# Catalyst

V 14.1

Spring/Summer 2019 Volume 14 • Issue 1

College of Chemistry • University of California, Berkeley

## Alumna Frances Arnold takes the gold

- The College's rich startup culture
- Rui Wang: Theoretical models
- Ke Xu: Super-microscopic visions

# Catalyst

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### ON THE COVER

Alumna Frances Arnold became the first American woman to receive the Nobel Prize in Chemistry on December 10, 2018 for the *directed evolution of enzymes.*

COVER PHOTO: HENRIK MONTGOMERY/AFP/GETTY IMAGES


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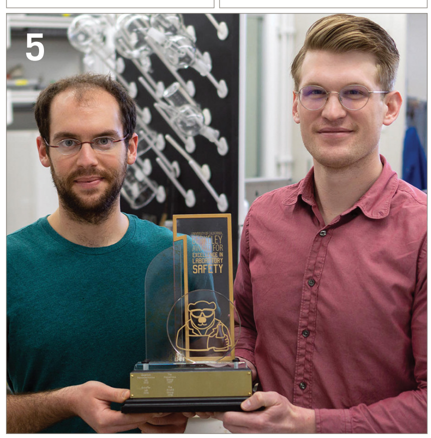


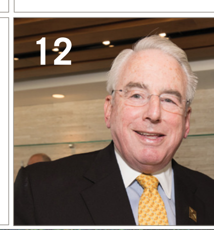


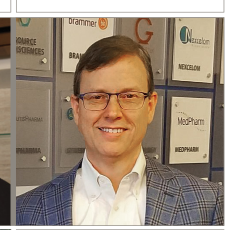

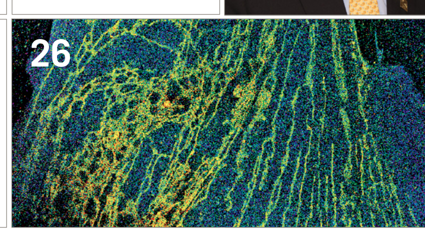

# Spring/Summer 2019

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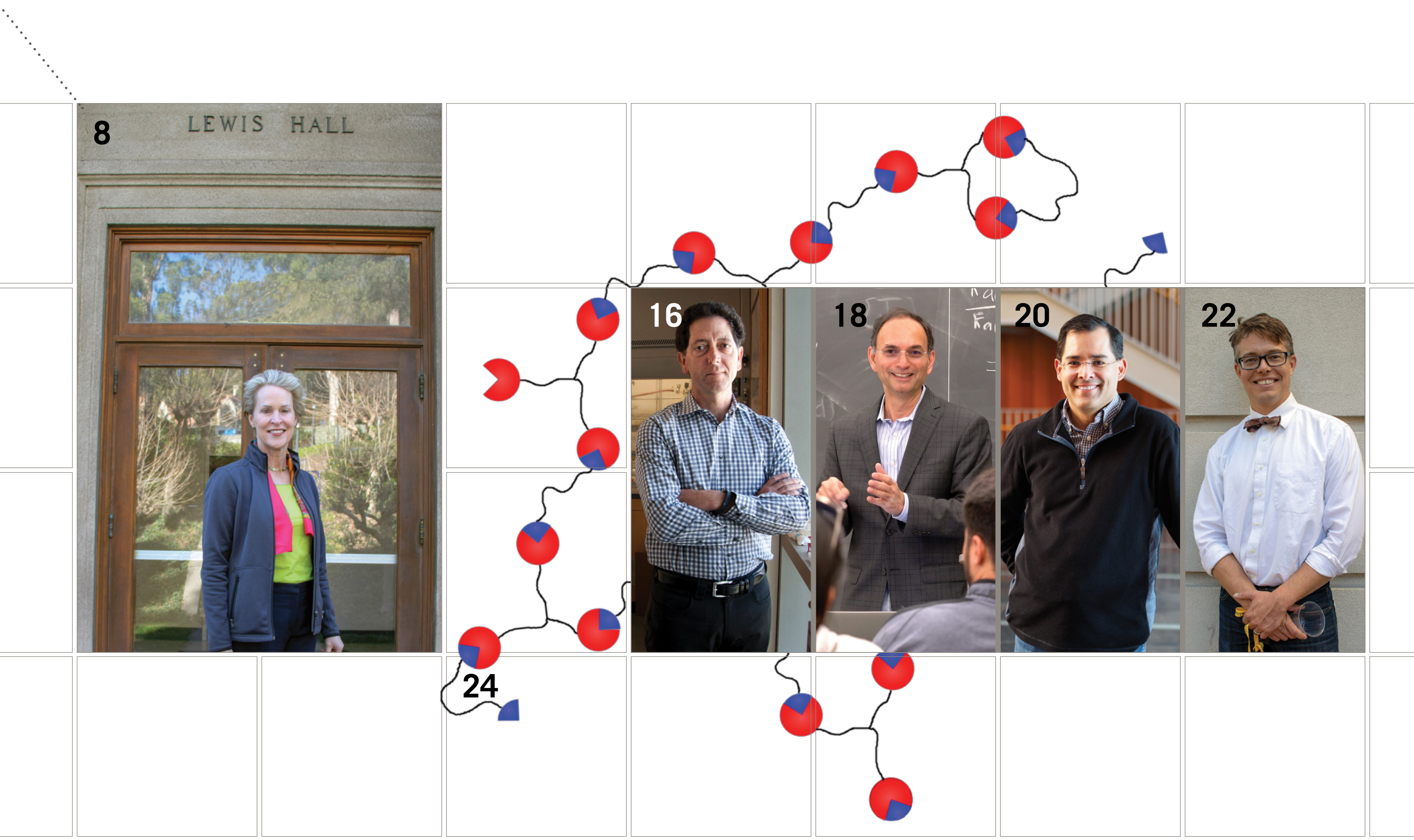


College of Chemistry
Nobel Laureate Alumni
FRANCES H. ARNOLD
Nobel Prize in Chemistry 2018
U.C. Berkeley College of Chemistry
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BERKELEY
ROBERT F. CURL, JR.
Ph.D. 1957
Nobel Prize in Chemistry 1996
U.C. Berkeley College of Chemistry
AHMED ZEWAIL
Postdoc 1974
Nobel Prize in Chemistry 1999
U.C. Berkeley College of Chemistry
KURT WÜTHRICH
Nobel Prize in Chemistry 2002
HENRY TAUBE
Ph.D. 1940
Nobel Prize in Chemistry 1983
U.C. Berkeley College of Chemistry
THOMAS CECH
Nobel Prize in Chemistry 1989 (with Sidney Altman)
U.C. Berkeley College of Chemistry
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Ph.D. 1972
Nobel Prize in Chemistry 1995 (with Paul J. Crutzen and F. Sherwood Rowland)
U.C. Berkeley College of Chemistry
HAROLD C. UREY
Ph.D. 1923
Nobel Prize in Chemistry 1934
U.C. Berkeley College of Chemistry
WILLARD F. LIBBY
B.S. 1931, Ph.D. 1933
Nobel Prize in Chemistry 1960
U.C. Berkeley College of Chemistry
GEOFFREY WILKINSON
Postdoc 1950
Nobel Prize in Chemistry 1973
U.C. Berkeley College of Chemistry


Jeffrey Reimer, Frances Arnold and Douglas Clark at the spring 2019 Dean's Dinner.

