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

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

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

draw a 3D bounding box around the lesion

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.
4DE Image Acquisition

Endo- and Epi-cardial Surface Segmentation (Dictionary Learning-based)

Local Curvature & confidence

Regularized Shape tracking (G-RPM)

GPU Correlator (using phase & magnitude)

Viterbi Filter

Integration

Shape-based displacements

Geometry/appearance

U_{shape}

Speckle-based displacements

U_{speck}

U_{dense}
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.

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.
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.

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

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

isaacslab.org

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“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

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

-Nicholas Wade, NY Times 2011

“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

Agricultural

Biomedical

Chemical

Energy
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

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.

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

Publications
- Journal of Biological Chemistry (cover)

THE iGEM TEAM SEEKS A FEW GOOD YALIES ... TO CHANGE THE WORLD

farren.isaacs@yale.edu
• 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?
Potential Undergraduate Projects

### Mapping Huntington's Disease-Associated Protein Phase Transitions

- Cells organize dysfunctional proteins into “droplets” like oil droplets in water
- 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
- We will create an assay that reproduces in-cell observations in a test tube

### 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 cells
- A complementary approach uses rapid mixing to quickly change the local environment (pH, salt, temperature, etc)
- A laser quickly heats the sample to induce a “temperature jump,” and microscopy monitors dynamics of protein or RNA
- We will design and test a microfluidic mixer for our infrared microscope
- 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 ruptured!
femtosecond broadband infrared microscopy

Beam propagation experiments

Beam propagation simulations

NA = 0.65

I(x,y,z=0)
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)
Sanah (gap year student, now grad student here) working with low temperature thermometry in the Dilution Refrigerator.

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

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.
Receiver noise testbed - led by graduate student Emily Kuhn

Emily and Ben building the foam insert

Maile constructing the fiberglass insert

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

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

Debating

One of two receiver noise test-beds done!
Drone beam mapping

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

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

Annie and Maile checking out the drone radio signal chain

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

- **Perceptrons**
- **Artificial Neural Networks**
- **Convolutional Neural Networks for Complex Recognition**
- **Spiking Neural Networks**
- **AlphaGo:** 1920 CPUs and 280 GPUs (~1MegaWatt)  
  Vs.  
  **Lee Sedol:** 1 human brain (~20 Watts)

**Neuromorphic Computing - Integrate-and-Fire Non-linearity**

**Simple Classification – Threshold Non-linearity**

**Multi-class Classification – Sigmoid, Tanh, ReLU**

**Output Spike Train**

**Input Spike Train**

**Research Focus:** Towards energy-efficient and robust machine intelligence with brain inspired ‘spikes’ computing
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
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/](https://intelligentcomputinglab.yale.edu/)

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

• Confinement of wavefunction
• Reduced dielectric screening

Electronic Confinement

Enhanced Optical Absorption

3D:

2D:

- Confinement of wavefunction
- Reduced dielectric screening

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

Electronic Properties

- We know how electrons interact
- Many-body Hamiltonian

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

- N+1 particle problem

\[ \text{N} \sim 10^{23} \text{ electrons!} \]

Cannot be solved exactly!

\[ E^0, p, m_e \]

Ground State Charge Density

electron

electron + "screening" cloud

quasielectron (quasihole)

\[ E^{\text{QP}}, p, m^*, \tau \]
Optical Properties

Incoming photon excites electron and hole

Electron and hole interact forming an exciton

Exciton State:

\[ \Psi_S(r_e, r_h) = \sum_{vck} A_{vck}^S \psi^*_v(r_h) \psi_k(r_e) \]

Like a hydrogen atom!
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
A catalyst is a substance that alters the rate of a reaction without being consumed in the reaction.

\[
\begin{align*}
A + B & \quad \text{slow or no reaction} \quad C + D \\
A + B & \quad \text{fast reaction} \quad \text{catalyst} \quad C + D
\end{align*}
\]

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.
Secure & privacy-respecting personal computing

Efficient, dependable edge

IoT  Mobile  Wireless/Edge  Cloud

Privacy. Security
5G & Edge data centers

IoT  Mobile  Wireless/Edge  Cloud

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
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.

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.

