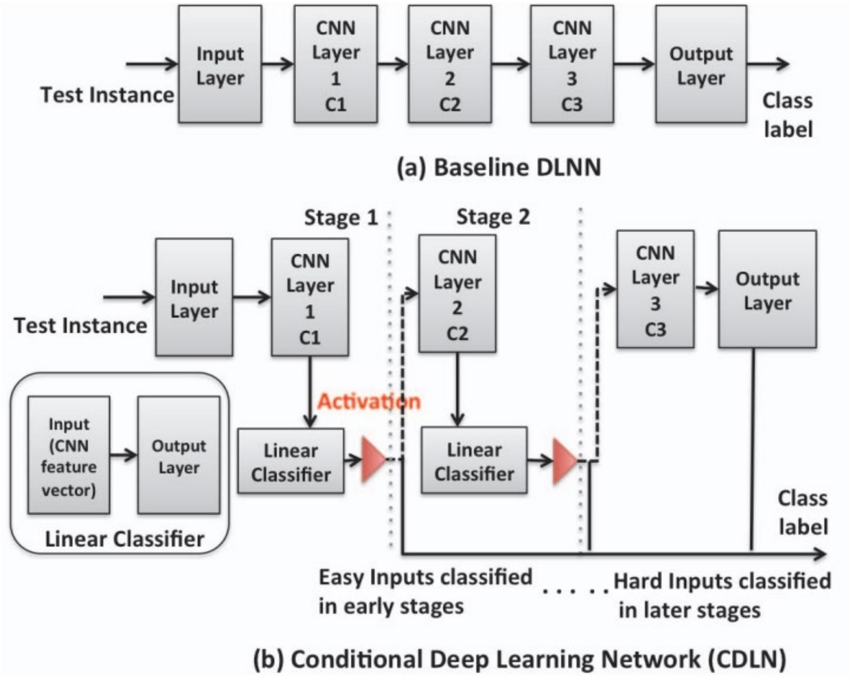
Yale U

Projects

- Adversarial Susceptibility of Spiking Neural Networks
- Design neural networks to say 'I don't know'
- Conditional Spiking Neural Network for real-time fast and efficient learning
- Action Recognition with brain-inspired neural network designs







Yale University

Logistics

Pre-Req: Having background in neural network and knowing basic Python skills will be good.

Mentoring: Will closely work with the students in defining the problem. Typically meet with me 1-2 times a week. Informal drop ins welcome

Funding: Looking for 2-3 students, encourage to find funding of your own!

Want to learn more? https://intelligentcomputinglab.yale.edu/

Prof. Priya Panda
Assistant Professor
Electrical Engineering
priya.panda@yale.edu

Yale University

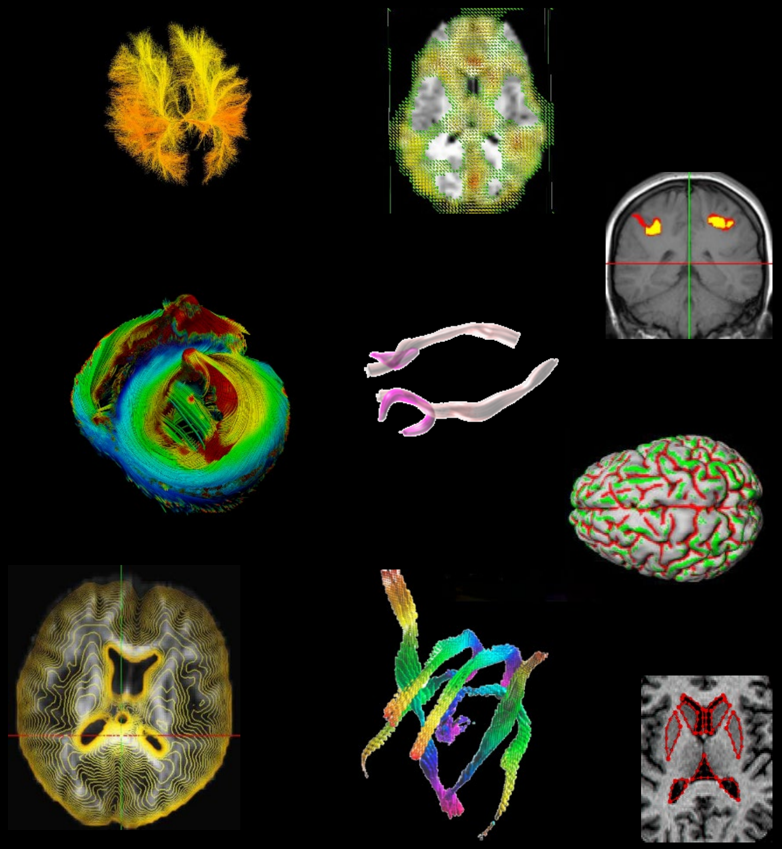
Lawrence Staib

Departments of Biomedical Engineering and
Radiology & Bioimaging Sciences

lawrence.staib@yale.edu

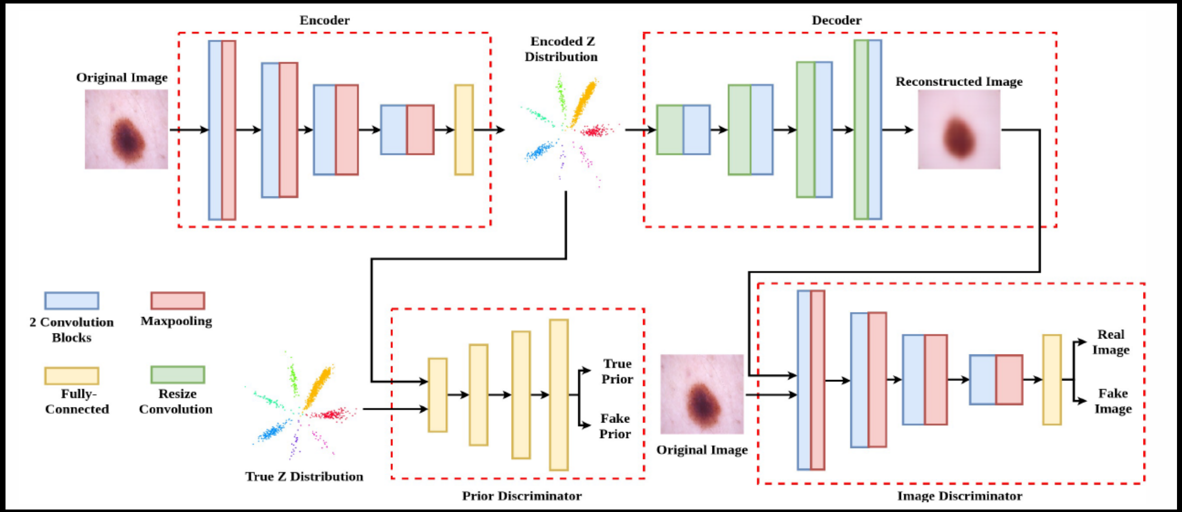
- Focus on:

Medical Image Analysis
and Machine Learning
for quantification
diagnosis,
prognosis, and
characterization
of normal and pathological
structure and function



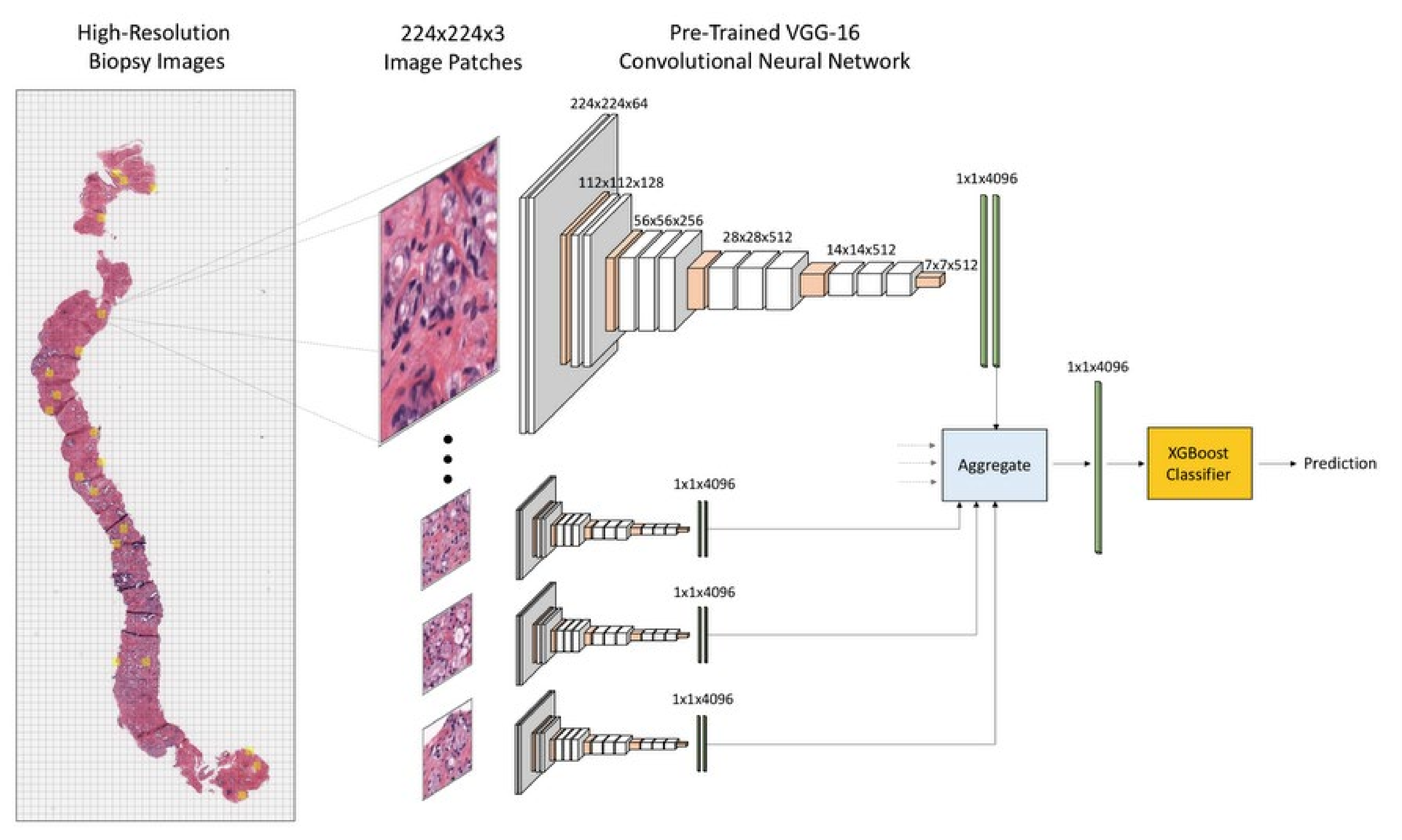
Potential Projects

- Applications in neuroimaging, cardiovascular disease, cancer, etc.

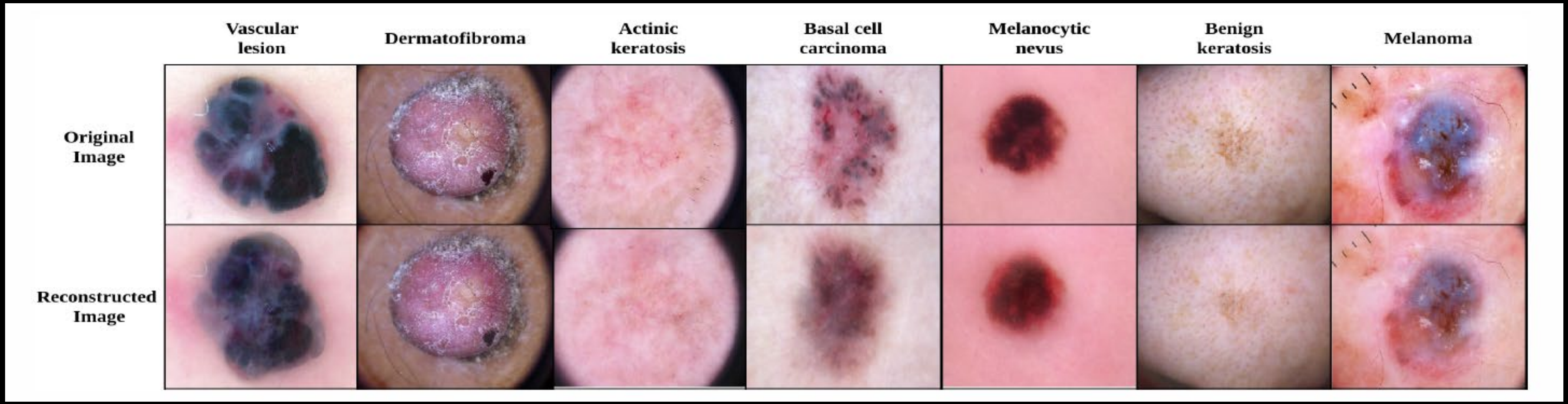


- Image segmentation
- Diagnosis from images
- Image registration
- Treatment selection
- Outcome prediction
- End-to-end quantification

Biopsy Analysis



- Mentoring: touch base with me every day with a longer meeting each week; open door policy
- Prior projects:
  - Predicting liver tumor growth from imaging features
  - Lung lesion segmentation/classification
  - Dermoscopic image generation
  - Uncertainty estimation



Lawrence Staib, lawrence.staib@yale.edu

Using Supercomputers to Design and Predict the Properties of Novel Materials

Diana Y. Qiu

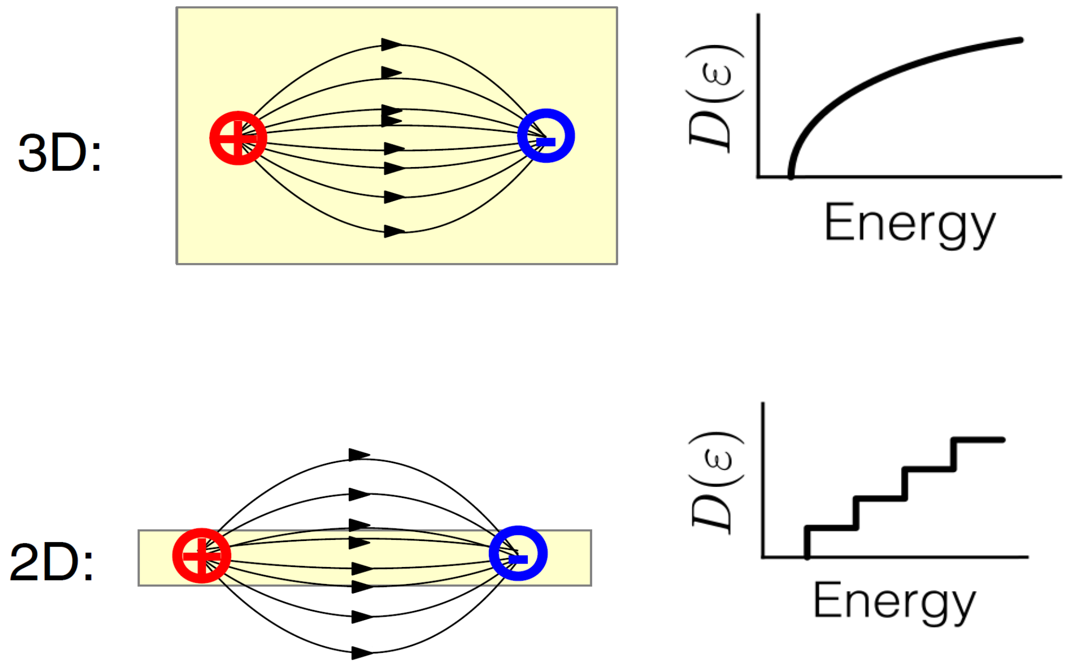
diana.y.qiu@gmail.com

Undergraduate Research Matchmaking Session

1/16/2020

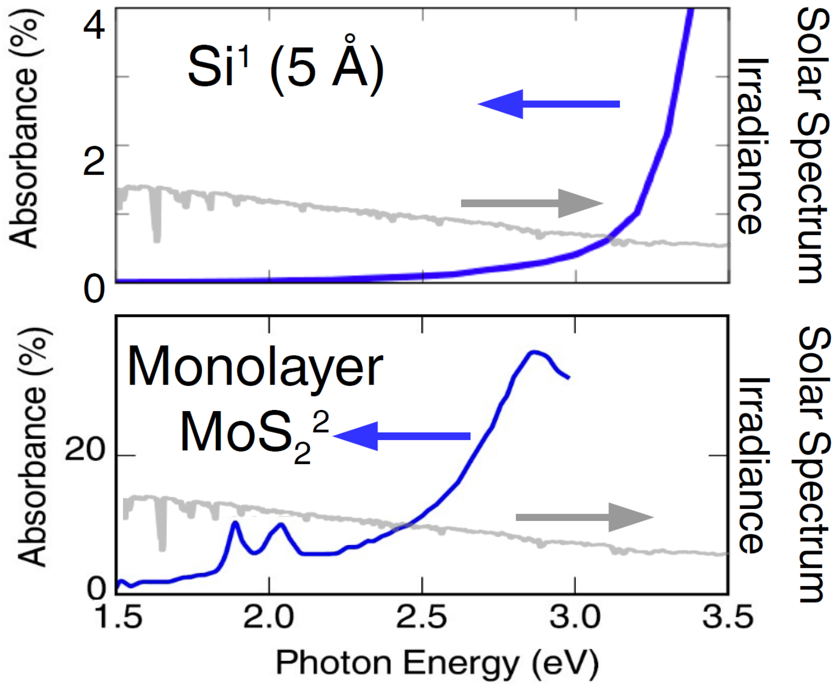
Reduced Dimensional Materials

Electronic Confinement



- Confinement of wavefunction
- Reduced dielectric screening

Enhanced Optical Absorption



- How can we design/calculate/predict the properties of a material?

[1]Aspnes, Studna, PRB 27, 985 (1983) [2]Mak, Lee, Hone, Shan, Heinz, PRL 105, 136805 (2010)

Electronic Properties

- We know how electrons interact
- Many-body Hamiltonian

N~10^{23} electrons!

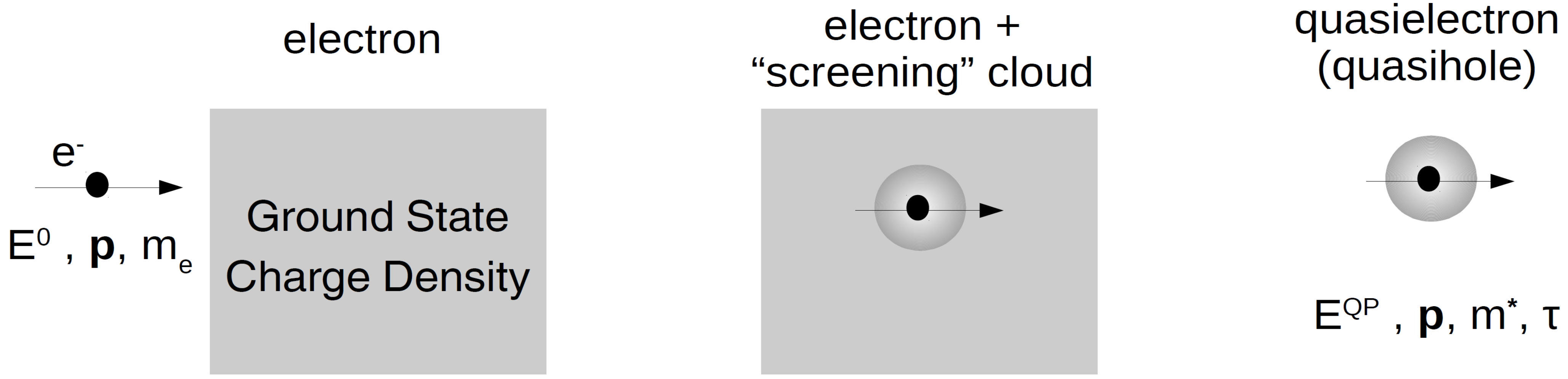
Cannot be solved exactly!