# The Riches of Fall

The fall conjures annual images of autumn colors, falling leaves, and students of all ages heading back to school. For our College of Chemistry, it also evokes visions of Nobel Prizes, which are announced in October. Our College has been recognized with many prestigious honors and awards, the most distinguished being the Nobel Prize. From 1934 to 2018, four of our faculty, three of our previous postdoctoral scholars, and seven of our former graduate students have been awarded this distinction. In this issue of Catalyst you will read about our latest Nobel Prize recipient, alumna Frances Arnold. A chemical engineering graduate student of Harvey Blanch and Ph.D. recipient in 1985, Frances has always been a trailblazer. She can lay claim to many firsts, including the first Ph.D. chemical engineer to receive a Nobel Prize, and the first female chemical engineer to receive the prize. Frances has also maintained her Berkeley connection; she was our 2018 Commencement Speaker and the 2013 Lewis Lecturer. We are immensely proud of her.

Another recent notable awardee from our College (among many) is Chemistry Professor John Hartwig, who shared the 2019 Wolf Prize with Stephen Buchwald of MIT. The Wolf Prize is generally regarded to be the most prestigious award in chemistry after the Nobel Prize, and this is the third year in a row it has been awarded to a Berkeley chemistry professor (Omar Yaghi shared it in 2018, and Robert Bergman received it in 2017). Including Paul Alivisatos in 2012, our College has garnered four of the last seven Wolf Prizes—a truly remarkable achievement (there was no award in 2015).

This issue also includes articles about two of our assistant professors, Rui Wang in CBE, and Ke Xu in Chemistry. We have a stellar group of assistant professors who are making their mark and we are hopeful that you will soon hear about three newly appointed assistant professors coming on board this July (and further down the road, future Wolf Prize awardees and even a Nobel Laureate or two).

We have also expanded and upgraded our facilities for educating the next generation of trailblazers. While our undergraduate students are tackling organic chemistry and thermodynamics, they now can access our new Peer Tutoring Center, located in Latimer Hall in what was previously called Bixby Commons. With generous support from Chevron and Fillmore Capital Partners (CoC alumnus Ron Silva's company), this Center provides students with space for review sessions, student group meetings, and one-on-one and group tutoring. Our Que Family Undergraduate Advising Center in Gilman Hall also now provides career counseling as well as undergraduate advising.

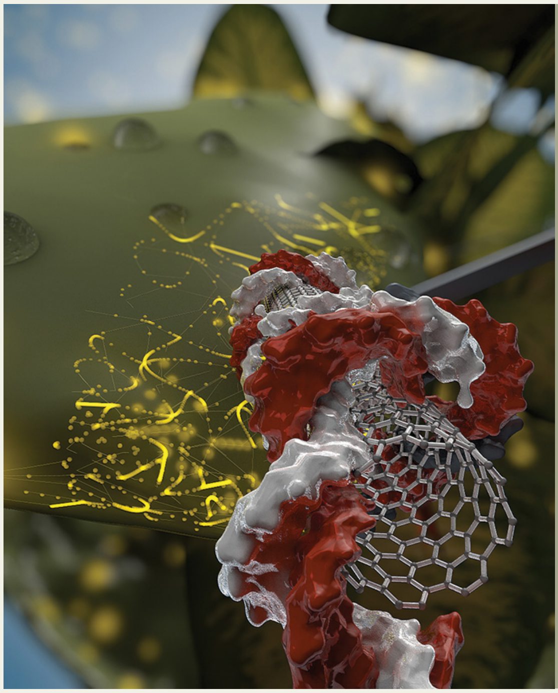
So, next year when the subtle signs of fall begin to catch your eye, think of it as a particularly exciting time for the College of Chemistry. We'll be waiting to see if the season brings us more distinction to add to our legacy. In the meantime, thank you for your continuing support, and for helping us make each and every year so rewarding.

**DOUGLAS S. CLARK**
Dean, College of Chemistry
Gilbert N. Lewis Professor

On the wall in Latimer Hall, alumni Nobel Laureates

# NEW & NOTABLE

RESEARCH • VIEWS
DISCOVERIES • AWARDS



## With nanotubes, genetic engineering in plants is easy-peasy

Inserting or tweaking genes in plants is more art than science today, but a new technique developed by University of California, Berkeley, scientists in the lab of Markita Landry could make genetically engineering any type of plant—in particular, gene editing with CRISPR-Cas9—simple and quick.

To deliver a gene, the researchers grafted it onto a carbon nanotube, which is tiny enough to slip easily through a plant's tough cell wall. Nanotubes are highly successful at delivering a gene into the nucleus and also into the chloroplast, a structure in the cell that is even harder to target using current methods.

The nanotube not only protects the DNA from being degraded by the cell, but also prevents it from being inserted into the plant's genome. As a result, the technique allows gene modifications or deletions that in the United States and countries other than the European Union would not trigger the designation "genetically modified," or GMO. Results of the research were reported in the journal *Nature Nanotechnology*.



## Yeast produce low-cost, high-quality cannabinoids

College of Chemistry synthetic biologists have engineered brewer's yeast to produce marijuana's main ingredients—mind-altering THC and non-psychoactive CBD—as well as novel cannabinoids not found in the plant itself—in new research from the lab of Jay Keasling, Professor of Chemical and Biomolecular Engineering and of Bioengineering and a faculty scientist at Lawrence Berkeley National Laboratory.

According to Keasling, "For the consumer, the benefits are high-quality, low-cost CBD and THC: you get exactly what you want from yeast. It is a safer, more environmentally friendly way to produce cannabinoids."

Medications containing THC have been approved by the Food and Drug Administration to reduce nausea after chemotherapy and improve appetite in AIDS patients. Medical research on more than 100 other chemicals in marijuana has been difficult, because the chemicals occur in tiny quantities, making them hard to extract from the plant. Inexpensive, purer sources—like yeast—could make such studies easier.

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## Awards & Nominations

### 1. John Hartwig awarded 2019 Wolf Prize in Chemistry

Henry Rapoport Professor in Organic Chemistry John Hartwig *(Ph.D. '90, Chem)* and co-awardee Professor Stephen Buchwald from MIT have been named 2019 Wolf Laureates for the development of efficient transition-metal catalysts that have revolutionized drug manufacturing, leading to a breakthrough in molecule and synthetics design.

Hartwig and Buchwald were also jointly awarded the Tetrahedron Prize for Creativity in Organic Chemistry in 2018 for their development of the Buchwald–Hartwig amination: a chemical reaction used for the synthesis of carbon-nitrogen bonds via the Palladium-catalyzed coupling reactions of amines with aryl halides. The process has gained wide use in the industrial preparation of numerous pharmaceuticals.

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### 2. Douglas S. Clark elected to the National Academy of Engineering

Douglas S. Clark, Dean of the College of Chemistry and Gilbert Newton Lewis Professor, has been elected a member of the National Academy of Engineering for advances in biocatalyst and bioreaction engineering for drug discovery, drug screening, and bioprocessing.

Clark's research is focused in the field of biochemical engineering, with particular emphasis on enzyme technology, biomaterials, and bioenergy.  Underlying these general topics is a longstanding interest in extremophiles and extremophilic enzymes. His work in biocatalyst engineering has created new opportunities for the application of enzymes in the pharmaceutical, chemical, and agrochemical industries, and his development of protein and cellular arrays has enabled high-throughput biosynthesis and activity/toxicity screening of potential drugs.

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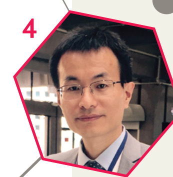
### 3. Alum David Oxtoby named president of the American Academy of Arts & Sciences

The American Academy of Arts and Sciences has named David W. Oxtoby *(Ph.D. '75, Chem)* the organization's new president starting in 2019. A chemist by training, he served as president of Pomona College from 2003 to 2017. He was elected a member of the American Academy in 2012.

In making the announcement, Nancy C. Andrews, chair of the Academy's Board of Directors and Dean Emerita of the Duke University School of Medicine said, "We are thrilled that David is ready and excited to help the Academy fulfill its mission to support this still-young nation through its work to understand complex issues and advance the common good."