**bioinformatics**

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

**peptidomics**

- lyse by boiling, acid extraction
- MWCO filter isolate peptides
- reduction, alkylation, trypsin digest
- analyze by 2D-LC-MS/MS

**Numbers and lengths of smORFs in K562 cells**

- 195 smORFs validated by proteomics
- Thousands ID’d by ribosome profiling

<table>
<thead>
<tr>
<th>Length (amino acids)</th>
<th>53</th>
<th>95</th>
<th>27</th>
<th>9</th>
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<td>26-50</td>
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<td>76-100</td>
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<td>101-125</td>
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<td>126-150</td>
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</table>

**PubMed references to smORFs and related keywords, by year**

References vs. Year
Small open reading frame (smORF) discovery: examples of functions

DNA double-strand break repair
- MRI-2/CYREN
- Ku70/80
- DNA-PK
- XRCC/Ligase IV

Cytoplasmic 5′-to-3′ RNA decay
- RNA decapping complex

Cellular stress responses
- Stress responsive smORFs in E. coli genome
  Also: oxidative stress, hypoxia, nutrient starvation

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, etc.)

**SNARE zipper hypothesis**: P. Hanson, ..., R. Jahn, J. Heuser, Cell, 90, 523 (1997)
Single-molecule manipulation of SNARE complexes

High-resolution optical tweezers

Hardware

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

Measurement range

Software

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)

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

- 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

‘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)
Undergraduate Summer Research Projects

1. Computational modeling of deformable particles
   - Reconstruction of bubble packing
   - Packing of bubbles

2. Dense packing in protein cores
   - Packing of deformable polyhedra
   - Packing of keratinocytes
   - Core residues
     - Voronoi polyhedron
     - Packing of residues
     - Void space
Details of Mentoring

1. Computational modeling of deformable particles: Lead: Jack Treado (4th 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 (2nd year Ph.D. student in Computational Biology & Bioinformatics) and Zhe Mei (4th 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
The Standard Genetic Code

Genetic Code Expansion

The Standard Genetic Code

Pyrrolysyl-tRNA Synthetase

Selenocysteine

Pyrrolysine

UAG

UGA

Pyl

ncAA

Mutant

AMP

PPI

Nascent Polypeptide

Ribosome

mRNA

5'

3'


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**


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

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.

Aldag et al., Angew Chem Int Ed. 2013, 52, 1441-1445.
• Materials for solar energy devices (solar cells, solar fuel cells, …)

• Charge transport physics (experiment and theory)

• Projects depend on your interests and background
Nanomaterial design considerations

Steve Konezny
steven.konezny@yale.edu

January 16, 2020
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.

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Steve Konezny
steven.konezny@yale.edu
January 16, 2020
Synthetic Biology @ Yale

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

Isaacs Lab

- Structural Diversity
- Biological Design
- High-Throughput Biology

Cellular Engineering & Evolution

- Starting Cells
- Diverse Population of Cells with New Function
- Synthetic DNA

Biological Discovery

- Drugs
- Chemicals, Materials

Biofuels

Biological Safeguards

• 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

isaacslab.org igem.org
Synthetic Biology: a new approach for meeting grand challenges and societal needs

“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

“the quest to hijack living systems and convert them to human-directed goals”
-Nicholas Wade, NY Times 2011

“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
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

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.

Publications
- Journal of Biological Chemistry (cover)

farren.Isaacs@yale.edu

THE iGEM TEAM SEEKS A FEW GOOD YALIES ... TO CHANGE THE WORLD
Quantum Information Science, Computing and Algorithms in High Energy Physics at the Large Hadron Collider

Oliver K. Baker
Department of Physics, Yale University
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
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Anthony E. Armenakas
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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

\[ \text{N}_2 \rightarrow \text{NH}_3 \]

140,000,000 tons NH\(_3\) in 2017

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<th>Material</th>
<th>Weight</th>
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<td>Air (N(_2))</td>
<td>1.1 ton</td>
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<tr>
<td>Water (H(_2)O)</td>
<td>0.8 ton</td>
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<td>Natural gas (CH(_4))</td>
<td>0.5 ton</td>
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<tr>
<td>Ammonia (NH(_3))</td>
<td>1.0 ton</td>
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<tr>
<td>CO(_2)</td>
<td>1.3 ton</td>
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180 atm, 500 °C, Catalyst
Lewis Acid Effects on the N-N Bond of N₂

N₂ 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

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?

- 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

Contact: themis.kyriakides@yale.edu
The power-delay metric

Courtesy D.J. Paul, Cambridge
Multiplexed FD SOI CMOS Nanowires
E. Coli and RBCs separation