Kinetic Energy

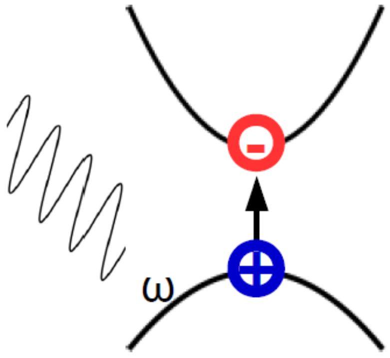
$$H_{\text{tot}} = T_e + V_{ee} + T_i + V_{ii} + V_{ei}$$

Coulomb Interaction

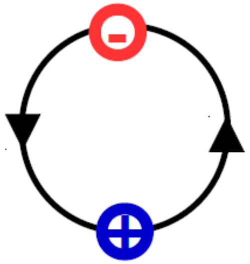
- N+1 particle problem



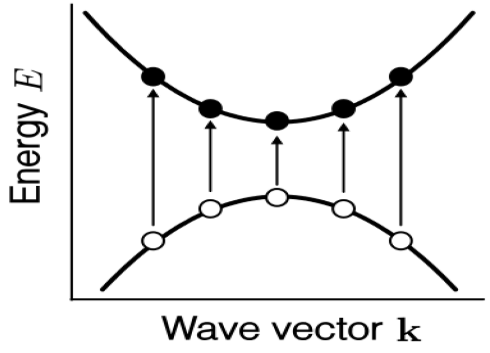
Optical Properties



Incoming photon excites electron and hole



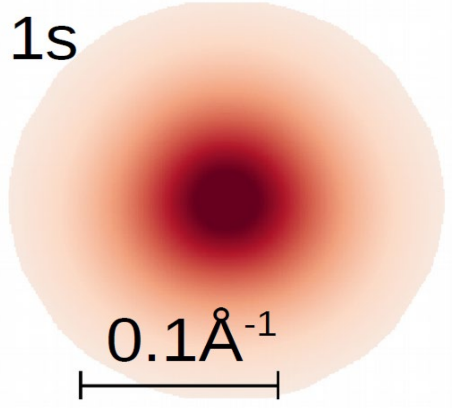
Electron and hole interact forming an **exciton**

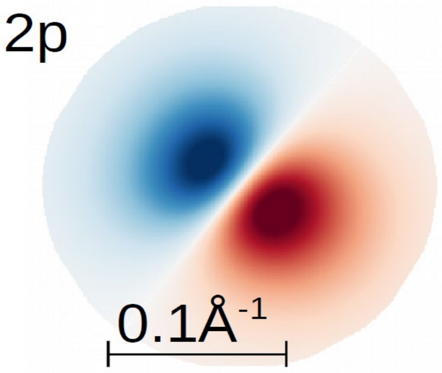


Exciton State:

$$\Psi_S(\mathbf{r}_e, \mathbf{r}_h)$$

$$= \sum_{vc\mathbf{k}} A^S_{vc\mathbf{k}} \psi^*_{v\mathbf{k}}(\mathbf{r}_h) \psi_{c\mathbf{k}}(\mathbf{r}_e)$$





Like a hydrogen atom!

Yale University

Undergraduate Student Research Presentation

- 25 undergraduates have worked in the group
- 10 went to graduate school in chemistry, 3 went to in medical school
- 5 received NSF Fellowships
- 8 were in the STARS program
- We would love to have more!

Hazari Group (nilay.hazari@yale.edu)

Inorganic Chemistry

Catalysts

A *catalyst* is a substance that alters the rate of a reaction without being consumed in the reaction

$$A + B \xrightarrow{\text{slow or no reaction}} C + D$$

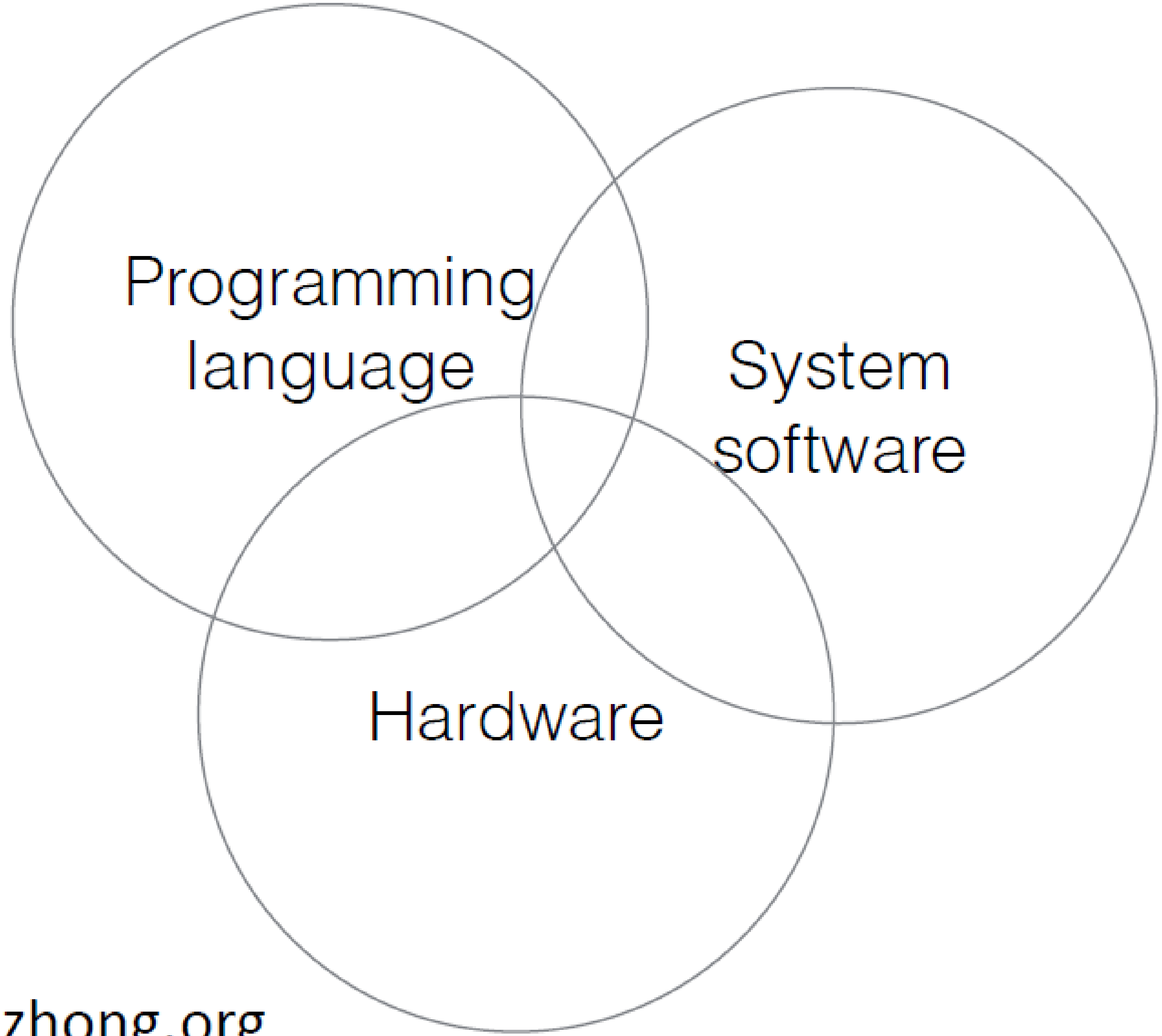
$$A + B \xrightarrow[\textit{catalyst}]{\text{fast reaction}} C + D$$

- **Almost 90% of chemicals that are produced commercially utilize a catalyst at some point in their synthesis**

We develop transition metal based catalysts for a variety of different applications

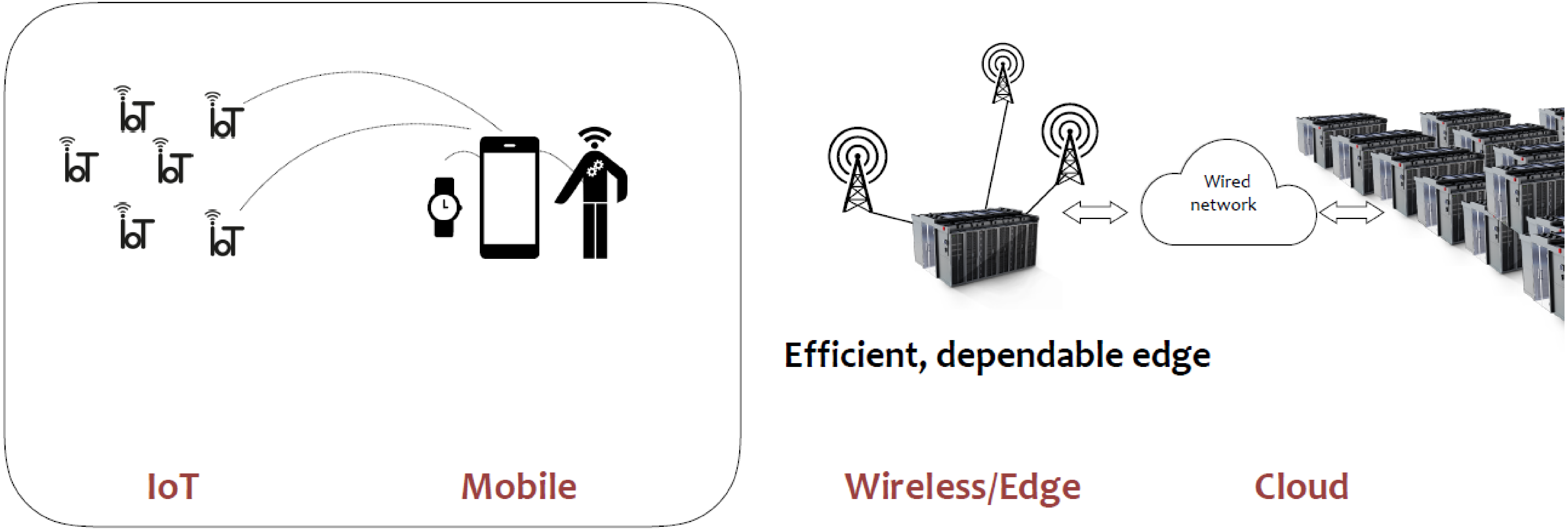
Yale Efficient Computing Lab

+



https://www.linzhong.org

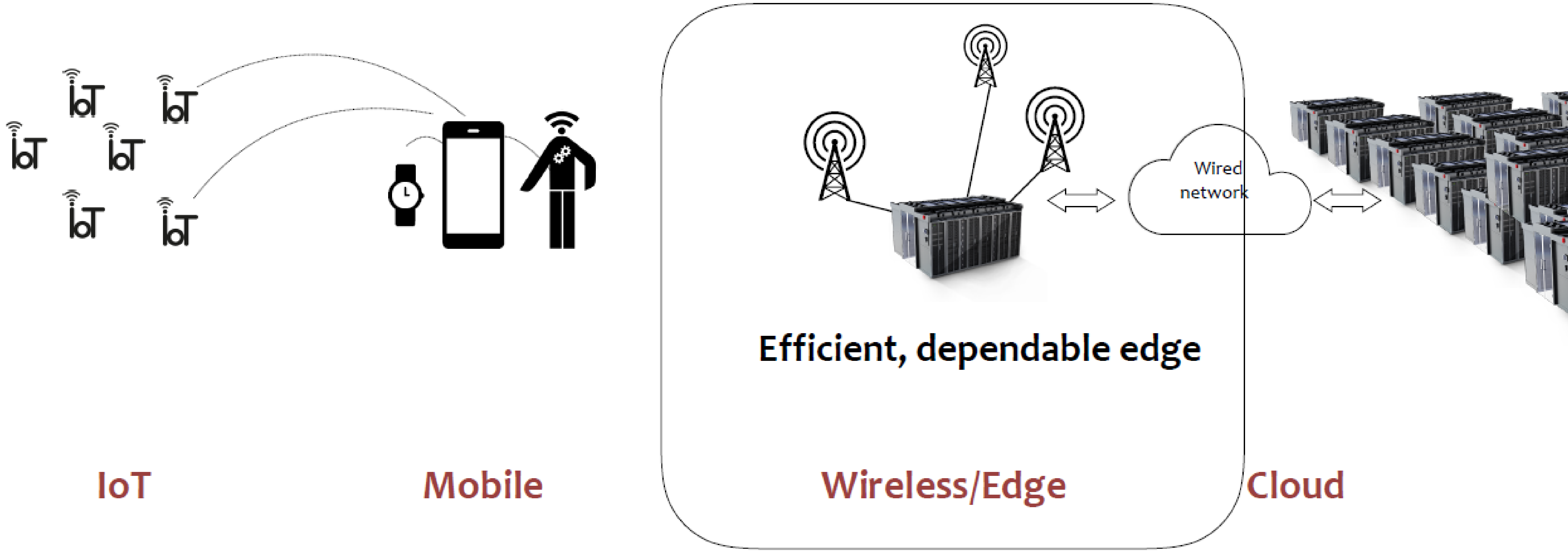
Secure & privacy-respecting personal computing



Efficient, dependable edge

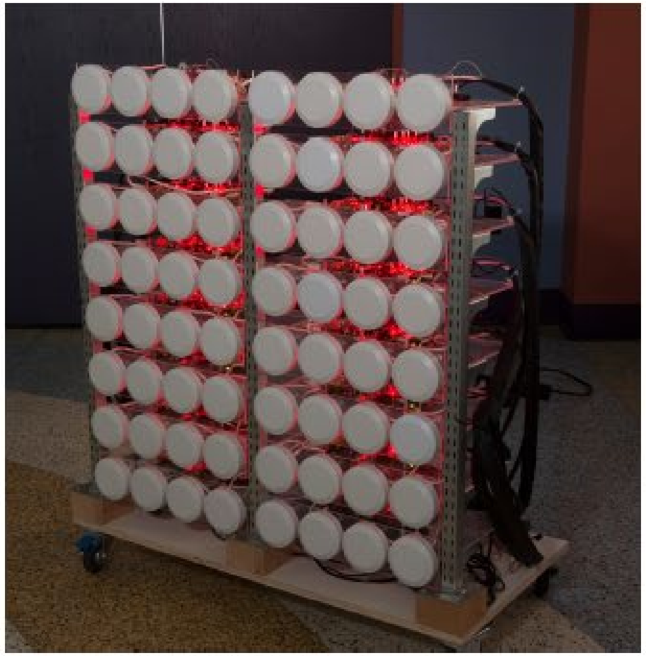
Privacy. Security

5G & Edge data centers

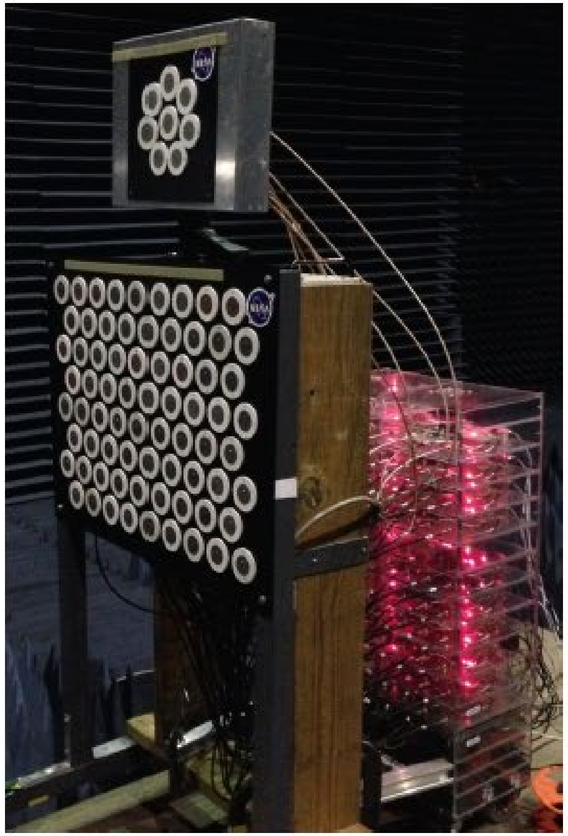


Efficiency. Reliability

Three generations of massive MIMO



Argos V1 (2011)
World's first Massive MIMO
base station

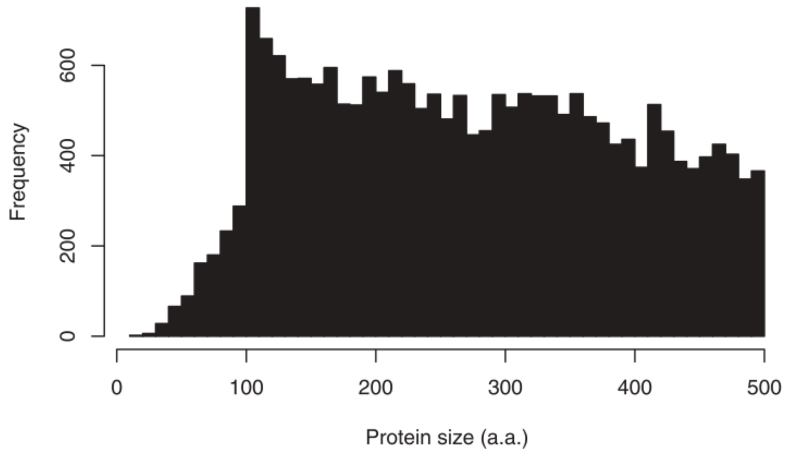


Argos V2 (2013)
World's first real-time Massive MIMO
system

Argos V3 (2017) and ArgosNet (2018)
World's first **network** testbed for massive MIMO

Slavoff Lab: Dark Matter of the Human Genome

Annotated mammalian protein size



>Ten years ago, the mean size of annotated proteins in mammalian genomes was 375 amino acids
Precipitous, artifactual drop off in annotated proteins <100 amino acids
In reality, there are thousands of small proteins, but they were invisible to geneticists – until now

Frith, M.C. et al. *PLoS Genet* **2**, e52 (2006).

Small Open Reading Frames: smORFs

The Slavoff lab develops and applies new technologies, including ribosome profiling and mass spectrometry-based proteomics, to discover small ORFs (smORFs) encoding *thousands of never-before-seen small proteins in human cells.*

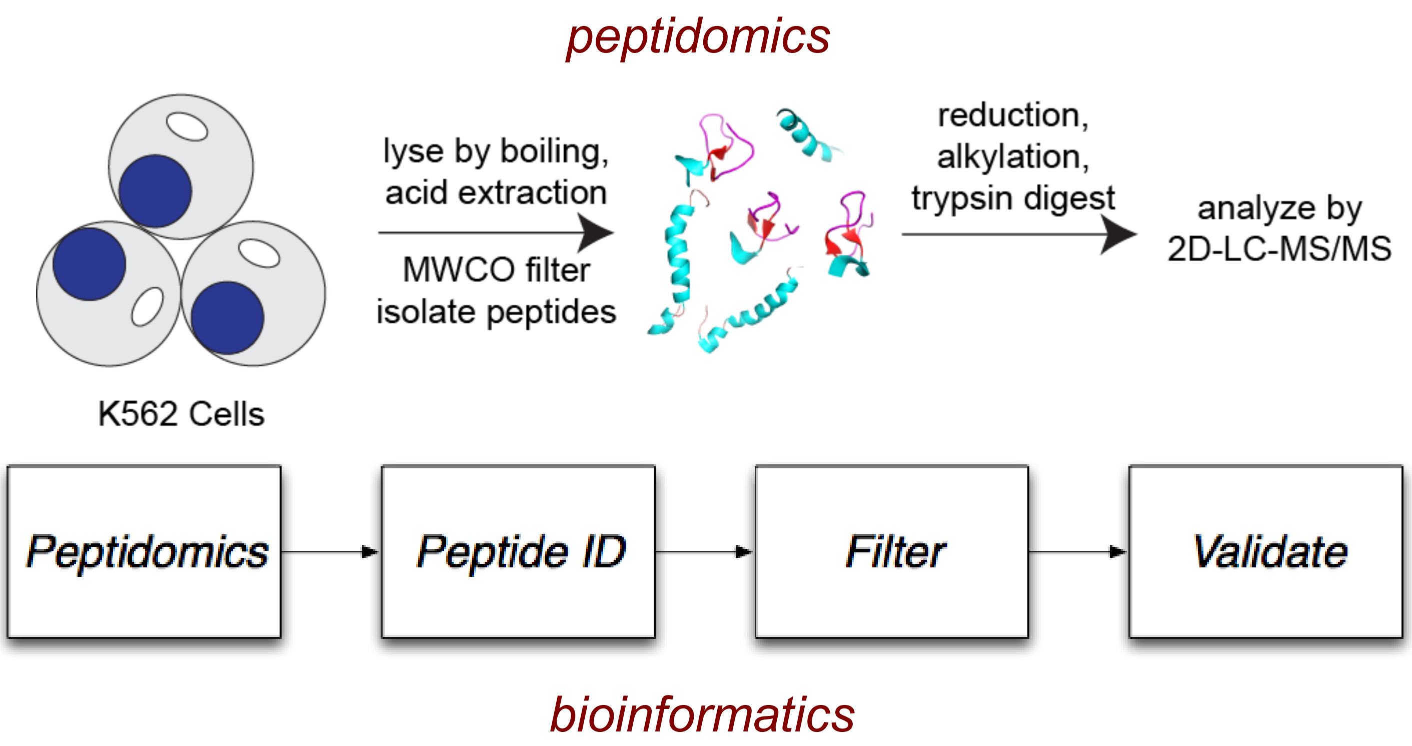
These smORFs were previously missed by genome annotation pipelines because (1) arbitrary size cutoffs for gene annotation of >100 amino acids were applied, and (2) small proteins and peptides are hard to detect with standard biochemical and proteomic approaches.