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### 4. Peidong Yang to direct Kavli Energy NanoScience Institute

Beginning in January, Peidong Yang, Professor of Chemistry and the S. K. and Angela Chan Distinguished Professor of Energy, took over the directorship of the Kavli ENSI. The Kavli ENSI focuses on scientific discovery to foster clean, affordable energy at the nano scale.

"Peidong Yang has been instrumental to the success of the Kavli ENSI since its inception," said UC Berkeley Vice Chancellor for Research Randy Katz. "A world-class scientist with a prominent international profile, he has all the attributes of an outstanding leader and will be an excellent successor to Paul Alivisatos. I am thrilled that Peidong has agreed to lead the Kavli ENSI."

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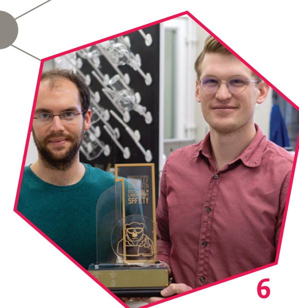
### 5. Alum John Adams re-elected chair of ACS board of directors

John E. Adams, *(Ph.D. '79, Chem)* has been re-elected chair of the board of directors of the American Chemical Society (ACS), the world's largest scientific society.

As chair of the board, Adams will preside over board and executive committee meetings, oversee the performance of the chief executive officer, appoint chairs and members of board committees and task forces, and ensure that strategic planning and evaluation of progress toward strategic goals occur, among other duties.



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### 6. Arnold Lab wins top Berkeley safety award

The winners of the 2018 Excellence in Laboratory Safety have been announced. The grand prize was awarded to the Arnold lab group in Chemistry, headed by Professor of Chemistry and Undergraduate Dean John Arnold. Lab safety coordinators and chemistry graduate students Michael Boreen and Trevor Lohrey were also acknowledged and accepted the award for the group in February. A total of 464 Berkeley labs were evaluated for safety practices.

Lohrey stated, "The way our group has dealt with lab safety has steadily evolved and improved over my five years as a graduate student. Thanks in large part to the efforts of both the College and University EH&S departments, implementing standard lab operating procedures along with a central chemical inventory system has made the process of training incoming students much more straightforward."

## Graduate and Undergraduate campaigns raise funds for diversity, inclusion and mentorship

Two student crowdfunding campaigns were launched this spring to raise money for student initiatives. The graduate student DEWI campaign committee raised money for diversity, equity, wellness and inclusion programs at the College. The committee also conducted several surveys to discover important issues that students felt needed a more supportive environment. The money will be used for seminars and events over the coming year.

The undergraduate committee focused their campaign on a mentorship program for aiding students in their search for post career roles after undergraduate school.

There will be an expansion of peer-to-peer student mentors, programs with alumni and professional affiliates, and a fund established to support career networking events.

## Drug sponge could minimize side effects of cancer treatment

New research from the lab of Nitash Balsara, the Charles W. Tobias Professor in Electrochemistry, reports that with the help of sponges inserted in the bloodstream to absorb excess drugs, doctors and scientists are hoping to prevent the dangerous side effects of toxic chemotherapy agents or even deliver higher doses to knock back tumors, like liver cancer, that don't respond to more benign treatments.

The "drug sponge" is an absorbent polymer coating a cylinder that is 3D printed to fit precisely in a vein that carries the blood flowing out of the target organ — the liver in liver cancer, for example. There, it would sop up any drug not absorbed by the tumor, preventing it from reaching and potentially poisoning other organs. The findings were published recently in *ACS Central Science*.



| | Gruppe I. $R^1O$ | Gruppe II. RO | Gruppe III. $R^1O^3$ | Gruppe IV. $RH^4$ $RO^7$ | Gruppe V. $RH^3$ $R^2O^5$ | Gruppe VI. $RH^3$ $RO^3$ | Gruppe VII. RH $R^2O^7$ | Gruppe VIII. — $RO^4$ |
|---|---|---|---|---|---|---|---|---|
| 1 | H = 1 | | | | | | | |
| 2 | Li = 7 | Be = 9.4 | B = 11 | C = 12 | N = 14 | O = 16 | F = 19 | |
| 3 | N = 23 | Mg = 24 | Al = 27.3 | Si = 28 | P = 31 | S = 32 | Cl = 35.5 | |
| 4 | K = 39 | Ca = 40 | — = 44 | Ti = 48 | V = 51 | Cr = 52 | Mn = 55 | Fe = 56 Co = 59 Ni = 60, Cu = 63. |
| 5 | (Cu = 63) | Zn = 65 | — = 68 | — = 72 | As = 75 | Se = 78 | Br = 80 | |
| 6 | Rb = 85 | Sr = 87 | ?Yt = 88 | Zr = 90 | Nb = 94 | Mo = 56 | — = 100 | Ru = 104, Rh = 104, Pd = 106, Ag = 104. |
| 7 | (Ag = 104) | Cd = 112 | In = 113 | Sn = 118 | Sb = 122 | Te = 125 | J = 127 | |
| 8 | Cs = 133 | Ba = 137 | ?Di = 138 | ?Ce = 140 | — | — | — | — — — — |
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| 10 | — | — | ?Er = 178 | ?La = 180 | Ta = 182 | W - 184 | — | Os = 195, Ir = 197, Pt = 198, Au = 199. |
| 11 | (Au = 199) | Hg = 200 | Tl = 204 | Pb = 207 | Bi = 208 | — | — | |
| 12 | — | — | — | Th = 231 | — | U = 240 | — | — — — — |

**Mendeleev's Periodic Table c. 1871**

## UN recognizes the Periodic Table's 150th anniversary

In 1869, Russian chemist Dimitri Mendeleev wrote out the known elements (there were 63 at the time) on cards and arranged them in columns and rows according to their chemical and physical properties, introducing the concept of the Periodic Table. In celebration of the 150th anniversary of his work, the United Nations has declared 2019 the "Year of the Periodic Table." UNESCO announced in their press release, "The Periodic Table of Chemical Elements is more than just a guide or catalogue of the entire known atoms in the universe; it is essentially a window on the universe, helping to expand our understanding of the world around us."

UC Berkeley faculty and alumni have long been involved in the discovery of elements on the Table. Starting with Ernest Lawrence's invention of the cyclotron in the 1930s, UC Berkeley researchers, including Nobel Laureate Glenn Seaborg, Darleane Hoffman, Albert Ghiorso, Matti Nurmia, Jim Harris, and Kari and Pirkko Eskola, were involved in the discovery of 16 elements between 1940 and 1974.

In 2016, the International Union of Pure and Applied Chemistry announced four more elements were to be added to the table. The Heavy Element Group at Lawrence Livermore National Laboratory, led by alumna and nuclear chemist Dawn Shaughnessy *(Ph.D. '00, Chem)*, worked with scientists in Russia and Japan on the newest elements' discovery.

## Alum Frances Arnold signs chair in Nobel tradition

Nobel Laureate Frances Arnold *(Ph.D. '85, ChemE)* carries on a fun Nobel tradition: signing the underside of the seat of one of the wooden chairs in the Nobel Museum Café in Stockholm. She co-signed her chair with fellow Chemistry Laureates George Smith and Gregory Winter. Then, settling in for an event at the museum, she chose to sit on the chair signed by the Dalai Lama, who won the Nobel Peace Prize in 1989. He signed his chair during a visit in 2011.

The tradition began in 2001. Felix Rosén, a museum guide, commented, "Any Nobel winner is allowed to leave their mark on a chair. The tradition is believed to have started with former U.S. President and philanthropist Bill Clinton, who has not won a Nobel Prize in any category. Attending the museum's opening in 2001, Clinton is said to have spontaneously signed and dated the bottom of a chair without being asked. We liked it and thought, 'Hey, let's make all the Nobel laureates do that.'"