We and other labs around the world continue to discover more smORFs all the time, and to use multidisciplinary approaches from biochemistry, cell biology and structural biology to characterize their functions.

smORF discovery methods and results

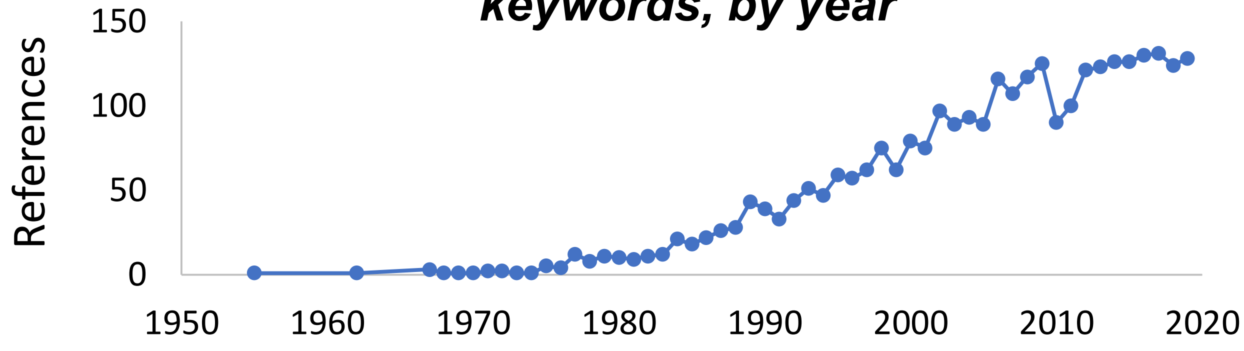
We primarily apply mass spectrometry-based proteomics, coupled with libraries of non-coding RNA sequences, to discover novel expressed smORFs in human cells.

Thousands have been identified to date, and more are being found all the time. Some also serve very important functions inside cells.

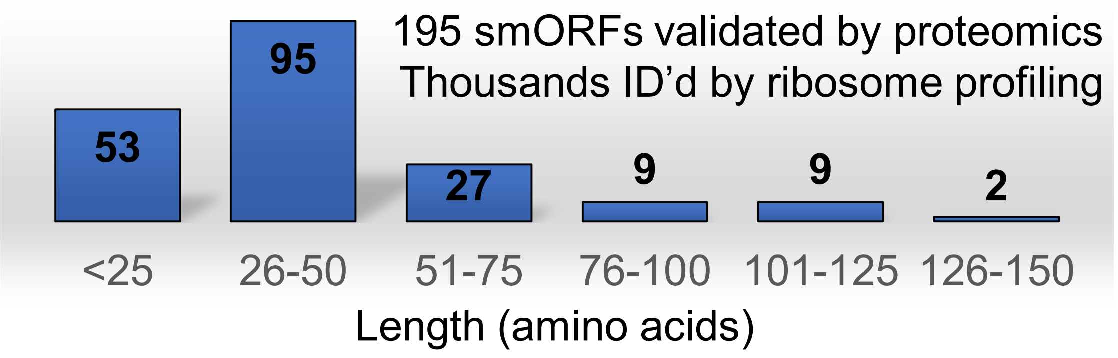


Highly stringent MS/MS criteria for a positive ID (i.e. false negatives for the price of no false positives)

PubMed references to smORFs and related keywords, by year

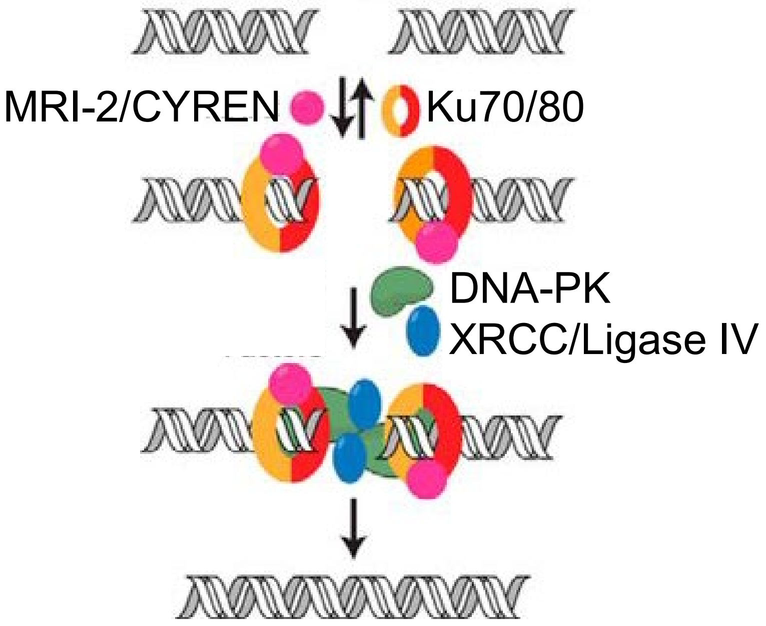


Numbers and lengths of smORFs in K562 cells



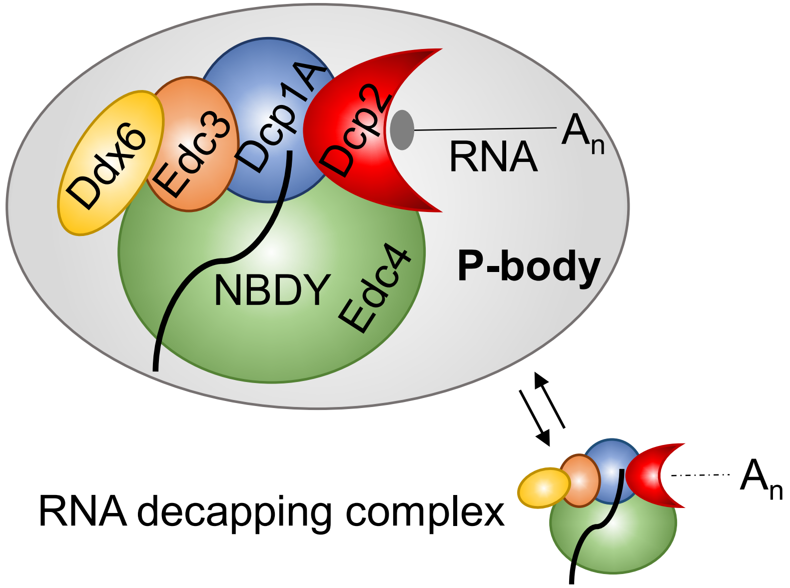
Small open reading frame (smORF) discovery: examples of functions

DNA double-strand break repair



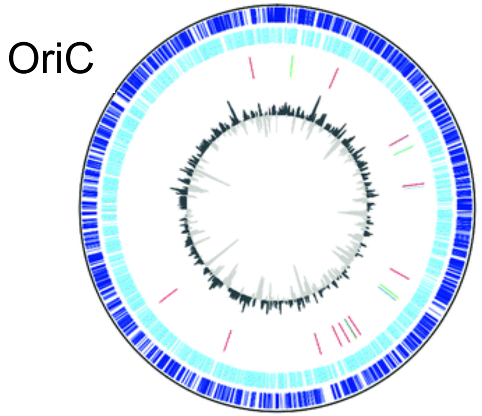
Slavoff et al., 2014

Cytoplasmic 5'-to-3' RNA decay



Slavoff lab, 2017

Cellular stress responses



Stress responsive smORFs in *E. coli* genome

Also: oxidative stress, hypoxia, nutrient starvation

Slavoff lab, 2018

Student Project Features

- Multi-disciplinary (mass spec, genetics, biochemistry, microscopy, bioinformatics)
- New discoveries (name your own gene!)
- Positive, engaged and exciting mentors
- Contribute to our understanding of the information content in the human genome

---

Interested? Contact Sarah Slavoff (sarah.slavoff@yale.edu) to discuss project ideas!

Protein Folding and Dynamics Revealed by Single-Molecule Force Spectroscopy

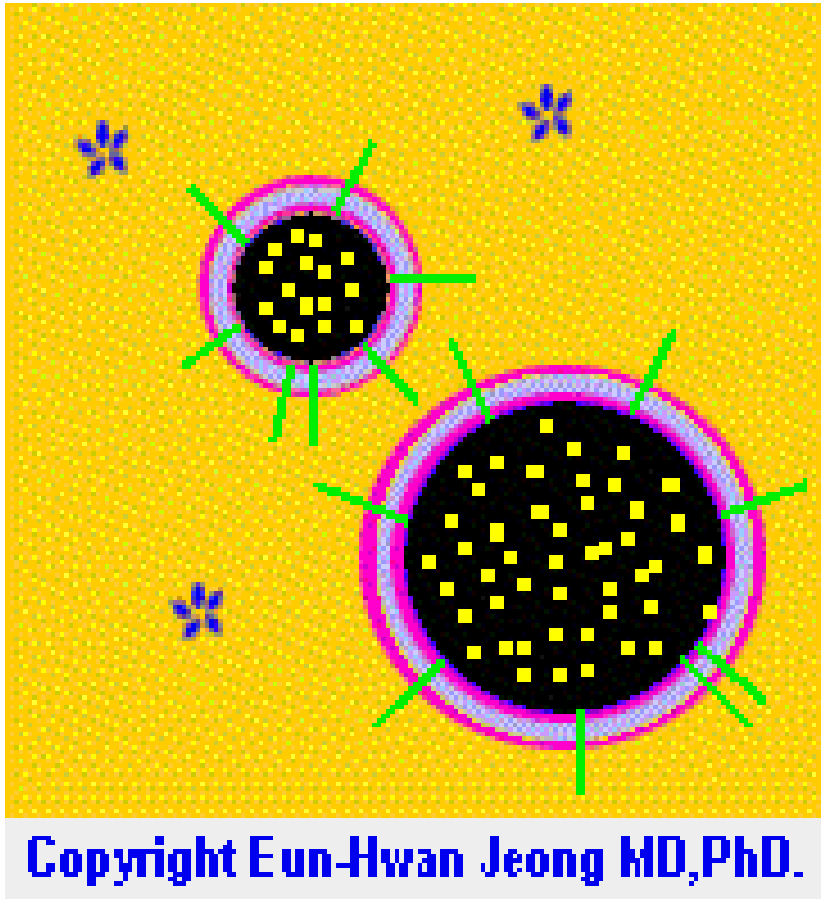
Yongli Zhang

Associate Professor
Department of Cell Biology
Yale University
Email: yongli.zhang@yale.edu

Some former Yale undergraduate students worked in the Zhang lab:

- Christina de Fontnouvelle, now medical student at Yale School of Medicine
- James Ting, now medical student at Johns Hopkins University
- Blessing Aghaulor, now medical student at North Carolina at Chapel Hill
- Gregory Gundersen, now graduate student at Princeton University

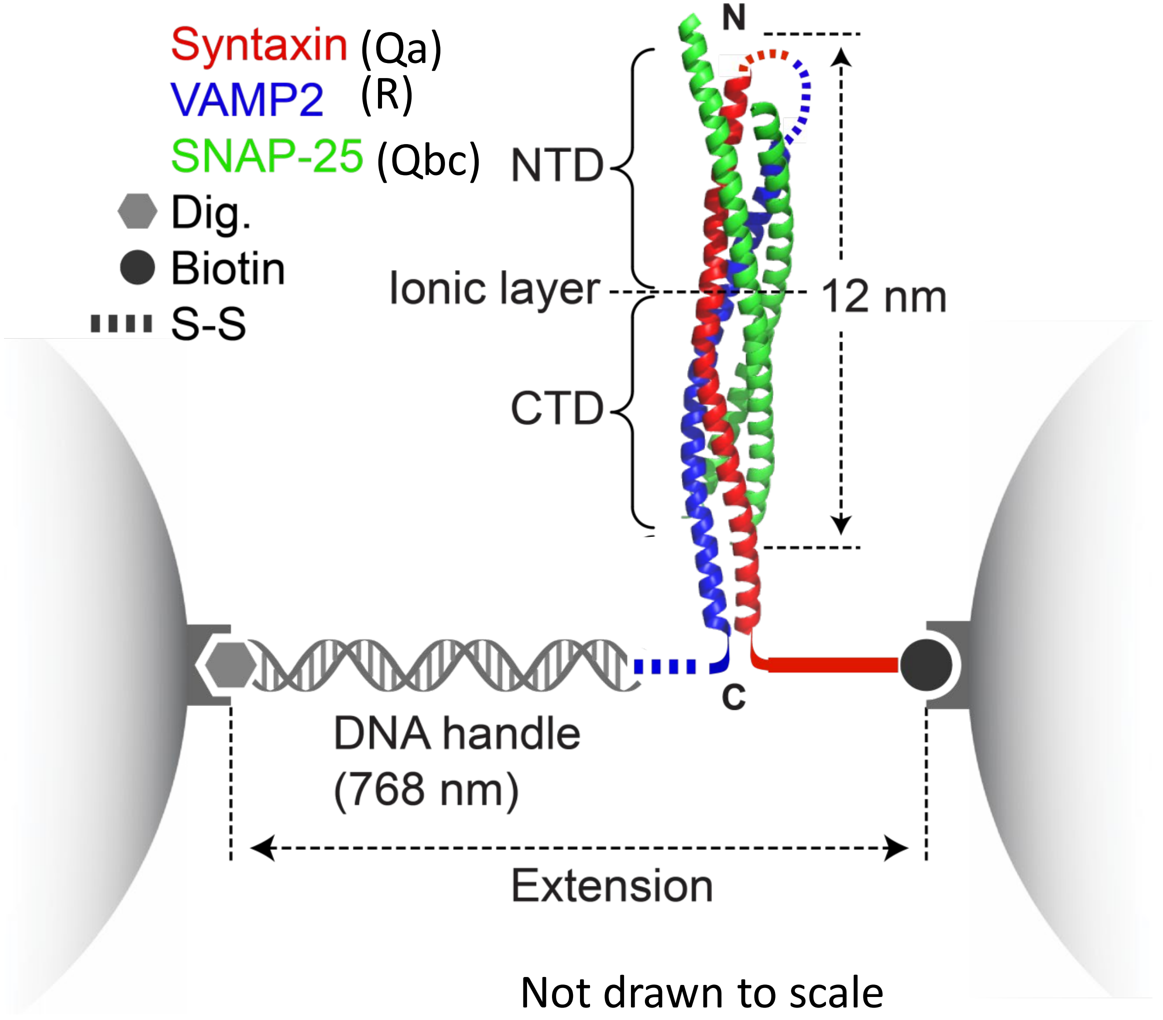
SNAREs couple their folding/assembly to membrane fusion



1. Energy barrier for fusion > 30 kT
2. Synaptic Vesicle fusion
   - Fast (<0.1 ms)
   - Frequent (>100 Hz)
   - Highly regulated
   - Related to many diseases
3. Complex kinetics of exocytosis (hemifusion, fusion pore flickering, itc.)

SNARE hypothesis: Sollner, T., …, Rothman, J.E. (1993). Nature *362*, 318-324.
SNARE zippering hypothesis: P. Hanson,,…, R. Jahn, J. Heuser, Cell, 90, 523 (1997)

Single-molecule manipulation of SNARE complexes

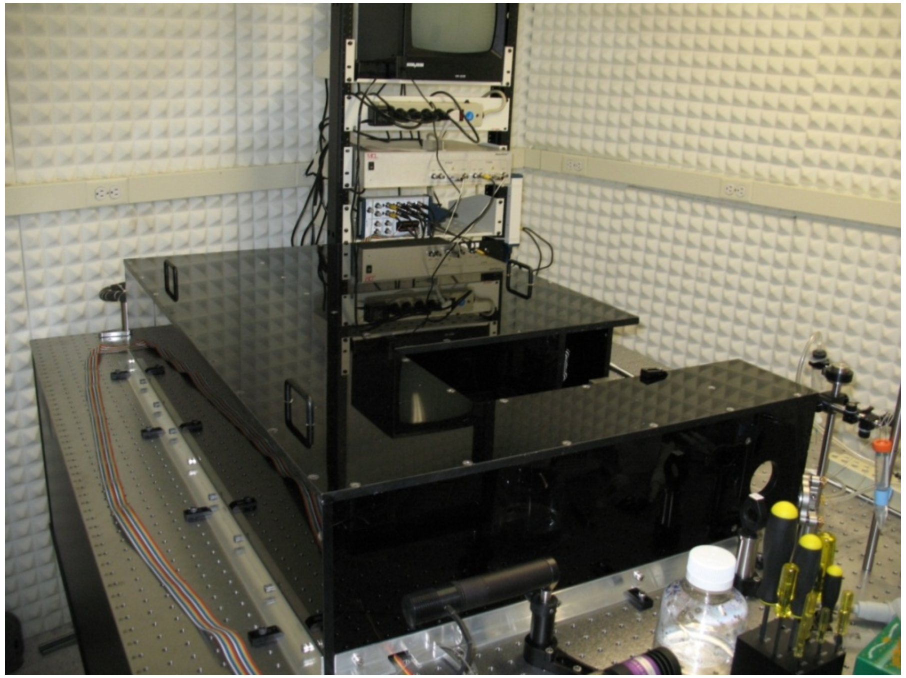


Not drawn to scale

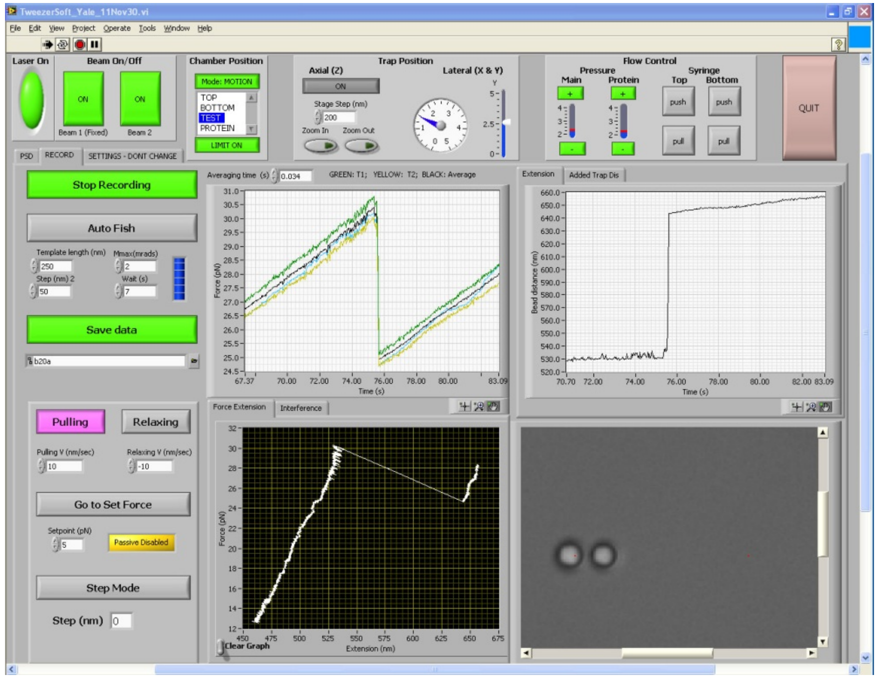
Y. Gao, …, J. E. Rothman, Y. L. Zhang, *Science* **337**, 1340 (2012).
Jiao, J., He, M., …, Hughson, F. and Zhang, Y., ***Elife***, 2018

High-resolution optical tweezers

Hardware



Software



Measurement range

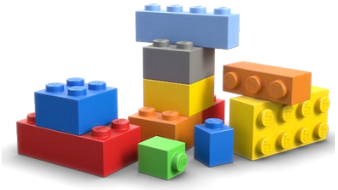
- Displacement: **0.2 nm** – 50 µm
- Force: **0.05 pN**– 200 pN (water); 10^{-21} N in vacuum
- Time: **20 µs** – 2 hours

Force to unfold macromolecules or generated by molecular motors: 1-40 pN

Force to break covalent bond: > 1000 pN

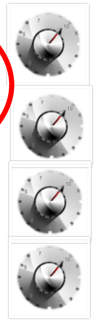
Ultracold Quantum Matter Lab @ Yale

Sloane Physics Laboratory



- Study complex quantum phenomena with highly-controllable synthetic quantum systems: ultracold atoms (***atomic legos***)

$$\hat{H} = \sum_{i=1}^{N} \frac{\hat{\mathbf{p}}_i^2}{2m} + \sum_{i=1}^{N} V_{\text{trap}}(\hat{\mathbf{r}}_i) + \sum_{i<j} V_{\text{int}}(\hat{\mathbf{r}}_i, \hat{\mathbf{r}}_j)$$



Temperature

Trapping landscapes

Interactions

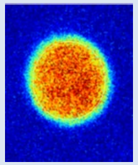
Quantum statistics

- Many ‘knobs’ external/internal degrees of freedom
  tunable interactions
  easily accessible observables

Fermi lab

(SPL 20)

Lego: Fermionic ^{6}Li atoms in programmable boxes



Research themes

Pairing with strong interactions

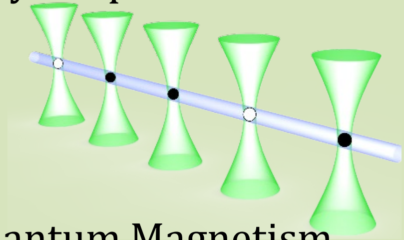
Exotic superfluid phases

Quantum vortices and rotation

Tweezer lab

(SPL 20A)

Lego: Single ^{88}Sr atoms in array of optical tweezers



Quantum Magnetism

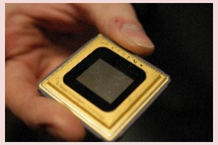
Dynamics of entanglement

Quantum cellular automata

Bose lab

(SCL 140D)

Lego: Bose-Einstein Condensates of ^{39}K



Atom interferometry

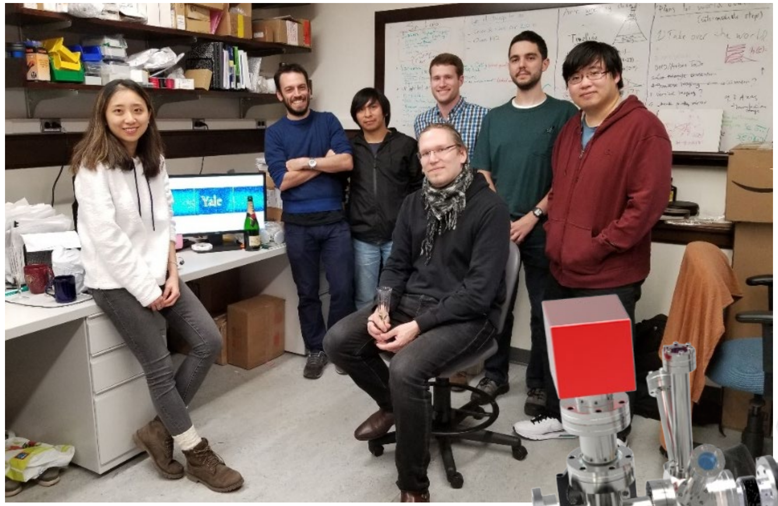
Thermodynamics

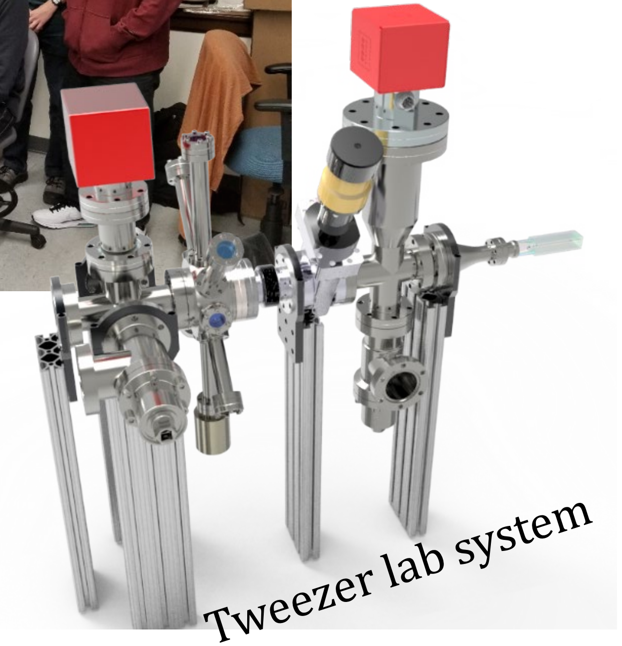
Matter-wave turbulence

Ultracold Quantum Matter Lab @ Yale

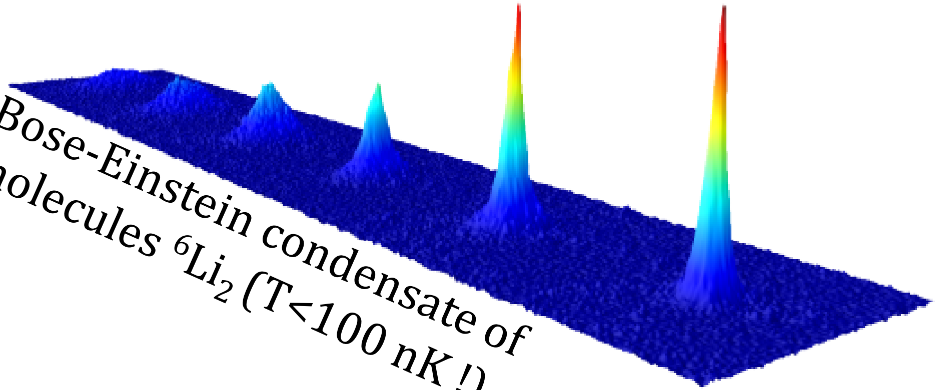
Join us!
Grad students: Yunpeng Ji, Grant Schumacher, Gabriel Assumpcao, Peter Zhou,
Postdocs: Jere Makinen, Franklin Vivanco

Undergraduate projects: ultrahigh-vacuum constructions, laser building, spectroscopy, optical setups, electromagnet design, control electronics, software design, quantum control



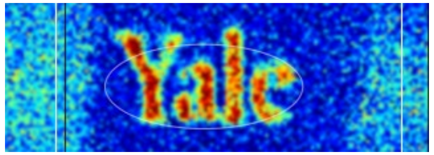


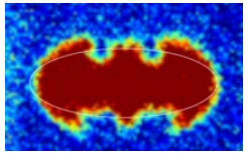
Tweezer lab system



Bose-Einstein condensate of molecules $^6Li_2$ (T<100 nK !)

'Atomic painting': strongly-interacting fermions in programmable potentials





Experimental Neutrino and Particle Physics at Wright Lab

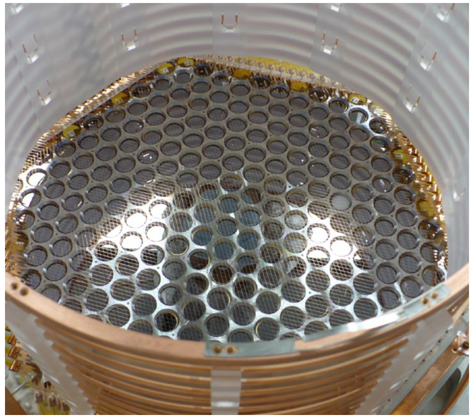
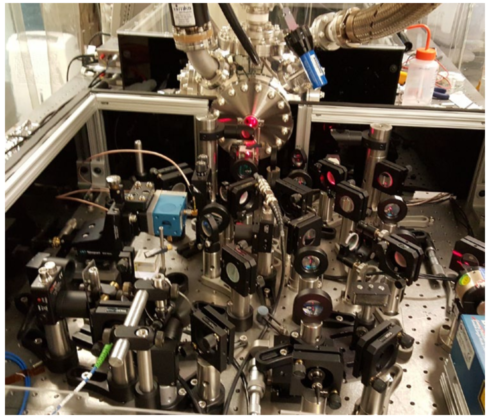
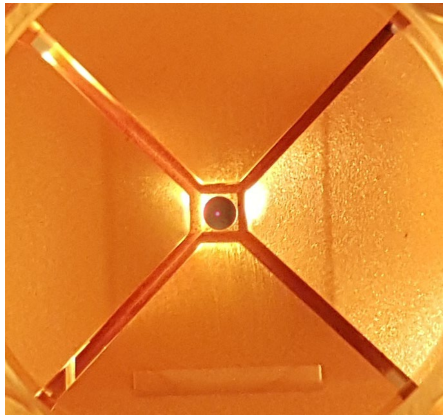
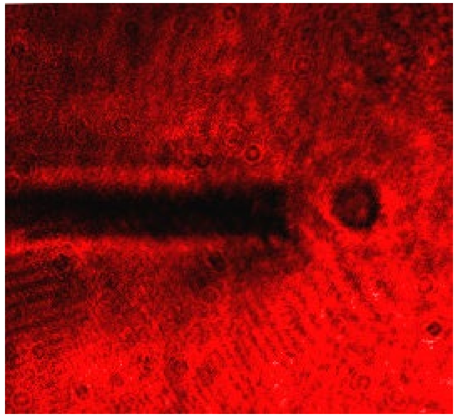
Prof. David Moore, *david.c.moore@yale.edu*

Our group is developing new technologies aimed at answering some of the major outstanding questions in nuclear and particle physics:

- What are the fundamental properties of neutrinos?
- What is the nature of dark matter and dark energy?
- Are there deviations from gravity that can be observed at microscopic distances?

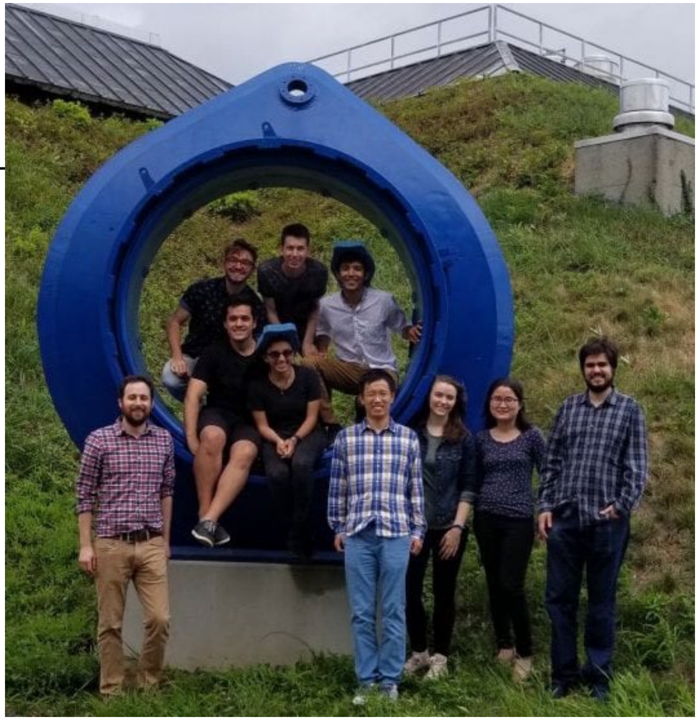
Answering these questions requires applying cutting-edge techniques from particle, nuclear, atomic, and optical physics.

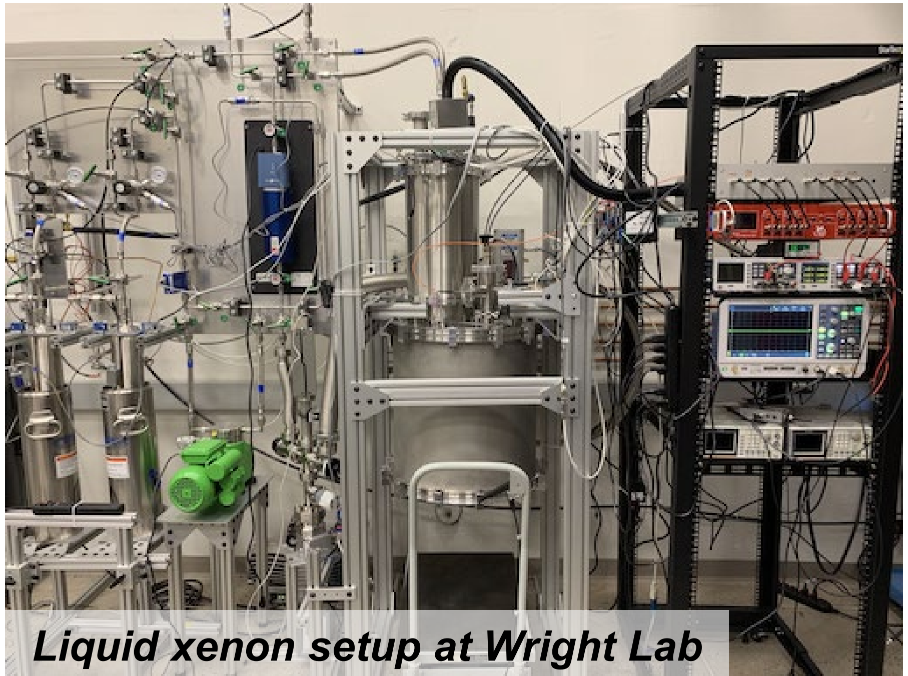
See http://campuspress.yale.edu/moorelab/ for more details

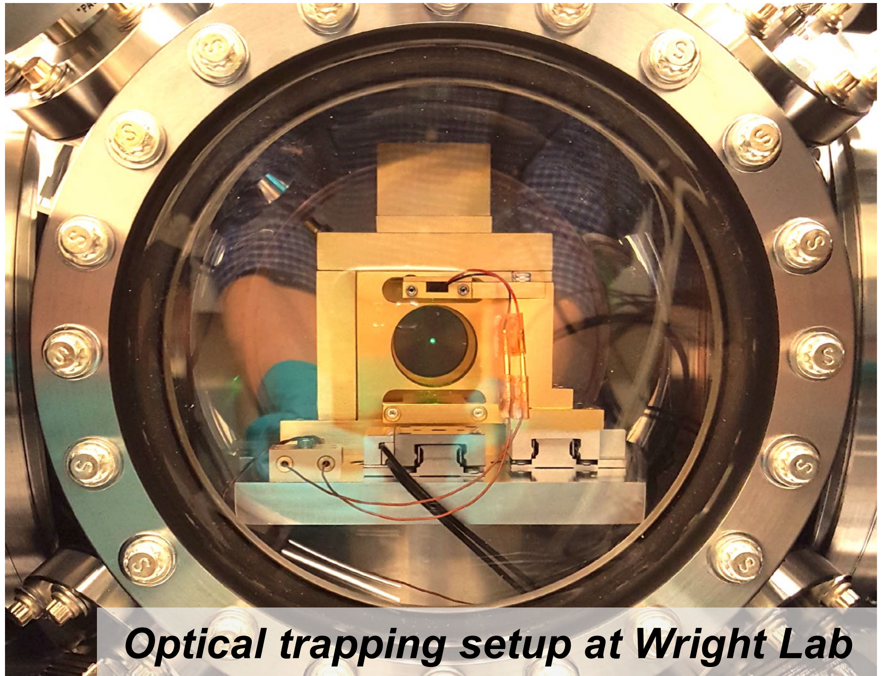
Join us!

- We typically have projects available for 2-3 students per summer to work in our labs
- Recent undergraduate researchers: Ilana Kaufman (YC17), Adam Fine (YC19), Cady van Assendelft (YC19), Alec Emser (YC19), Michael Mossman (YC19), Sam Day-Weiss (YC20), Shoumik Chowdhury (YC21), Charlotte Kavaler (YC21), Sam Borden (YC20)





Liquid xenon setup at Wright Lab



Optical trapping setup at Wright Lab

Prof. Corey S. O'Hern

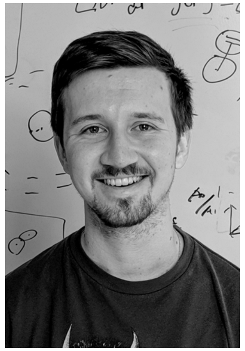
Laboratory for computational modeling of soft and biological materials

Departments of Mechanical Engineering & Materials Science, Physics, and Applied Physics

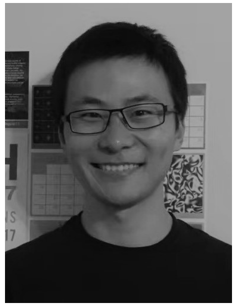
Graduate Program in Computational Biology & Bioinformatics

http://jamming.research.yale.edu

corey.ohern@yale.edu

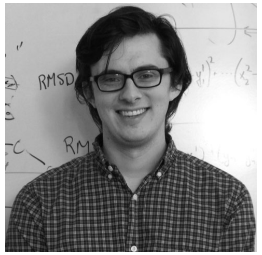


Alex Grigas

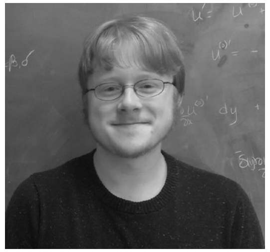


Weiwei Jin

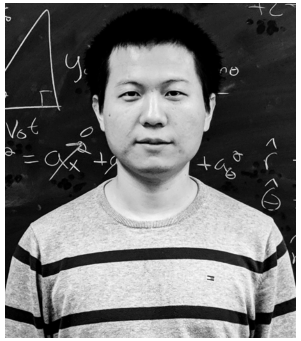
Cameron Lerch



Jack Trado



Kyle Vanderwerf



Dong Wang

Zhe Mei

Aya Nawano

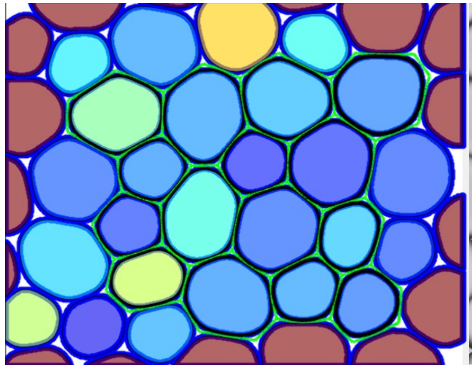
Philip Wang

Peter Williams

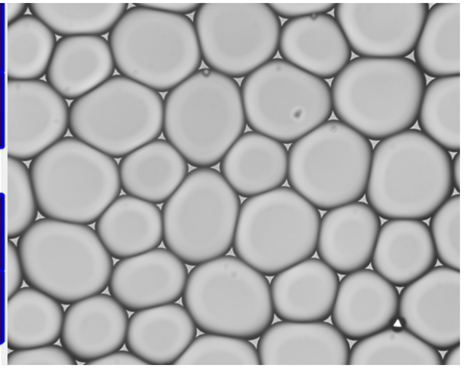
2 postdocs, 8 Ph.D. students, 2 undergraduates

Undergraduate Summer Research Projects

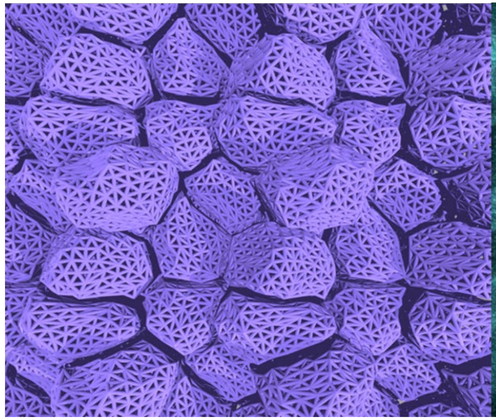
1.Computational modeling of deformable particles