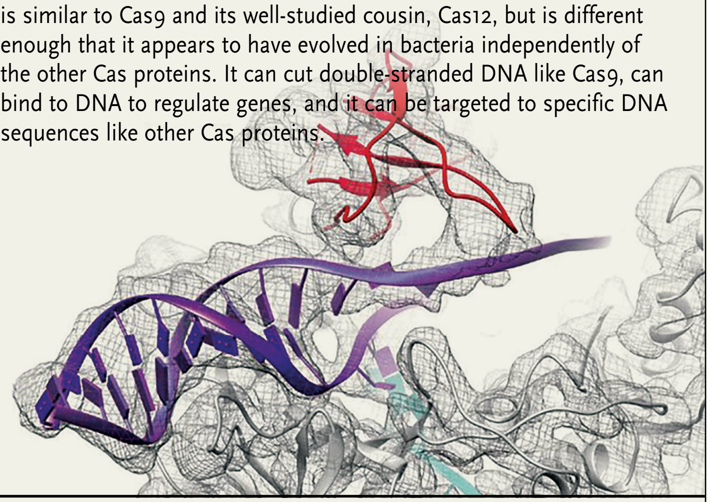
## Scientists find new and smaller CRISPR gene editor: CasX

In a mere seven years, Cas9 has shown itself to be a formidable gene editor, employed in humans, plants, animals and bacteria to quickly and accurately cut and splice DNA, transforming biology and opening new avenues for treating disease.

But a new kid on the block, CasX, may give Cas9 a run for its money. Discovered two years ago by UC Berkeley scientists Jill Banfield and Jennifer Doudna in some of the world's smallest bacteria, the protein is similar to Cas9, but quite a bit smaller: a big advantage if you're trying to deliver a gene editor into a cell.

But would it work outside its native bacteria?

According to a study published in *Nature,* CasX is, in fact, a potent and efficient gene editor in both bacteria and human cells. Its design is similar to Cas9 and its well-studied cousin, Cas12, but is different enough that it appears to have evolved in bacteria independently of the other Cas proteins. It can cut double-stranded DNA like Cas9, can bind to DNA to regulate genes, and it can be targeted to specific DNA sequences like other Cas proteins.



FRANCES ARNOLD

# From graduate student to Nobel Laureate


COURTESY FRANCES ARNOLD


MICHAEL BARNES

**Frances in front of Latimer Hall in the 1980s and 2019.**

BY MICHAEL BARNES

In the early 1980s, the lab of College biomolecular engineer Harvey Blanch brought together an adventurous group of young researchers and launched them on long and successful careers. One of them, Caltech professor Frances Arnold, has won the 2018 Nobel Prize in Chemistry for her discoveries in the directed evolution of enzymes. Arnold is the fifth woman to win the Nobel Prize in Chemistry since it was first awarded in 1901.

Arnold received her chemical engineering Ph.D. in 1985 at UC Berkeley. She went on to postdoctoral research with Ignacio "Nacho" Tinoco for one year and then six months at Caltech, starting her academic career there in 1987. While at Caltech, she has developed techniques for the directed evolution of enzymes, the achievement that won her the Nobel. But the groundwork for her later success was nurtured in the early heady days of genetic engineering here at the College of Chemistry in the lab of Harvey Blanch.

At the time, along with a handful of academic biochemical engineers at Caltech, MIT, Cornell, and Purdue, Blanch was exploring the possibilities of recombinant DNA technology. He developed bioreactor techniques for growing hybridomas, genetically engineered mammalian cells that produced monoclonal antibodies, which are now the basis for several important drugs that target human cancer cells.

Says Blanch, "It was obvious that recombinant DNA had tremendous potential. As a result, my lab attracted a terrific group of really sharp students, who have all gone on to have successful careers in academia and

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COURTESY FRANCES ARNOLD

**Frances after she has received her Nobel Prize and in her lab in the 1980s at Berkeley.**

industry. One of those students with exceptional drive and ability was Frances Arnold, who arrived in the winter of 1981." Once in Blanch's lab, Arnold got to work on affinity chromatography, a new separations process that could recover biochemicals from extremely dilute solutions.

Jeff Reimer, Professor and Chair of Chemical and Biomolecular Engineering, recalls when he first met Arnold. "Frances took her qualifying exam on October 7, 1982. I had just celebrated my 28th birthday. I showed up at UC Berkeley on Labor Day weekend that year, and Frances' exam was the first one of my career (other than my own). I had not met her prior to the exam, nor knew anything about her, or her work. I am not sure, but I think I was placed on her committee because someone was sick. I do recall it was pretty last minute."

He continues, "Before her exam started one of the committee members said something to the effect that this was going to be the easiest exam, ever. As most junior professors would, I took offense at this notion and grilled Frances on just about every sentence she spoke. And she was brilliant."

In 1982 Arnold mentored two undergraduate students, Matt Croughan *(B.S. '83)* and Jeff Chalmers *(B.S. '83)*, who joined the lab to conduct honors research with her. They learned to grow cell cultures with the help of a senior graduate student, William Miller *(Ph.D. '87, ChemE)*, who had come to do his Ph.D. after eight years' industry experience. At the time, he was perfecting the environment inside bioreactors to keep mammalian cell lines flourishing. These cells were far more difficult to grow than the simpler yeast and bacterial cells that produced earlier generations of biochemicals, from ethanol to antibiotics.

Chalmers and Croughan were co-authors with Arnold on a seminal 1985 paper on the rational approach to the scale-up of affinity chromatography. Affinity chromatography was a new concept at the time. Croughan relied on what he learned in ChemE 162 (Process Dynamics and Control) taught by Professor of Chemical Engineering Alan Foss to guide him in the research.

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In 1982 this tight-knit group was joined by another ChemE graduate student, Linda Griffith, who wrote her 1988 Ph.D. thesis on hollow fiber bioreactors. Says Griffith, "My lab desk was right next to Frances. She had incredibly high standards, and all the best undergrads wanted to work with her. She was very good at motivating people, tough but generous. She threw fabulous dinner parties—I'll never forget the braised apricots. Frances loved talking with and learning from other people."

Doug Clark, G.N. Lewis Professor and dean of the College, remembers meeting Arnold for the first time. Clark says, "I was attending an AIChE meeting in Chicago in 1985. I was still at Cornell, and Harvey Blanch was trying to recruit me to come to Berkeley. He suggested I meet Frances. She impressed me right away. And although hindsight is 20/20, I like to think I could see greatness in her then."

He continues, "I was incredibly impressed with her 1993 paper on engineering enzymes that introduced the world to her techniques for directed evolution. At the time, many scientists were struggling to use rational design techniques to create new enzymes and other proteins. Frances told them they didn't need to understand the exact structure of the enzyme target, they could just let evolution design it for them. Her solution was both simple and elegant. I said to myself, 'Why didn't I think of that?'"



The techniques Arnold launched are used widely today in industry, from making the enzymes used in laundry detergents to biofuels and pharmaceuticals. Directed evolution can replace hazardous chemicals and expensive catalysts with green chemistry approaches that use enzymes in mild conditions.

© NOBEL MEDIA AB 2018/PHOTO: ALEXANDER MAHMOUD

Arnold has remained at Caltech since she joined the faculty there in 1987. She became a full professor in 1996, three years after her ground breaking paper. The accolades began flowing soon after. In 2000, she was elected to the National Academy of Engineering, becoming one-half of the only father-daughter pair in the Academy with her father, nuclear engineer William Howard Arnold Jr.

She was elected to the National Academy of Medicine in 2004 and the National Academy of Sciences in 2008, making her the first woman to be elected to all three of the National Academies. She is also the first

© NOBEL MEDIA AB 2018/PHOTO: DAN LEPP

woman to receive the Charles Stark Draper Prize from the NAE, in 2011.