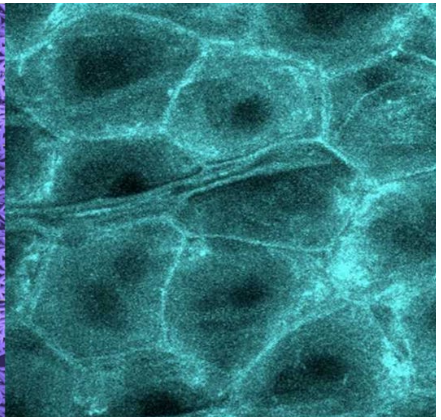
Reconstruction of bubble packing



Packing of bubbles

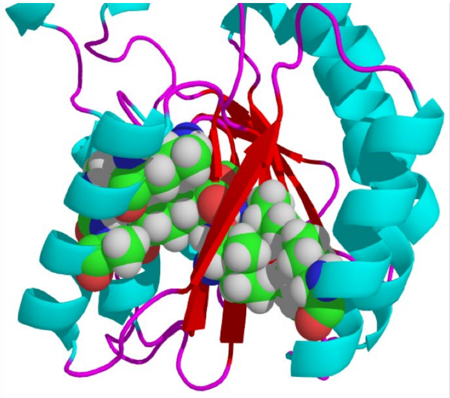


Packing of deformable polyhedra

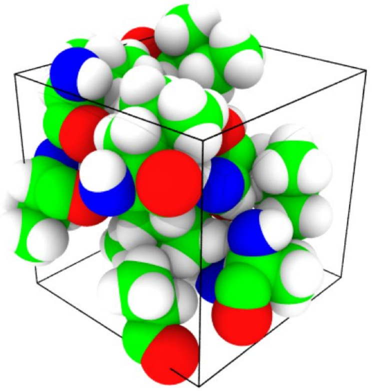


Packing of keratinocytes

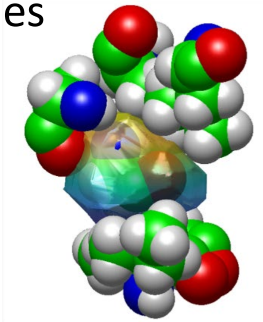
2. Dense packing in protein cores



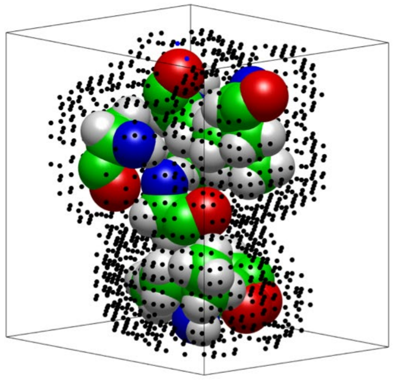
Core residues



Packing of residues



Voronoi polyhedron



Void space

Details of Mentoring

1. Computational modeling of deformable particles: Lead: Jack Treado
(4^{th} year Ph.D. student in Mechanical Engineering & Materials Science), daily meetings with Jack, weekly updates at subgroup meetings with PI, graduate students, and undergraduates on Fridays; Office in Mason Lab, Room 227

2. Dense packing in protein cores: Lead: Alex Grigas (2^{nd} year Ph.D. student in Computational Biology & Bioinformatics) and Zhe Mei (4^{th} year Ph.D. student in Chemistry), daily meetings with Alex and Zhe, weekly updates at subgroup meetings with PI, graduate students, and undergraduates on Thursdays; Office in Mason Lab, Room 227

3. Skills to be learned: computer programming in C++, python, Matlab, and Cuda; running codes on Yale's High Performance Computing facilities, molecular dynamics simulations, computational modeling; research at interface of physics, biology, and engineering

4. Interested in 2-3 undergraduate researchers in summer 2019

5. Since 2002, hosted more than 50 undergraduates in summer research; 6 undergraduates have appeared as authors on publications

Prof. Wenjun Hu

Dept. of EE & CS, YINS

wenjun.hu@yale.edu

Research themes in my group

Edge, Cloud

Backend
system
support

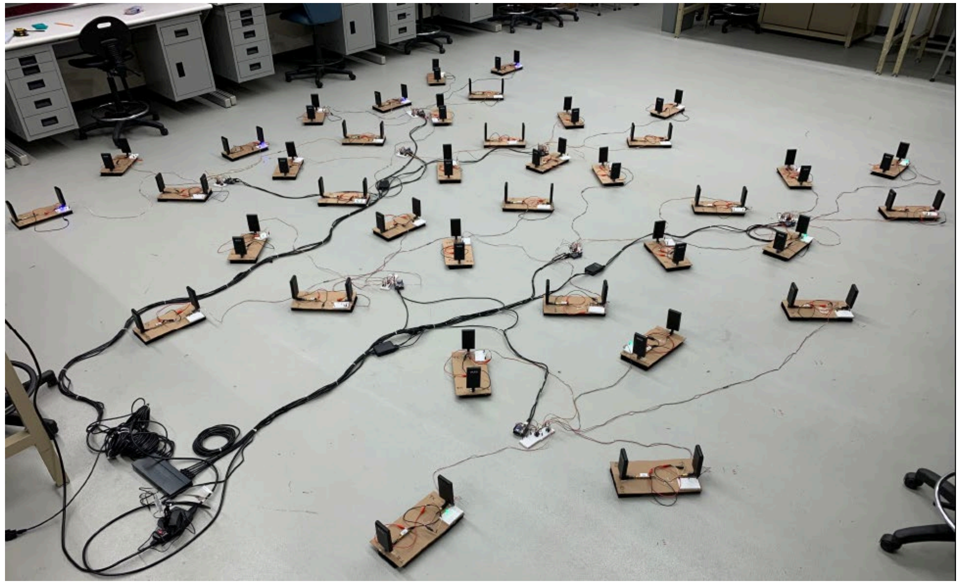
Wireless connectivity

Mobile

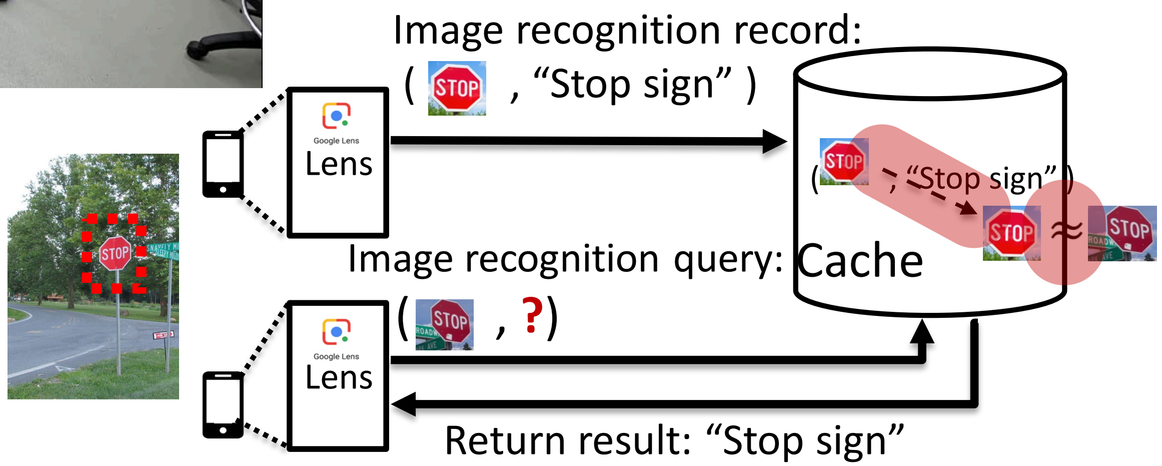
Device-centric
optimizations

Invisible and/or virtual…

Projects



(i) Programmable Radio Environment
(ii) Self-Upgrading Radios
(iii) Edge system support for machine learning



Logistics

- Target: 2-3 undergrads
- Work closely with the PhD student leads
- Typically meet with me 1-2 times a week
- Previous summers:
  - 2017: Josh Chavez
  - 2018: Josh Chavez, Michael McNamara
  - 2019: Jeacy Espinoza, Julia McClellan, Will Sussman

Dieter Söll Lab

Jeffery Tharp

Natalie Krahn

Jonathan Fischer

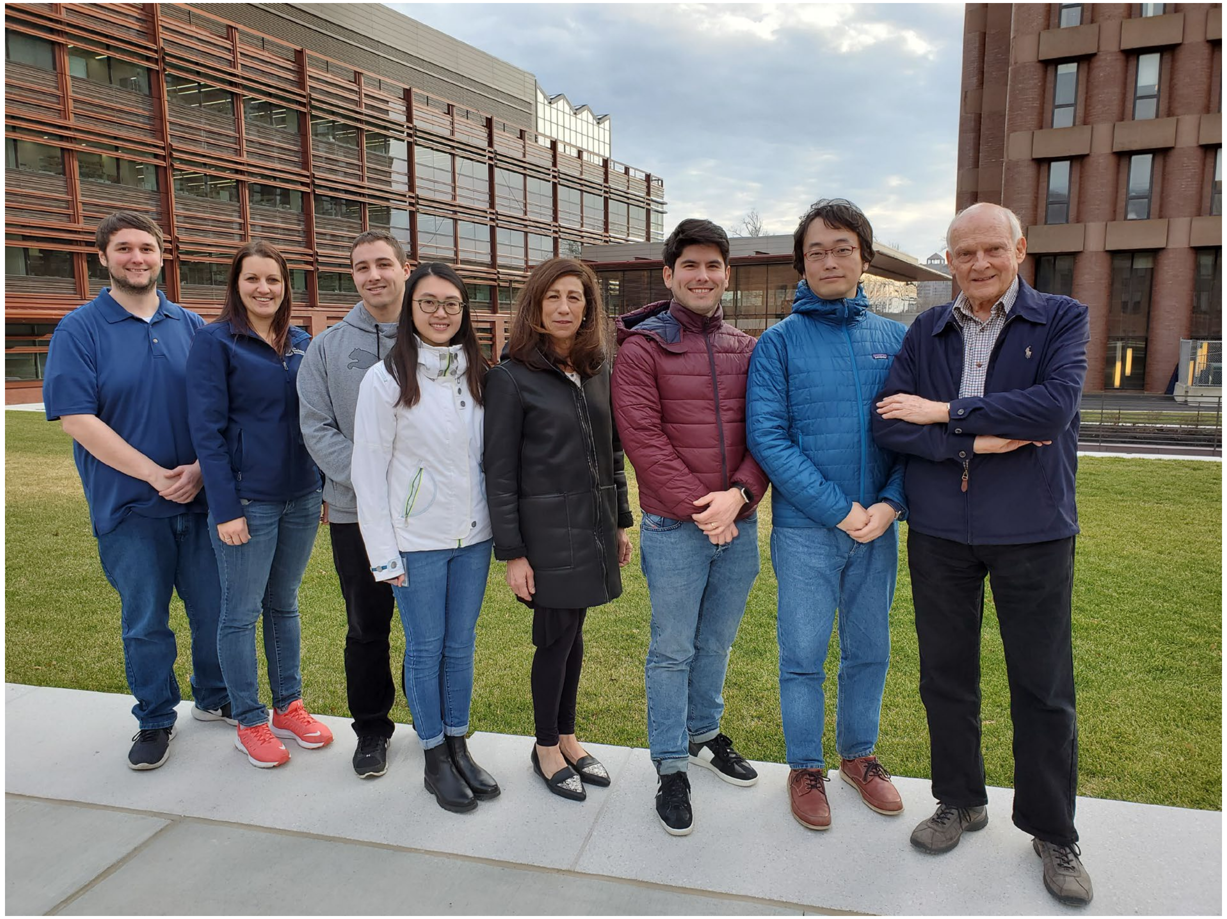
Christina Chung

Ava Artaiz

Oscar Vargas-Rodriguez

Kazuaki Amikura

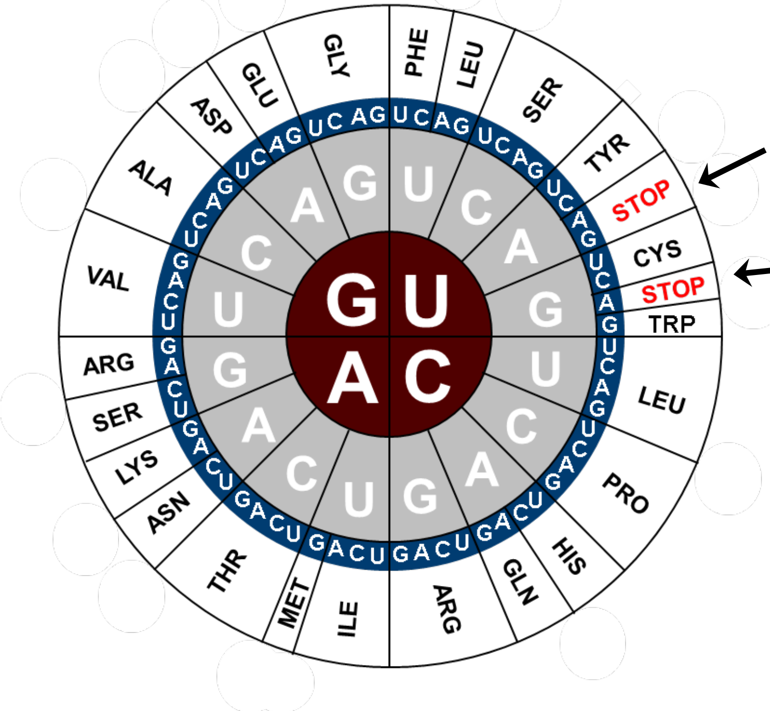
Dieter Söll

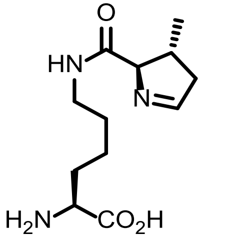


dieter.soll@yale.edu

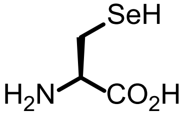
Genetic Code Expansion

The Standard Genetic Code





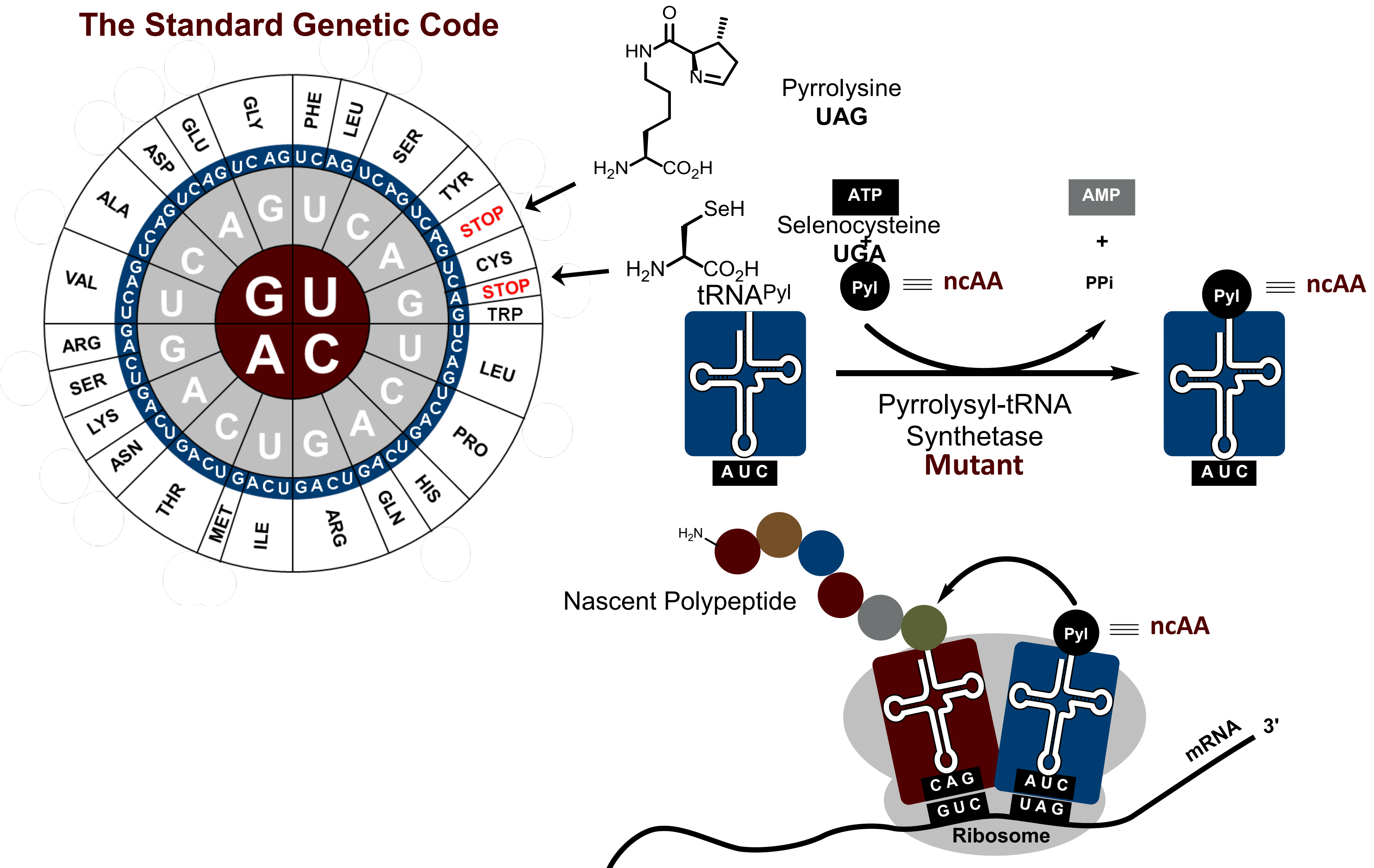
Pyrrolysine
UAG



Selenocysteine
UGA

Tharp et al., *RNA Biol.*, **2017**, *14*, 1-12.
Wan et al., *Biochim. Biophys. Acta.*, **2014**, *1844*, 1059-1070.

Genetic Code Expansion



Tharp et al., *RNA Biol.*, **2017**, *14*, 1-12.

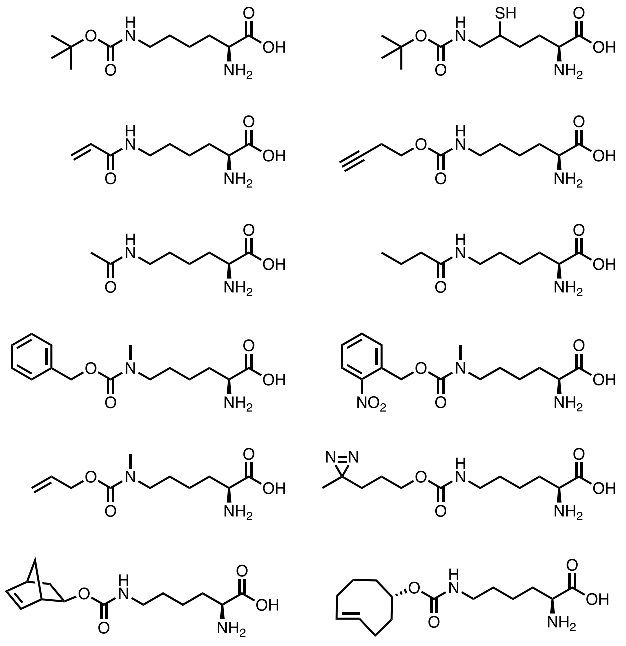
Wan et al., *Biochim. Biophys. Acta.*, **2014**, *1844*, 1059-1070.

Pyrrolysyl-tRNA Synthetase

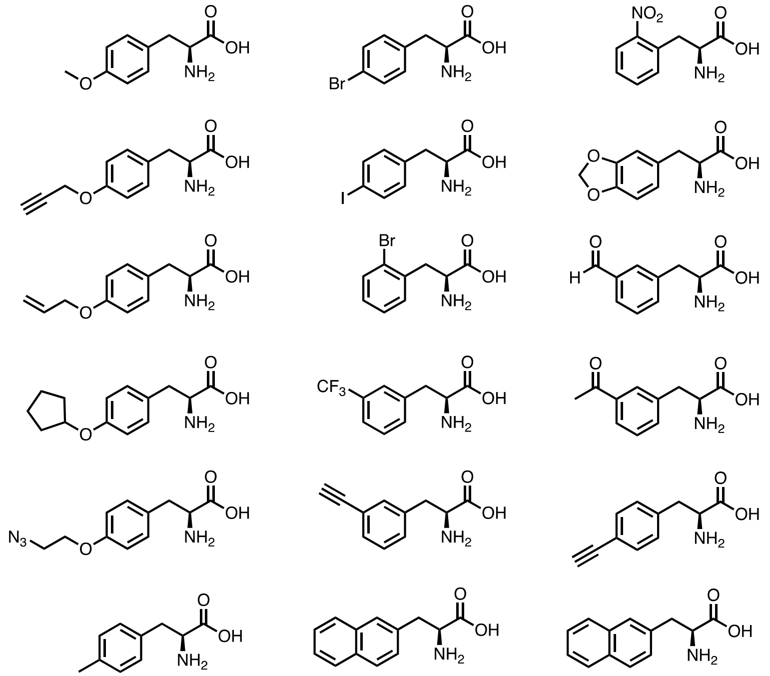
The pyrrolysyl-tRNA synthetase has been used to genetically encode >150 non-natural amino acids which have numerous purposes.