She currently holds 61 US patents and has cofounded three companies: Gevo, which is utilizing yeasts to make isobutanol as a replacement for ethanol in fuel production; Provivi, focused on rethinking pest control by using natural pheromones for more sustainable food production, and a new startup Aralez Bio using engineered enzymes to make sustainable products.

And on Dec. 10, 2018, the anniversary of Alfred Nobel's death, Frances Arnold was handed her Nobel medal by King Carl XVI Gustaf of Sweden. She continues to inspire us all.

# *Frances Arnold's thoughts on winning the Nobel Prize*

***Q:* Where were you when you got the news you had won the Nobel prize?**

*A:* I was in deep sleep in a Dallas hotel room having arrived at midnight to give a lecture the next day. The phone rang at 4am. I was worried that it was some emergency at home. Then I saw that the telephone number was from Europe and I thought maybe I had better answer it.

***Q:* What turned you on to biotechnology?**

I studied mechanical engineering at Princeton and worked on solar energy after graduation. But the industry's prospects changed for the worse in the early 1980s and I decided to do my Ph.D. in chemical engineering at the University of California, Berkeley. I had initially intended to work on biofuels but I stumbled on this new field of biotechnology.

***Q:* Your Nobel prize was awarded for the "directed evolution of enzymes". What's that?**

It is basically breeding, similar to mating cats or dogs to bring out desired traits, but at the level of molecules. The aim is to create new and better biological material in the form of enzymes, which are proteins that catalyze chemical reactions. And this allows us to use greener biological manufacturing processes to make the fuels, chemicals and materials we use in our daily lives.

***Q:* Some people find it remarkable that there are two female winners this year of Nobel prizes because it is usually all men.**

It is remarkable – and wonderful. But also not surprising because there are women doing fabulous physics and chemistry. I predict this is the beginning of a steady stream.

—Excerpt from *The Guardian,* "Frances Arnold: 'To Expect a Nobel Prize is rather silly'" | Oct 21, 2018

# Advisory Board members Herbert Hooper and Alan Mendelson discuss the Berkeley Catalyst Fund

BY MARGE D'WYLDE




## HERBERT HOOPER

After Herbert Hooper *(Ph.D. '90, ChemE)* graduated from UC Berkeley, he began his career as the product and business development manager at Air Products and Chemicals. He joined Ampersand Capital in 2002, initially as an entrepreneur, eventually becoming a managing partner. Ampersand is focused exclusively on growth equity investments in lower middle market healthcare companies.

Hooper notes, "Air Products and Chemicals was a great company to work for, but it was too large for me. I had a very successful experience there but realized it wasn't the right environment. I wanted something smaller – more impactful – so I cofounded Aclara, my first startup, in 1993. The company's focus was on developing replaceable gels for microchannel DNA electrophoresis. I learned several important lessons from that initial startup. Most importantly, I learned you really need a mentor when you are getting started."

Hooper initially had to go the self-educated route in the startup world. During his years in graduate school, the College of Chemistry did not include an entrepreneurial focus. Private universities like Stanford and MIT were starting to explode as incubators for science and technology at about that time, because startups were more favored at private institutions, being seen as a way to raise funds for the campuses. UC Berkeley, as a public institution, got a later start. Of the roughly 1,300 startups that have spun out of University of California research since 1968, three-quarters have been launched in the last 15 years.

Hooper continues, "When Rich Mathies became dean in 2008, there was a change of focus at the College. Mathies was very entrepreneurial and wanted to figure out how to make a chemistry investment fund work at UC Berkeley. Mathies laid the groundwork for BCF, and Dean Douglas Clark helped make it a reality. BCF is unique in a couple of ways. First, it is focused on the chemical sciences and, second, it looks to invest in research coming out of the College principally via the faculty, students, postdocs, and alumni. Another positive is that the fund can help create awareness at the College about company formation and creation.

"The College's advisory board sees a lot of potential with BCF. Currently it is too

## Berkeley Catalyst Fund

The Berkeley Catalyst Fund (BCF) is in its second year as an investment resource for entrepreneurial startups from the College of Chemistry. The fund is primarily focused on startups run by faculty, students, postdocs and alumni. BCF invests in new companies; long-term it will channel investment returns back to the College of Chemistry via the UC Berkeley Foundation.

BCF was established in partnership with UC Berkeley and the UC Berkeley Foundation and is managed by Laura Smoliar *(Ph.D. '95, Chem)*, Ted Hou *(Ph.D. '95. Chem)* and Drew Lanza *(MBA '87, Harvard)*. Smoliar and Hou first met as graduate students in the lab of Nobel Laureate Yuan T. Lee. With the guidance of the team's commercial experience and industry knowledge, the College is creating a unique entrepreneurial ecosystem focused on the chemical sciences.

The sector focus of BCF is biopharma, agriculture, medical device, clean air, clean water, energy storage, and sensors. The stage is primarily Seed and Series A.

early to say how well it will do. We need five to ten years and two to three winners to really get it off the ground. That said, BCF can help expose more students to how the startup process works."

When asked about the future of BCF, Hooper continues, "BCF is a very innovative concept that can benefit the College, faculty and students at multiple levels of involvement. It will be very exciting to see how it grows over time."

### ALAN MENDELSON


Alan Mendelson and Laura Smoliar

Alan Mendelson *(B.A. '69, PolSci; J.D. '73, Harvard)* represents emerging and public growth companies, primarily in the life sciences. He has handled a variety of major business transactions, including public offerings, venture capital financing, and mergers and acquisitions. He explains, "It was due to a lucky break that I started working in the life science area. As a young attorney in my first job, I happened to be there when the partner came down the hallway one day looking for someone to establish a new life science company. That company turned out to be Amgen. It took about eight to nine months to initially get it established.

"The first ten years of my practice I worked on all but one of Amgen's major transactions. Because of Amgen's success, it helped with referrals, and I started representing other biotech companies in Silicon Valley such as Acuson, which was eventually sold to Siemens, and Intuitive Surgical, specializing in robotic surgical devices."

Besides helping startups grow into major biotech organizations, Mendelson also serves on a number of important boards, including the College of Chemistry's advisory board. He comments, "Being on boards is an interesting extension of the work I do. The first board I sat on was the National Kidney Foundation. Amgen's first product, Epogen, was for the treatment of anemia associated with chronic kidney failure. This drug changed people's lives, as they could spend less time in dialysis and more time leading normal lives. It was a pleasure to sit on that board, see the progress being made, and how a drug could make such a difference."