We are engineering this enzyme to 1) improve its activity and 2) encode new non-natural amino acids

Lysine Derivatives



Phenylalanine Derivatives

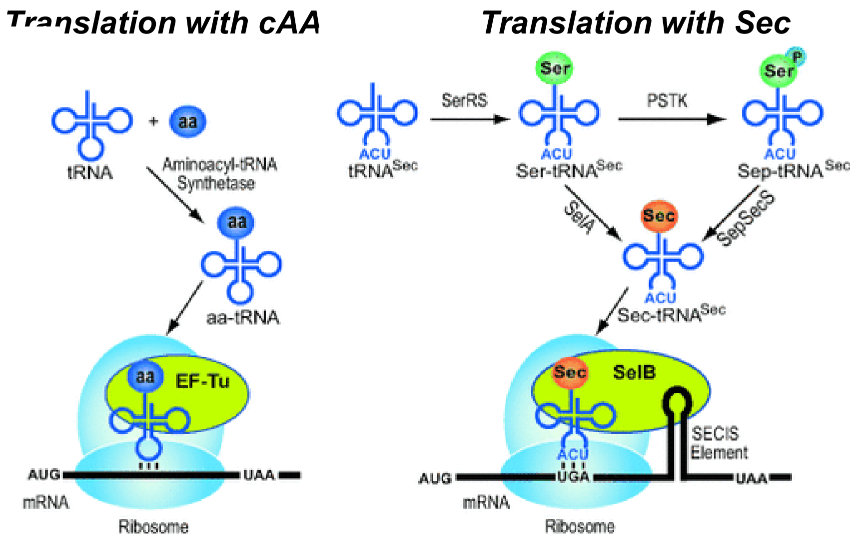


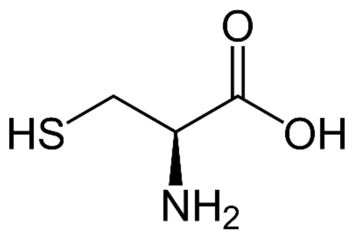
Tharp *et. al*, *RNA Biol.*, **2017**, *14*, 1-12.
Wan *et. al*, *Biochim. Biophys. Acta.*, **2014**, *1844*, 1059-1070.

Rewiring translation for selenocysteine incorporation

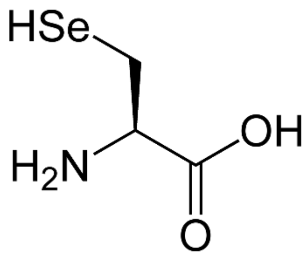
Humans have at least 25 selenoproteins which provide us with the essential micronutrient selenium

Selenocysteine incorporation in proteins is complicated and not fully understood





Cysteine
pKa=8.18



Selenocysteine
pKa=5.47

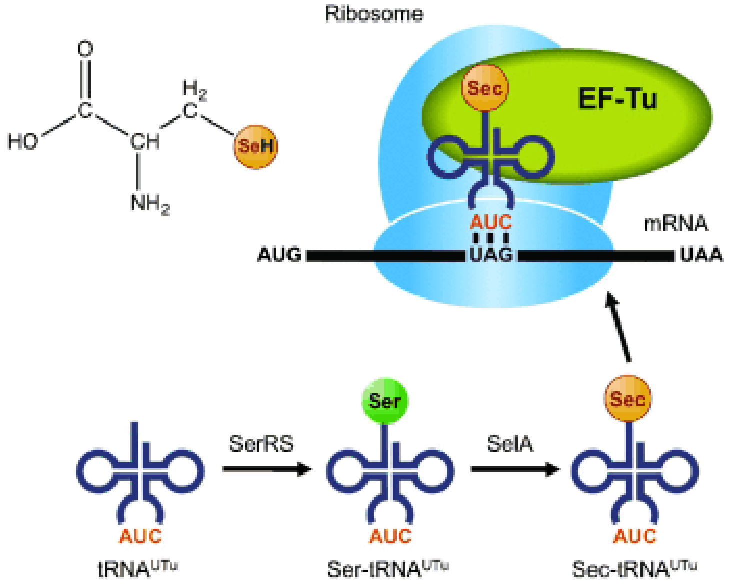
Aldag *et. al,* Angew Chem Int Ed. **2013**, 52, 1441-1445

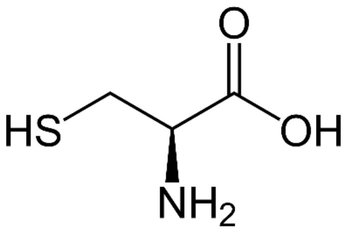
Rewiring translation for selenocysteine incorporation

Humans have at least 25 selenoproteins which provide us with the essential micronutrient selenium

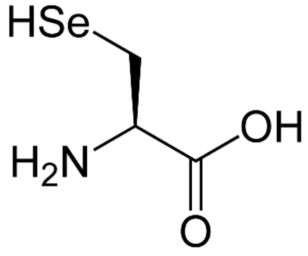
Selenocysteine incorporation in proteins is complicated and not fully understood

Rewired translation with Sec

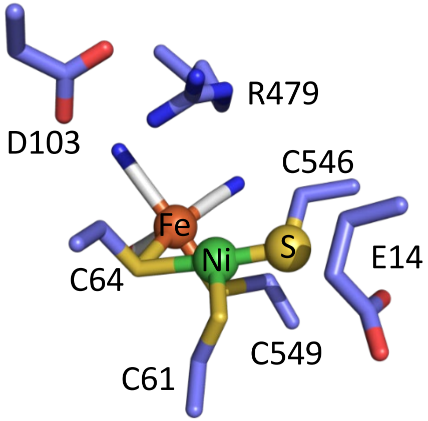


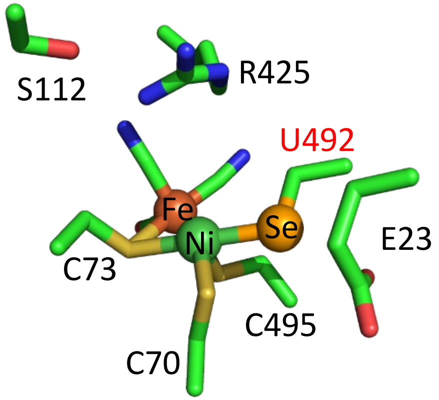


Cysteine
pKa=8.18



Selenocysteine
pKa=5.47



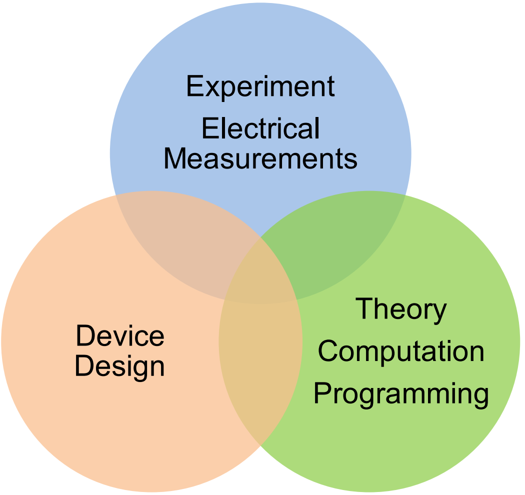


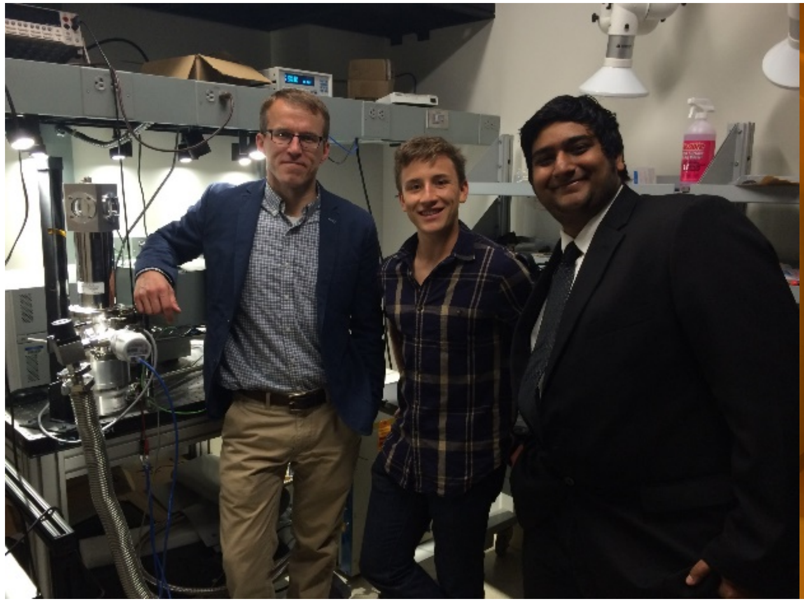
up to 1000x activity

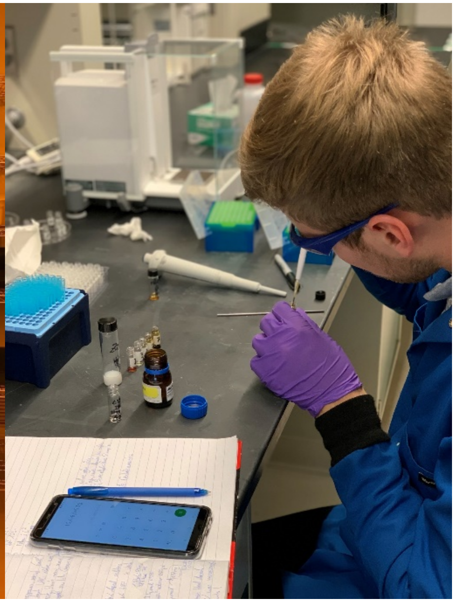
Aldag *et. al,* Angew Chem Int Ed. **2013**, 52, 1441-1445

Konezny Lab

- Materials for solar energy devices (solar cells, solar fuel cells, …)
- Charge transport physics (experiment and theory)
- Projects depend on your interests and background

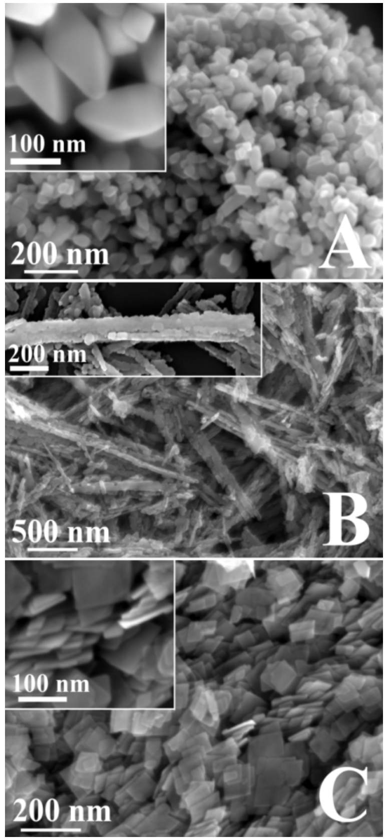


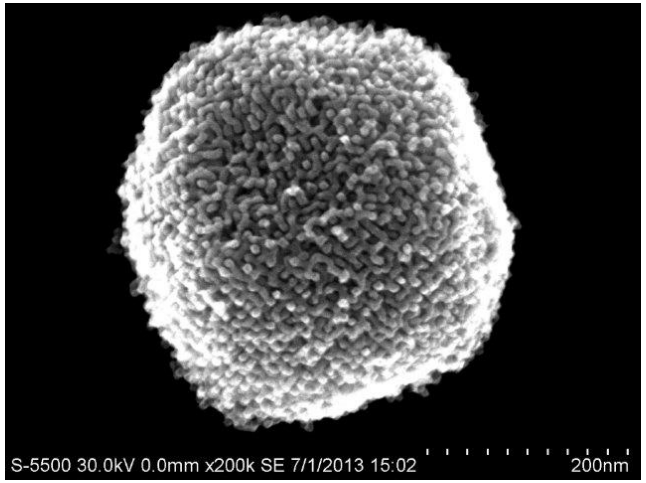


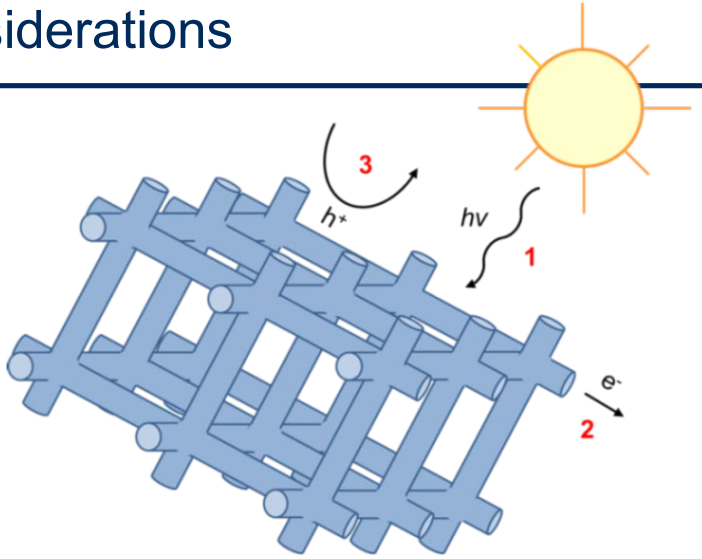


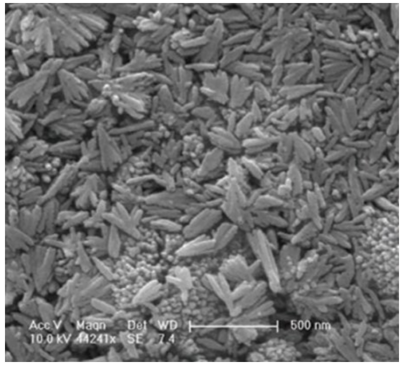
Steve Konezny
steven.konezny@yale.edu

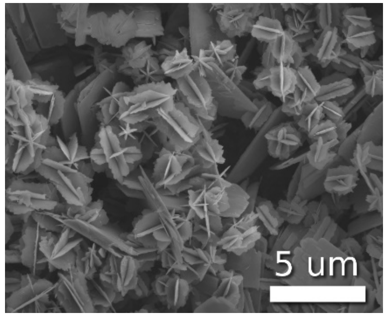
Nanomaterial design considerations

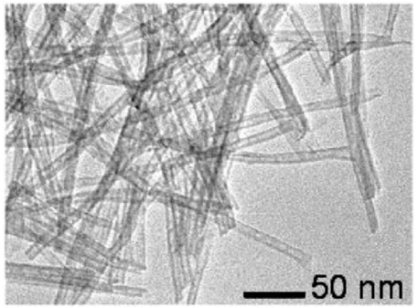


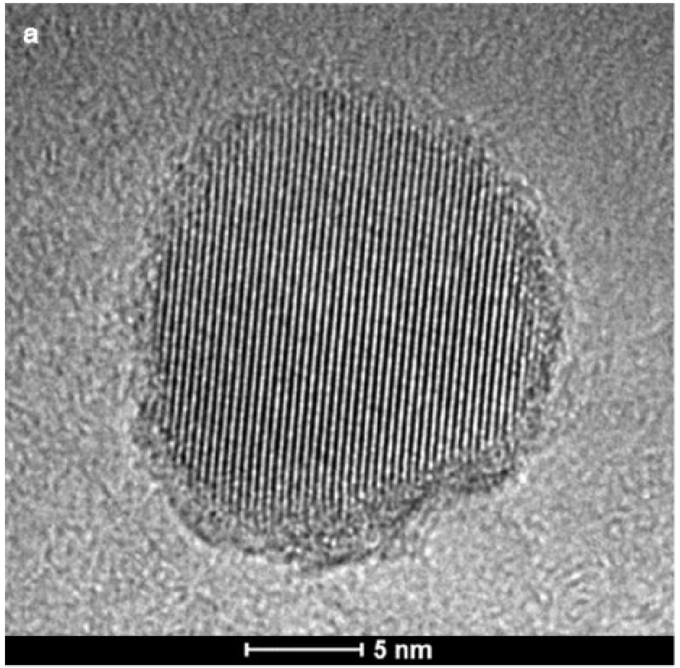


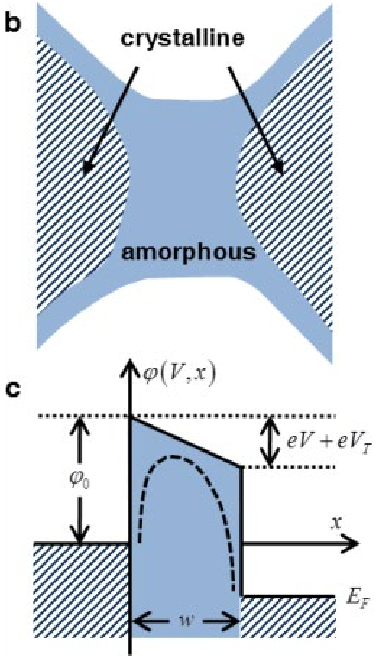












Steve Konezny
steven.konezny@yale.edu

Open Undergraduate Research Projects

Open Projects: I have 4 research projects that are focused on fabrication, measurement, and/or theory, depending on student interest and experience:

Project 1. *Device Design and Characterization for Energy-Related Materials*

This project involves studying charge transport in materials for solar energy conversion using various device architectures and methods. The student will learn thin-film fabrication and microscopy characterization methods, how to design and deposit electrodes, and useful techniques in the west campus clean room such as photolithography and optical profilometry.

Project 2. *Theory of Charge Transport in Nanostructured Materials*

Studying charge transport is important from a fundamental physics perspective, but also can provide guidance for material design. This project involves studying the mechanisms of charge transport important to nanostructured materials used for solar energy conversion. The student will learn how to apply these models to temperature-dependent electrical data. Programming experience recommended.

Project 3. *Temperature-Dependent Charge Transport Measurements in Energy Materials*

Our lab on west campus has a cryostat capable of accessing temperatures between ~7 and 315 K. By measuring the conductivity of materials in this range, one can decipher the mechanism of charge transport and learn valuable information about improving device performance. Because important materials for energy applications are often highly porous by design for achieving high surface area, conductivities are often very low. The cryostat is therefore equipped with highly sensitive electrical equipment capable of measuring currents on the order of femtoamps. This project is a study of charge transport as a function of temperature under various light and ambient gas conditions. Prior experience in LabView and Python would be helpful, though experience can be swapped for an interest to learn.

Project 4. *Impedance Spectroscopy for Studying Materials for Energy Applications*

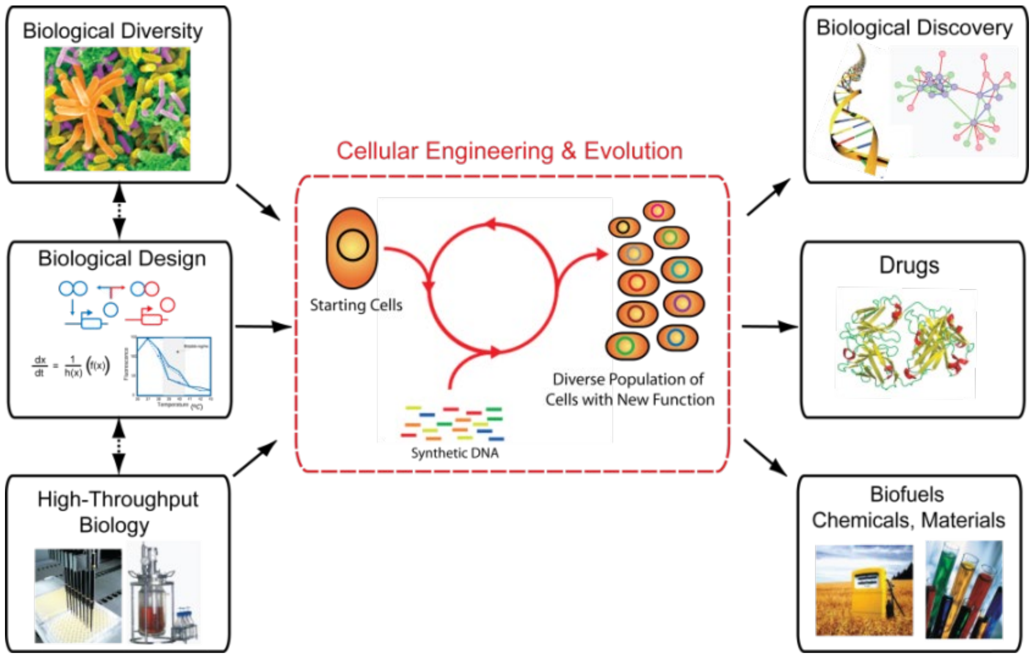
Studying the resistance and capacitance properties of a material upon application of an ac signal can potentially provide much more information than dc methods. These data can be fit with an equivalent circuit model, each component of which corresponding to a particular physical process in the device. This project is an application of this powerful method, which allows complicated systems such as thin-film devices or electrochemical cells to be studied systematically. Some programming experience will be useful.