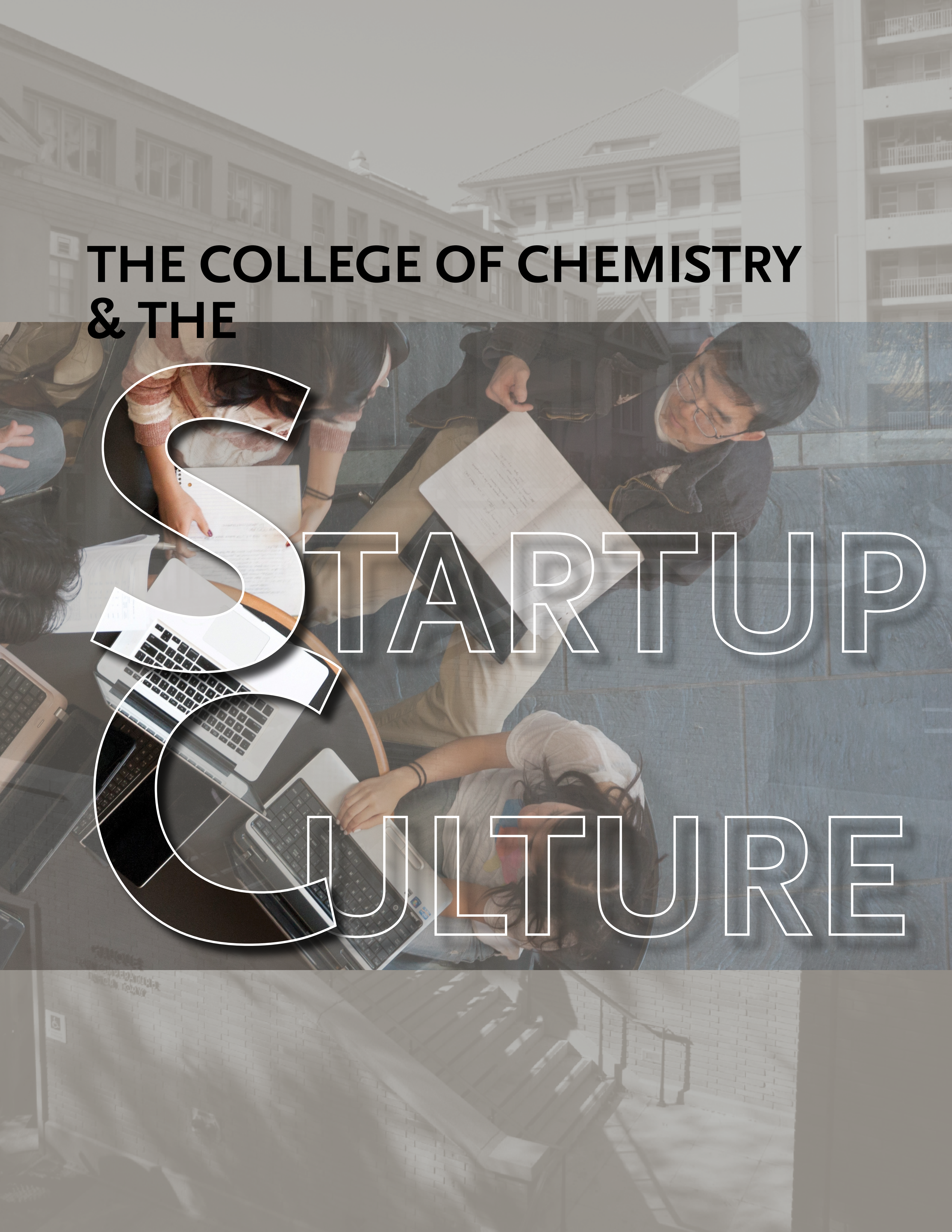
Mendelson joined the board of the College in 2007 at the suggestion of Michael Marletta who was Chair of Chemistry at the time. Once on the board, Mendelson began discussing development of the startup culture with then dean Rich Mathies. "Rich is a very entrepreneurial guy and understood the challenge of trying to raise seed capital for startups. There were people interested in investing in the College — but who also wanted to support commercial opportunities. Rich wasn't sure initially how to make that happen."

Mendelson was asked to sit on a task force to look at better ways to make full use of the University's patent portfolio. There he met, and worked with, Janet Napolitano, the president of the University of California. He credits her with really kick-starting the entrepreneurial culture on campus. The University's incubators and BCF are outgrowths from that period.

He recalls, "It took several years and a lot of hard work for Laura, Ted and Drew to get BCF up and running. I was approached to support them through their fundraising arm, the Berkeley Catalyst Philanthropic Fund. At the time, this was a unique way to help create the initial venture fund, as it was an opportunity to donate to UC Berkeley and have it tied to the venture capital investment fund. They were responsible for creating the first program of its kind at UC Berkeley."

Mendelson continues, "I think the fund is doing fine. They are working on getting more visibility for research endeavors in the College, and more researchers are learning that the fund exists. The question is, what should we do now to expand community and public awareness of this very unique and important fund? It's exciting to see the startup culture taking hold at the College. I hope to see a day when students are getting recommendations for their startup skills like they do for research skills today."

# THE COLLEGE OF CHEMISTRY & THE STARTUP CULTURE



BY MARGE D'WYLDE

> "As innovation and entrepreneurship becomes an even greater force in economic growth, U.S. universities and colleges will be in the vanguard of discovering innovation and nurturing entrepreneurs that can create products, services, economic value, and high-quality jobs."
> —US DEPARTMENT OF COMMERCE, 2013

The headline in a recent Dow Jones editorial called out, "3 technologies that could create trillion-dollar markets over the next decade." A bold headline indeed and then you read the article and realize that research in the three technologies — CRISPR, quantum theory, and materials science — are being led by researchers at UC Berkeley's College of Chemistry.

The numbers are heady. According to a 2018 report from the National Science Board, U.S. research and development performance totaled nearly $500 billion in 2015. The business sector accounted for more than two-thirds of the total. Academia and the federal government were the next largest performers at $50 billion. Chemistry research (including chemistry, biochemistry, and chemical engineering) is the largest single science sector funded, because it tends to produce the largest return on investment.

For academic researchers and their students, in order to get to those "trillion-dollar markets," both time and money are needed to make their scientific breakthroughs, and then turn them into real-world products. As the cost of science research escalates (everything costs more today, from the support of Ph.D. and postdoctoral students; to state-of-the-art labs; to clinical trials), university faculty and students are looking to a more flexible range of funding, which now includes government, corporate, and private venture capital investment. They are also becoming more likely to create startups, so as to maintain control of their research and patents if the research appears promising.

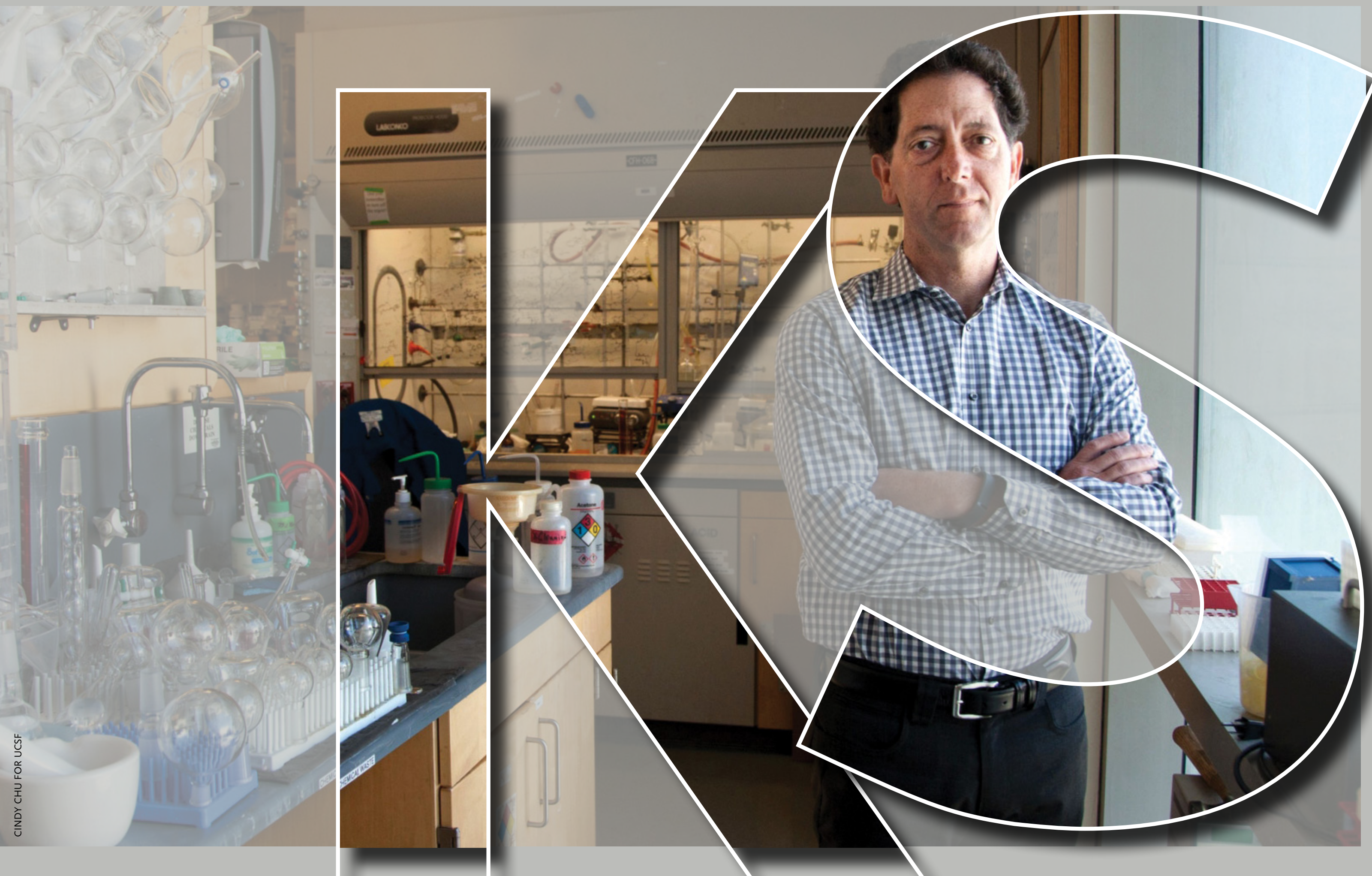
According to Jeffrey Reimer, Chair of Chemical and Biomolecular Engineering (CBE), "There is definite synergy between startups and the Ph.D. research happening at the College. In recent years, a number of startups have come out of both the chemistry and CBE departments." Some recent companies include Mosaic Materials, cofounded by Professor of Chemistry and CBE Jeff Long, Thomas McDonald *(Ph.D. '15, Chem)*, and Steven Kaye *(Ph.D. '07, Chem)* for developing MOFs for the oil and gas industry; Atom Computing, cofounded by Jonathan King *(Ph.D. '12, ChemE)* and Benjamin Bloom *(Ph.D. '14, CU Boulder)*, focused on building scalable quantum computers; and Ripple Foods, cofounded by Neil Renninger *(Ph.D. ChemE, '02)*, who did his postdoctoral work in the lab of synthetic pioneer and CBE professor Jay Keasling, with Adam Lowry *(B.S.'96; Stanford)*. They have developed a plant-based milk product from peas.

UC Berkeley houses a series of incubators and venture funds geared toward the University's support of students and faculty. The University has long maintained a patent program, but its entry into the startup culture began around 1968. It is now considered one of the best university incubators for student startups, with a solid track record of success. UC Berkeley incubators can offer as much as $100K to give student startups a much-needed leg up in the beginning of their development, along with ongoing mentorship from the faculty overseeing their research.

Matthew Francis, Chair of the Department of Chemistry, notes, "Students have become more 'mission oriented' in the last five years. However, along with creating companies, we need them to develop a solid and ethical framework for their research. There are legal and environmental issues that should be contemplated at the beginning of any new venture. The College now offers the opportunity to take business courses as part of the degree process, to learn more about both the business and ethics behind running a startup."

We wanted to know what it's currently like to be involved in the College's startup culture. So, we asked four of our faculty and alumni to share some of their experiences with us. Kevan Shokat *(Ph.D. '91, Chem)*, a professor of chemistry and cellular and molecular pharmacology, discusses some of the leaps needed to get research from the lab to market. Nitash Balsara, a professor of CBE and a senior scientist at Berkeley Lab, shares insights about creating startups based on scientific breakthroughs made by Ph.D. students and postdocs in his lab. David Schaffer, a faculty member in the Departments of CBE and Bioengineering as well as the Helen Wills Neuroscience Institute, discusses how ground-breaking research has been translated from his lab to a series of startups. And Martin Mulvihill *(Ph.D. '09, Chem)*, who helped establish the Berkeley Center for Green Chemistry, discusses his work that is changing the way people buy chemical products, focusing on funding promising green startups.

There is a revolution happening at Berkeley's College of Chemistry. With ground-breaking research being explored, and an increased ability to help move discoveries to market, the future is looking bright.



CINDY CHU FOR UCSF

# KEVAN SHOKAT: DISCOVERY SCIENCE AND THE PATH TO CREATING NEW DRUGS

Kevan Shokat *(Ph.D. '91, Chem)* is professor and vice-chair of cellular and molecular pharmacology at UCSF, professor of chemistry in the Berkeley College of Chemistry, and a Howard Hughes Medical Institute investigator. He is a pioneer in the field of chemical genetics, focusing on the development of chemical methods to decipher the role of individual kinases and their cellular signaling networks.

After completing his Ph.D. in chemistry at UC Berkeley with advisor and then-faculty member Peter Schultz (who now leads Scripps Research), Shokat went to Stanford for postdoctoral research in immunology. It was there he first suggested that, rather than modify cell genetic structures to manipulate kinases, one could design small molecules that could block kinase signal paths directly. He states, "When I got to Stanford I threw myself into immunology, debating the fundamental questions of the day. I went from looking at molecules to cells."

"Once you make a discovery — you've opened a door. Then it becomes a question of how to raise the funds to make it available to the public. If you plan to start a company, you need a really good team." —KEVAN SHOKAT, 2019

In 1994 he took his first faculty position, at Princeton. In a 1997 paper published in the *Proceedings of the National Academy of Sciences,* Shokat and three collaborators reported ground-breaking research that showed that complex proximal signaling cascades, controlled by cellular tyrosine kinases, could potentially be blocked using genetically programmed molecules.

He returned to the Bay Area in 1999, joining the faculties of both UCSF and UC Berkeley. Current research in his lab focuses on discovery of new chemical-based tools to decipher cellular signaling networks, with an emphasis on protein kinases and more recently, GTPases. The analysis of signal transduction pathways has proven challenging using the traditional tools of biochemistry, genetics, and chemistry. His lab has solved this fundamental problem for the largest family of enzymes in the human genome, protein kinases, by the development of a strategy based on a combination of protein engineering and organic synthesis.

In addition to pursuing cutting-edge research, Shokat is also committed to bringing new effective medicines to patients. He has cofounded three biotechnology companies that have taken multiple drugs through varied stages of clinical trials (including drug approval of Duvelisib in 2018), with more in development. The companies include Intellikine, established in 2007; Araxes Pharma, founded in 2012; and eFFECTOR Therapeutics, started in 2013.

Intellikine was established to focus on the development of small-molecule drugs that would specifically fight various aggressive cancers. Four years after its founding, Takeda Pharmaceuticals of Japan acquired Intellikine, boosting the odds that discoveries from the Shokat lab could make it into approved therapies that would reach patients.

Shokat notes, "It was hard to raise funds for Intellikine. Finding money is a constantly moving target in a capital environment. The early series funding was a real lesson in how to work with venture capitalists and the stock market. No matter your fundraising approach, they all have challenges. In the academic environment, you can have more control over the money you raise."

After Intellikine was sold, Shokat and Troy Wilson *(Ph.D. '96, Biochem; J.D., NYU),* who had been CEO of Intellikine, cofounded Araxes Pharma, based on additional pioneering research from the Shokat lab that uses small-molecule, covalent inhibitor approaches to develop safer, more effective ways to drug the KRAS mutant genes that cause many aggressive cancers.

According to Shokat, "Right now this is probably the mainstream approach for cancer treatment. Twenty years ago, nobody thought you could make a drug specific and potent enough to inhibit the kinases. Historically the term for this kind of discovery was 'basic science,' but I like to think of it as 'discovery science'!"