Steve Konezny
steven.konezny@yale.edu

Synthetic Biology @ Yale

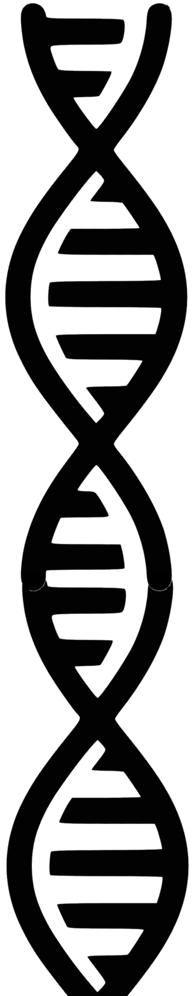
Farren Isaacs
Associate Professor & DGS
Molecular, Cellular & Developmental Biology
Biomedical Engineering
Systems Biology Institute
Yale University

Isaacs Lab



- Invent new genome engineering technologies
- Construct organisms with new genetic codes
- Engineer novel proteins & biomaterials
- Develop biological safeguards

➢ **Undergrads publish papers!** Isaacslab.org



iGEM

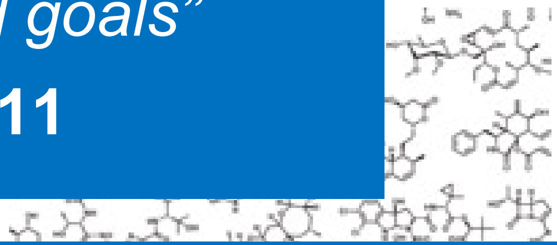
- International genetically engineered machines
- Multidisciplinary teams work together to build, design, and test novel biological systems
- Push the boundaries of science by tackling real-world global problems

➢ Compete against 6,000 people from around the world at annual Jamboree @ MIT igem.org

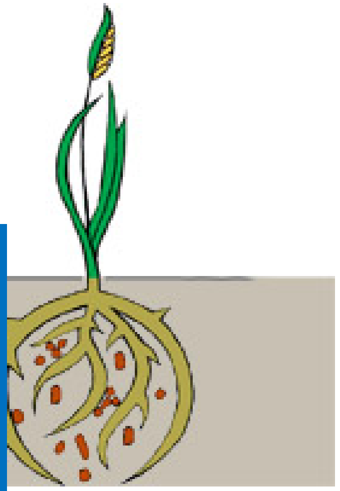
Synthetic Biology: a new approach for meeting grand challenges and societal needs

"the quest to hijack living systems and convert them to human-directed goals"

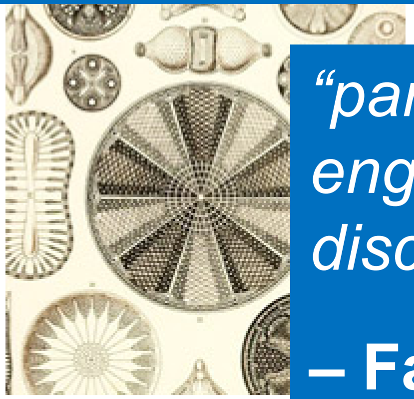
-Nicholas Wade, NY Times 2011



"By combining elements of engineering, chemistry, computer science, and molecular biology, synthetic biology seeks to assemble the biological tools necessary to redesign the living world."
– New Yorker 2009



ricultural



"part of the natural maturation of biotechnology, in which the engineering of biological systems is becoming a formal discipline"

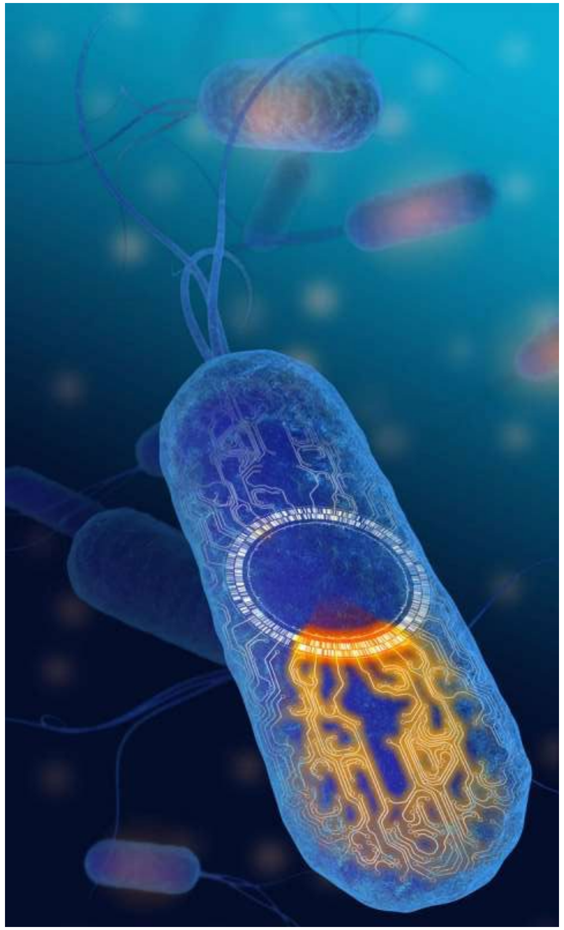
– Farren Isaacs & Lingchong You, Genome Biology 2009

Materials **Energy** **Global Health**

Synthetic Biology is "Engineering Biology"

- the design and construction of new biological parts, devices, and systems

- the re-design of existing, natural biological systems for useful purposes



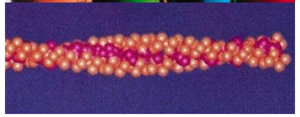
Medicine

Food

Energy

Chemicals

Materials



iGEM at Yale

Team History

Yale iGEM was **founded in 2009** by a group of undergraduates passionate about the **potential of synthetic biology**. Inspired by the iGEM foundation mission, they set out to make their own contributions, completing their first project in 2010.

Nature's Antifreeze: Microbial Expression and Characterization of a Novel Insect Antifreeze Protein for De-Icing Solutions

Developing a Framework for the Genetic Manipulation of Non-Model and Environmentally Significant Microbes

Publications

- Journal of Biological Chemistry (cover)
- Nature, eLife, ACS-Synthetic Biology, Nucleic Acids Research

Team Awards

- Food/Energy Project Grand Prize
- Best Natural Biobrick
- Gold Medal
- Grand Finalist

Individual Awards

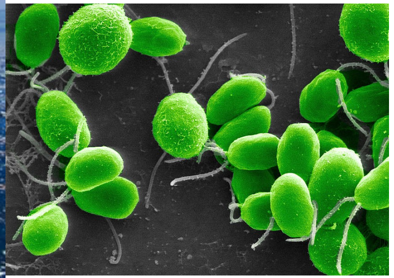
- Gates Fellowship
- Hertz Fellowship
- Goldwater Award
- Beckman Scholar
- Schwartzman Scholarship

iGEM Alumni

- Grad School @ Yale, Duke, Stanford, Harvard, Princeton
- Regeneron
- NIH
- Microsoft
- Promega
- McKinsey & Co., BCG

Recent Project

"its all about plastics"



To mitigate PET microplastic waste build-up, the Yale iGEM team has been working to engineer a strain of *Chlamydomonas reinhardtii,* a freshwater green algae, with the ability to secrete proteins capable of breaking down plastics.

WE WANT YOU!

THE iGEM TEAM SEEKS A FEW GOOD **YALIES** …
… TO CHANGE THE WORLD

farren.Isaacs@yale.edu

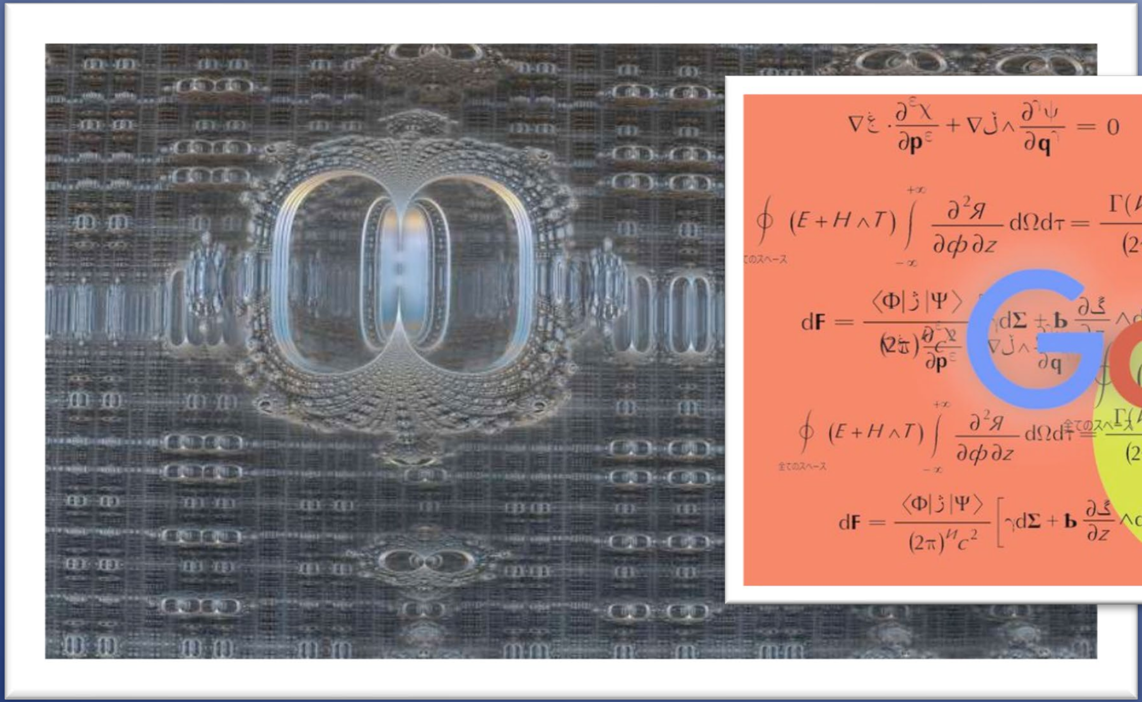
Quantum Information Science, Computing and Algorithms in High Energy Physics at the Large Hadron Collider

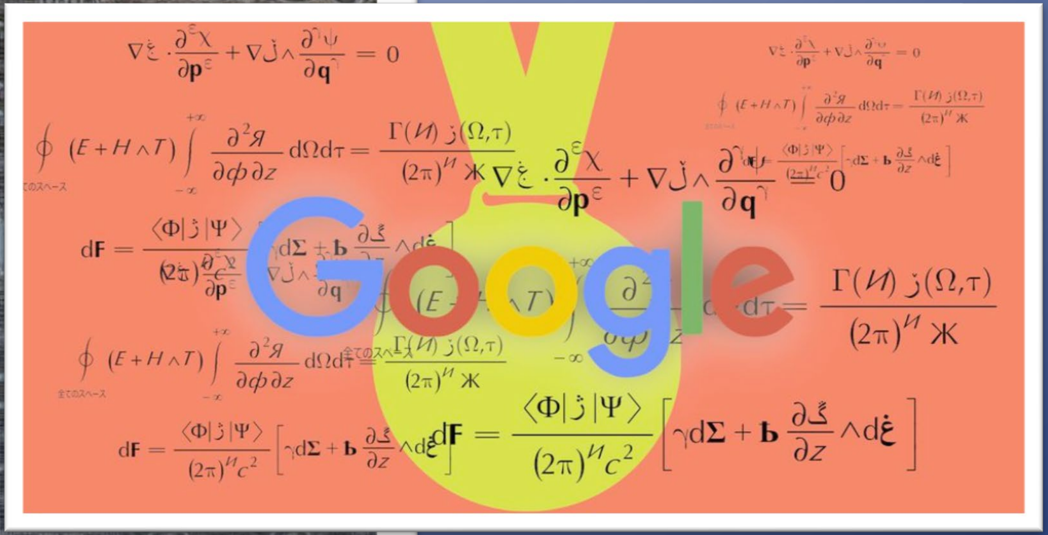
Oliver K. Baker
Department of Physics, Yale University

October 25, 2019 PHYS.ORG

What Google's 'quantum supremacy' means for the future of computing

by Deborah Netburn





Quantum computing algorithms in HEP in collaboration with Anthony E. Armenakas (high school student from NYC)

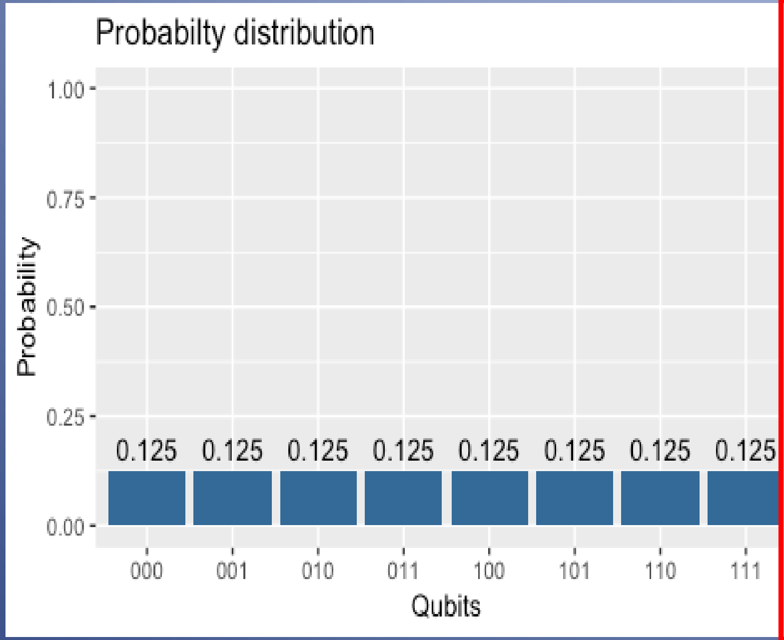
1. Rstudio (R-programming package)
2. QCSimulator (quantum computing simulator)
3. Used 3 qubits in simulator along with modified Grover algorithm
4. Converted code to python
5. Ran on IBM 4-qubit quantum computer

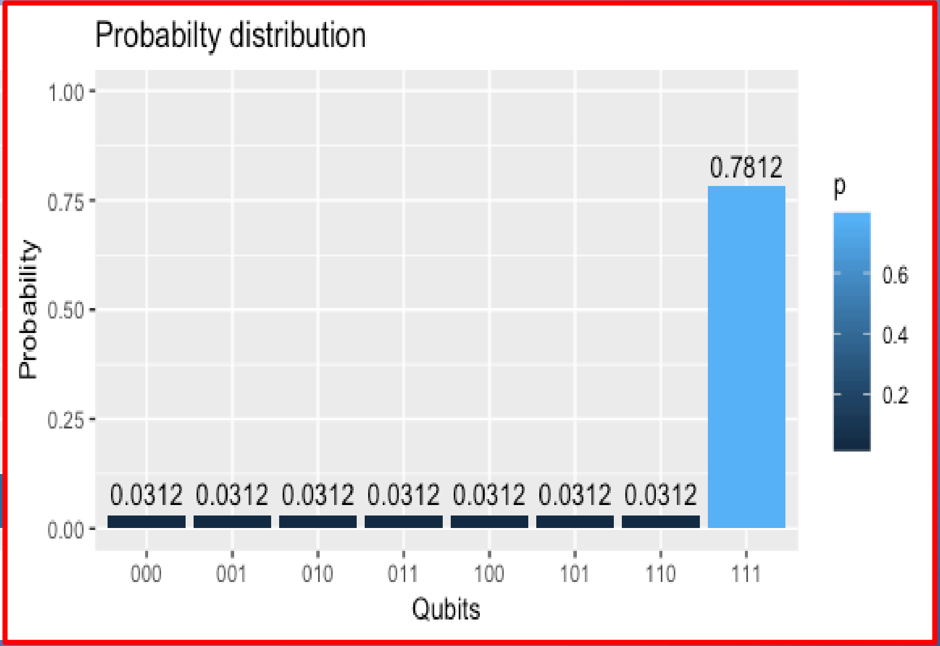
Quantum computing algorithms in HEP
in collaboration with
Anthony E. Armenakas
(high school student from NYC)

- a = TensorProd(TensorProd(Hadamard(I2),Hadamard(I2)),Hadamard(I2))
- …
- plotMeasurement(a)
- . . .

	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]	[,7]	[,8
[1,]	0.3535534	0.3535534	0.3535534	0.3535534	0.3535534	0.3535534	0.3535534	0.3535534
[2,]	0.3535534	-0.3535534	0.3535534	-0.3535534	0.3535534	-0.3535534	0.3535534	-0.3535534
[3,]	0.3535534	0.3535534	-0.3535534	-0.3535534	0.3535534	0.3535534	-0.3535534	-0.3535534
[4,]	0.3535534	-0.3535534	-0.3535534	0.3535534	0.3535534	-0.3535534	-0.3535534	0.3535534
[5,]	0.3535534	0.3535534	0.3535534	0.3535534	-0.3535534	-0.3535534	-0.3535534	-0.3535534
[6,]	0.3535534	-0.3535534	0.3535534	-0.3535534	-0.3535534	0.3535534	-0.3535534	0.3535534
[7,]	0.3535534	0.3535534	-0.3535534	-0.3535534	-0.3535534	-0.3535534	0.3535534	0.3535534
[8,]	0.3535534	-0.3535534	-0.3535534	0.3535534	-0.3535534	0.3535534	0.3535534	-0.3535534

Quantum computing algorithms in HEP in collaboration with Anthony E. Armenakas (high school student from NYC)





Can quantum entanglement be used to address open problems in other fields?

Making Molecules Out of Thin Air

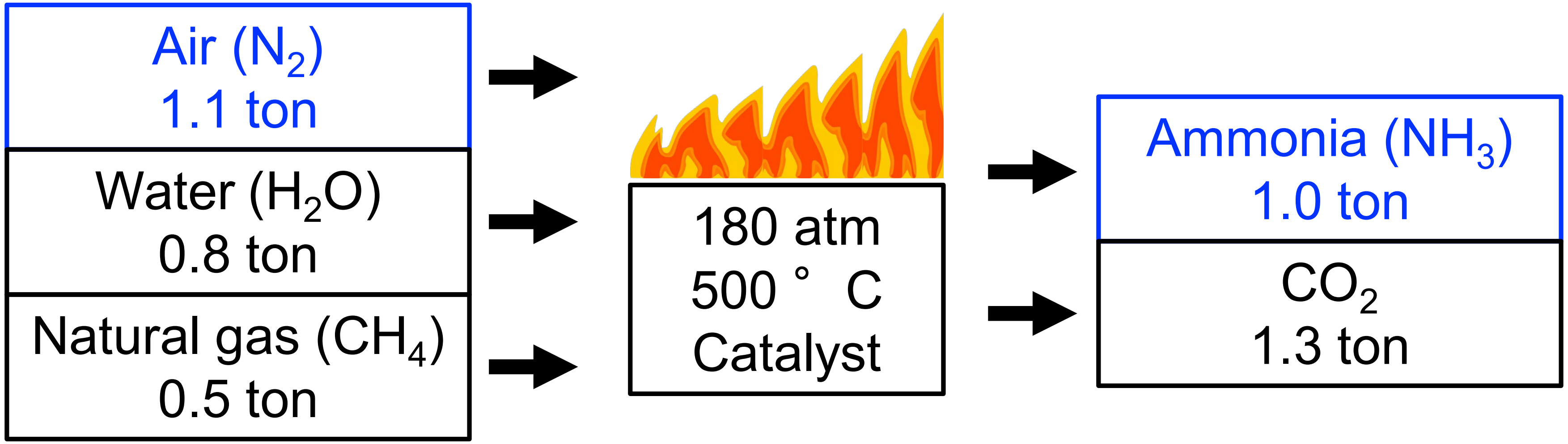
Patrick Holland
Chemistry Department

patrick.holland@yale.edu

Haber-Bosch Process

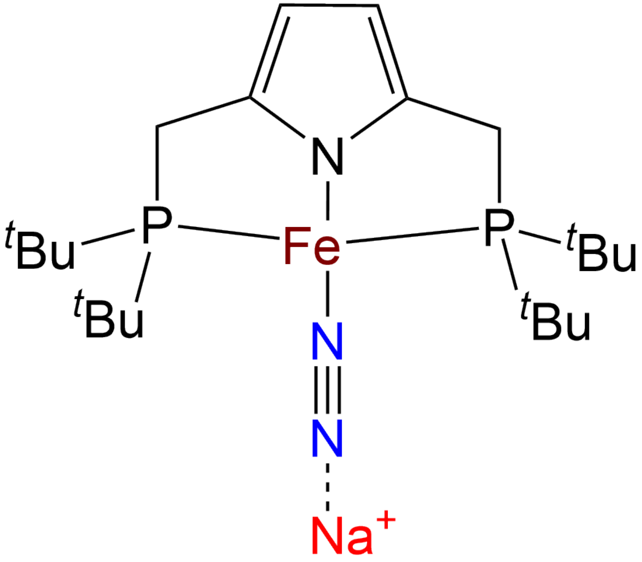
$$N_2 \longrightarrow NH_3$$

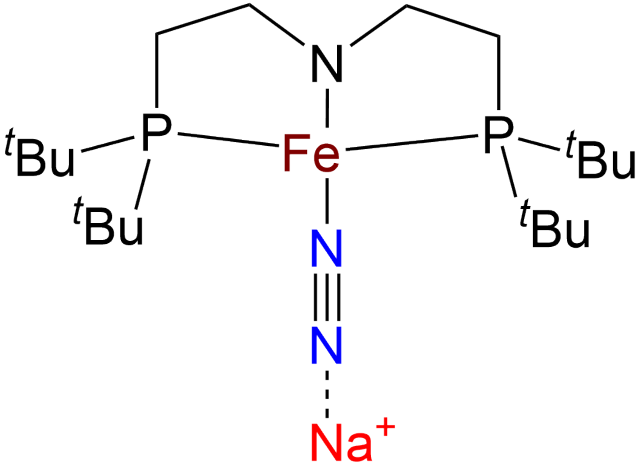
140,000,000 tons NH_3 in 2017

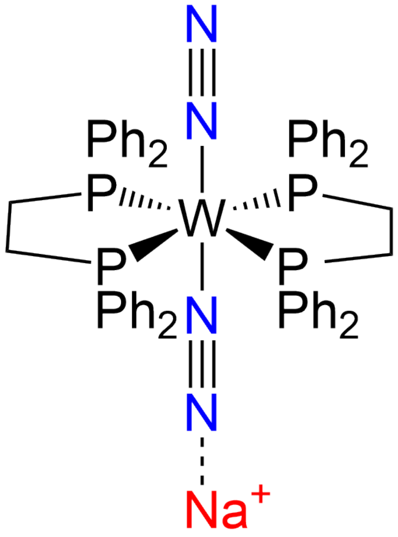


http://cse.ksu.edu/REU/S14/rinaldi/
US Geological Survey, *Mineral Commodity Summaries 2017*

Lewis Acid Effects on the N-N Bond of N_2







- N_2 is held together by a strong triple bond
- Triple bond must be broken to produce ammonia and other useful products
- When Lewis acids coordinate, N–N bond is weakened

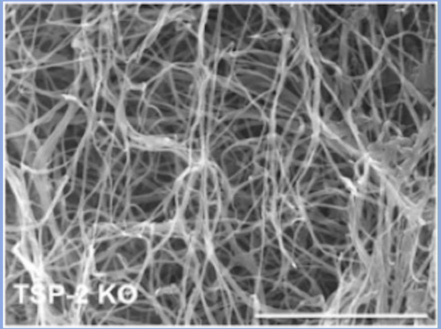
Kuriyama, S.; Arashiba, K.; Nakajima, K.; Matsuo, Y.; Tanaka, H.; Ishii, K.; Yoshizawa, K.; Nishibayashi, Y. *Nat. Commun.* **2016**.
Chatt, J.; Crabtree, R.H.; Jeffery, E.A.; Richards, R.L. *Dalton Trans.* **1973**.

Contact: themis.kyriakides@yale.edu

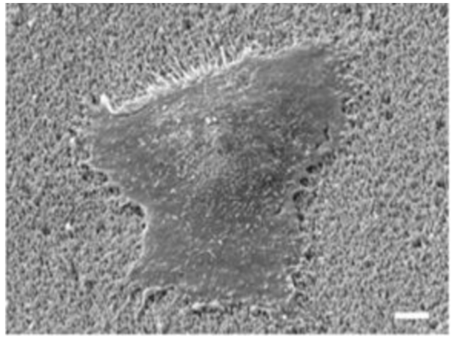
Kyriakides Lab

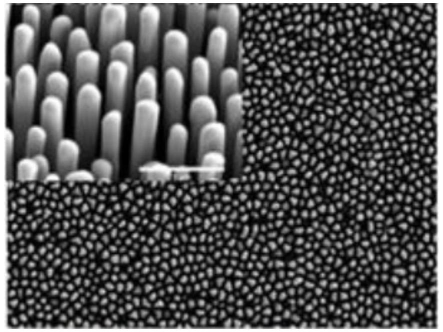
Where discovery meets application

TISSUE ENGINEERING

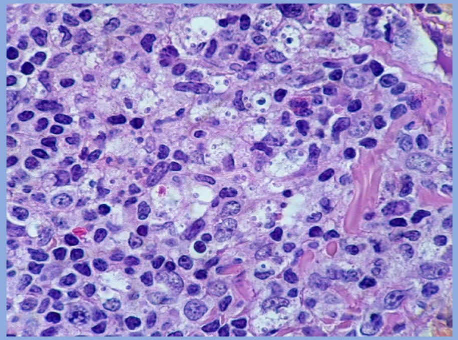


BULK METALLIC GLASS





TOPICAL TREATMENT



Contact: themis.kyriakides@yale.edu

Potential Summer/Semester Project

- Diabetic Kidney Fibrosis and Treatment
- Growth-factor imbedded biomaterials
- Tissue-derived hydrogel
- BMG Implant in Rodents
- Skin lesion mimic prototyping

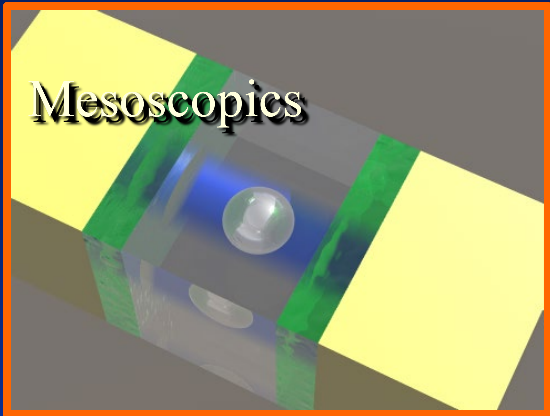
How can you get involved?

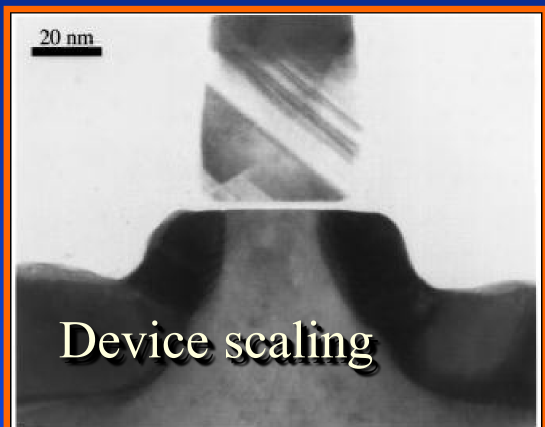
themis.kyriakides@yale.edu

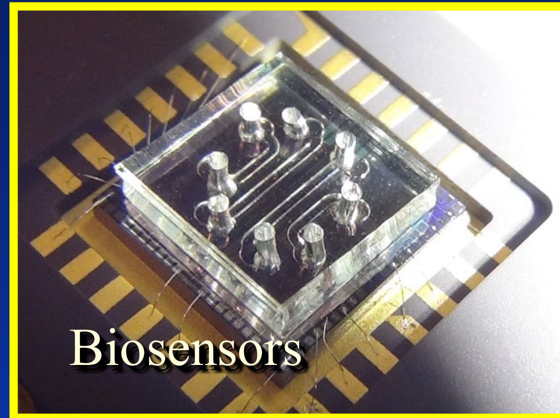
- Graduate students as day-to-day mentors
- Bimonthly project meetings followed by journal club
- 2 funded students
- 2 BME students completed their senior thesis with us past year

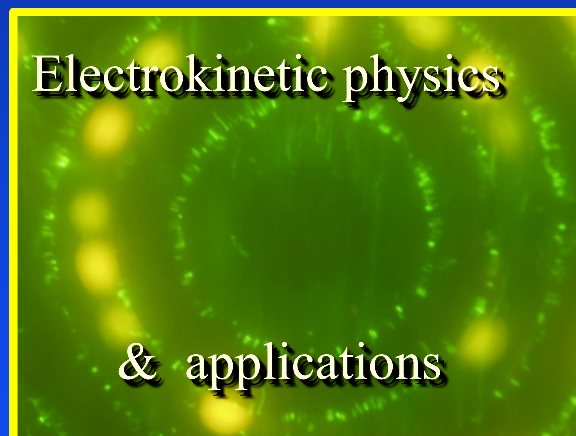
Reed Lab

mark.reed@yale.edu

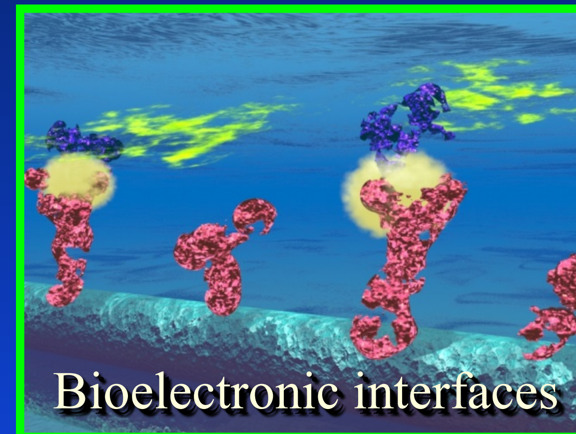


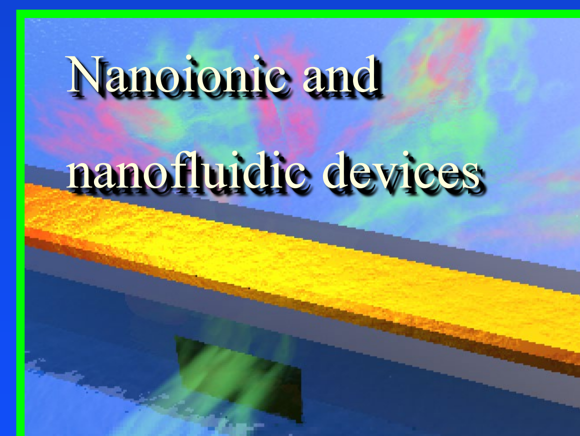




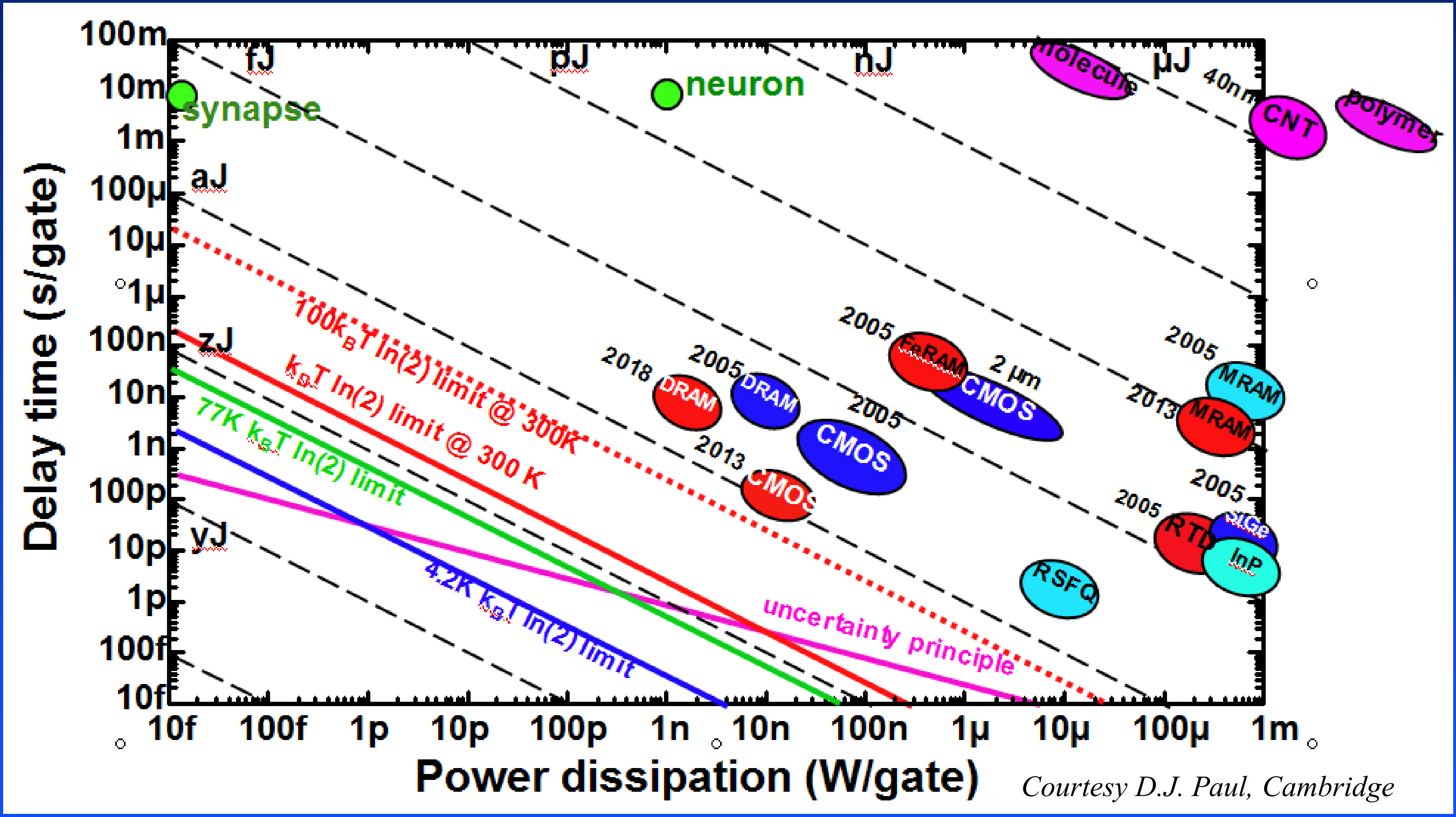


https://www.eng.yale.edu/reedlab/



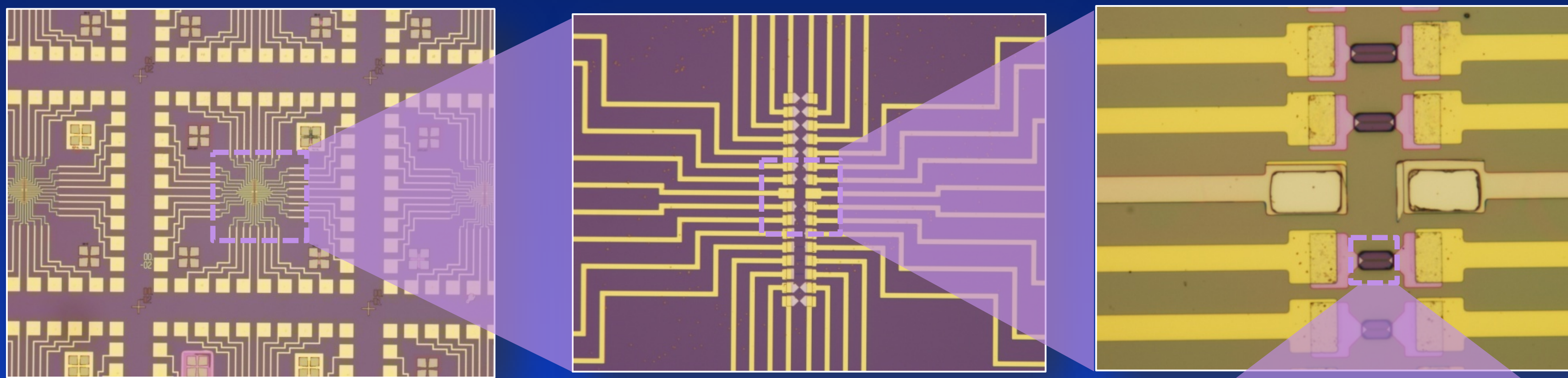


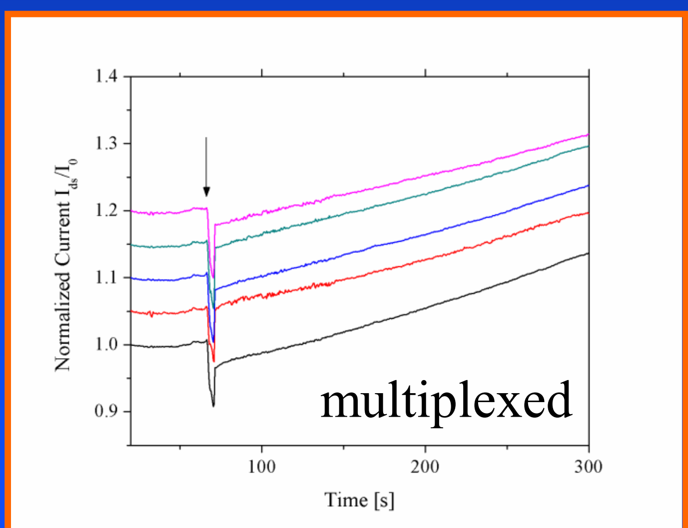
The power-delay metric

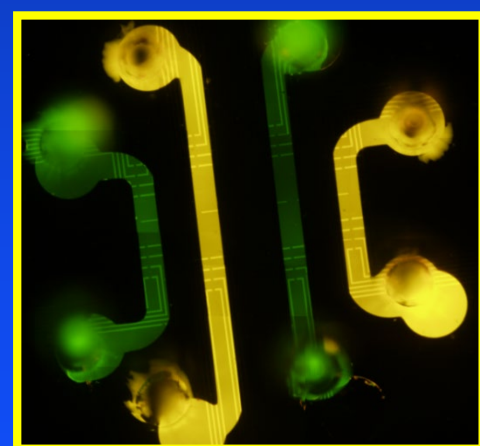


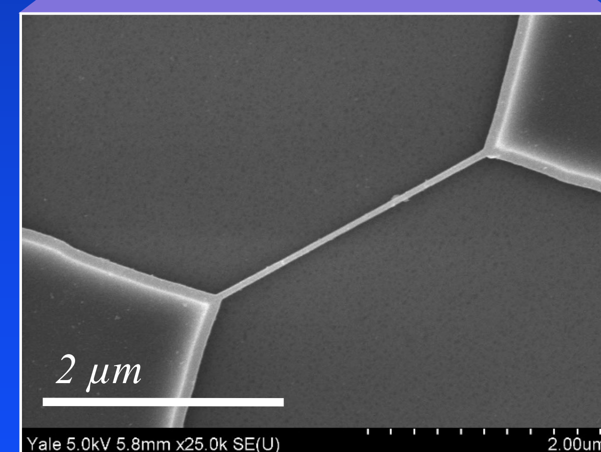
Courtesy D.J. Paul, Cambridge

Multiplexed FD SOI CMOS Nanowires









E. Coli and RBCs separation