He continues, "It's very hard to plan to 'discover a drug.' Pharma companies have billions of dollars to invest in new drugs every year. Currently, however, there are only about 21 drugs a year making it through the FDA process to market — out of hundreds tested. It's helpful to work inside a university research environment because you are part of a team of researchers who can support each other through the ups and downs of the process."

In 2013, Shokat and his UCSF colleague Davide Ruggero cofounded San Diego–based eFFECTOR Therapeutics (eFFECTOR) along with CEO Steve Worland *(Ph.D. '84, Chem),* focusing on the development of selective translation regulators for the treatment of cancer. To date, the company has raised multiple rounds of series funds to test drugs through FDA-approved trials. eFFECTOR recently established a partnership with Merck to evaluate the combination of eFFECTOR and Merck therapies for the treatment of patients with metastatic triple negative breast cancer.

"Once you make a discovery — you've opened a door," Shokat comments. "Then it becomes a question of how to raise the funds to make it available to the public. If you plan to start a company, you need a really good team — including members with serious business acumen. It's also special that the CEOs of these companies both received their Ph.D.s in chemistry from UC Berkeley."

RICK CHAPMAN, PIONEERSOFCLEANENERGY.ORG.

# NITASH BALSARA: GRADUATES, POSTDOCS, AND THE STARTUP CULTURE

Nitash Balsara, the Charles W. Tobias Professor in Electrochemistry and a senior scientist at Berkeley Lab, is an internationally recognized expert in polymer materials who joined the senior faculty in the College of Chemistry in 2000. Among other innovations, his research team is responsible for the discovery of nanostructured polymer electrolyte technology, a solid electrolyte designed for use in rechargeable lithium batteries.

Balsara is no stranger to bringing startups from research to market, companies that include his students as key collaborators. He cofounded Seeo in 2006 with former graduate student Hany Eitouni *(Ph.D. '04, ChemE)* and former postdoctoral researcher Mohit Singh *(2004-'06, ChemE)*. At Seeo, what began as research to create an electro-responsive polymer for an artificial muscle became the basis for a solid dry polymer for an electrolyte battery.

In 2015, Seeo sold its technology to Bosch, a German multinational, for an undisclosed amount. It only took 12 years to progress from the original research to a functional lithium-ion battery that is safer to use than the ones currently on the market. Not only did the founders of Seeo benefit financially from this discovery, so did the University of California, which co-holds some of the patents used in the battery design. Elsie Quaite-Randall, Berkeley Lab's chief technology transfer officer, notes, "It takes time for the Lab's breakthrough technologies to reach this stage. It's exciting to see the progression from fundamental science, to startup technology, to sought-after opportunity."

Eitouni was Balsara's first Berkeley graduate student. "Nitash was a polymer guy. I was the first student in his career to work on electrochemistry," Eitouni says. "He has a good ability to take a problem and break it down to fundamental pursuits. His charisma is contagious. He's a lot of fun to work with."

Balsara states, "In the 1980s, there were no startups on college campuses. We went to industry to develop products. Because of the increasing costs, it appears that large companies have become more risk adverse, and that kind of funding has dried up. There doesn't seem to be the motivation now for established companies to develop new ideas, and startups have filled this void.

"Students are looking for startups today as part of their college experience. It's really a people thing. Startups are small and comforting, akin to research groups. Also, the lead person in the startup can now be a student. The limiting steps to success are not the money, but the good ideas and execution. We have remarkable students here at Berkeley who are ambitious, talented, and grounded. They want to be successful. Undergrads are also coming with knowledge and a keen interest in research."

In a second startup, Balsara teamed up with Joseph DeSimone of 3D Carbon and another former graduate student, Alex Teran *(Ph.D. '13, ChemE)*, to form Blue Current in 2014. Blue Current is now led by Kevin Wujick *(Ph.D. '16, ChemE)*, another former graduate student, who left the battery group at Ford to join the team. This group is also working on new lithium battery research that will take the risk out of batteries catching fire. When asked about the current status of the company Balsara states, "We are at a very interesting point in time at Blue Current."

For Balsara, the holy grail of battery research is developing one that will last forever. "Lithium ion batteries are already a miracle," he says. "You can recharge it over hundreds of cycles. The problem about longevity is degradation of the electrolytes. The focus is to make it more stable, but then the ions don't go fast enough. I think we will see a time fairly soon when a battery lasting 20 years is not a challenge. Lasting for a century will be next."

In a new project, Balsara has teamed up with Steven Hetts, a physician and chief of interventional neuroradiology at UCSF, to work on a drug sponge to lessen the side effects of chemotherapy. Today, some chemo treatments are limited to the amount a heart can take without being either damaged or stopped by chemo toxicity. Hetts knew that chemical engineers are keenly interested in removing pollutants from the environment – and chemotherapy can be thought of as a major "pollutant." Hetts came to Balsara with the idea that if they could "mop up" chemotherapy (the way chemical engineers determine how to mop up chemical spills) right after it transfers through the liver, this could stop the chemical from going straight on to a patient's heart and thus permit a more effective dose.

When she read about this concept of a new type of medical drug-capture device, Xi Chelsea Chen *(2012-'16, ChemE)*, a former postdoc in Balsara's group, had a realization. She had been investigating polymer membranes which help current to flow in a fuel cell that converts hydrogen and oxygen into electricity. She realized that the benefit from the identical property in the fuel-cell material – which allows it to attract and capture certain molecules by their electric charge, while allowing other types of molecules to flow through – could be translated conceptually to the drug sponge.

"Originally, we used this material for transporting protons in a fuel cell," Chen said. "I was really excited when I found this could be used for chemotherapy — this was branching out in a totally different direction."

Balsara called on his long-time collaborator Joseph DeSimone, at 3D Carbon, to turn the research into a 3D printed prototype device for testing. Says Balsara, "We have been working on this research for four years now and, thanks to 3D printing, have produced working prototypes." The team is currently in the midst of experiments to determine how much drug is absorbed when the device is implemented.

Balsara states, "We are doing research in some very exciting fields here at Berkeley. One of the reasons I work with startups is because my students are interested in it. I think of it as a component of their education. In addition to students having compelling ideas for technology that can generate a startup, I also think it's a human endeavor. I value the opportunity to contribute to their advancement, well after they graduate."

> "What has surprised me is the positive impact that startups have had on research on campus. It has made me a better academic. I feel we are doing more interesting work than ten years ago."
> —NITASH BALSARA , 2019

MARK JOSEPH HANSON



# DAVID SCHAFFER: PUTTING RESEARCH TO WORK FOR THE PUBLIC GOOD

Professor David Schaffer is a luminary in the chemical engineering field. He is the Hubbard Howe Jr. Distinguished Professor of Biochemical Engineering in the CBE department of the College of Chemistry. He is also a member of the faculties of Bioengineering and the Helen Wills Neuroscience Institute, and director of the Berkeley Stem Cell Center. Schaffer has accumulated more than 20 years of research experience in this span of disciplines, developing specific expertise in the molecular engineering of biologic therapeutics, resulting in over 50 patents filed to date.

His first introduction to bioresearch was during his undergraduate studies at Stanford. "I was working on an early recombinant DNA research project in the lab of Charles Goochee, which resulted in my first published author-

> "The campus really recognizes that translating research to clinical use is central to its mission to have an impact on society. It's also a potential source of funds for the campus." —DAVID SCHAFFER , 2015

ship in 1994. It was a great experience because we did the research in conjunction with Genentech."

He went on to earn his Ph.D. in chemical engineering at MIT (1993-98). While there, he became interested in epidermal growth factor receptor-mediated gene delivery. In a recent interview he noted, "Gene therapy was a new concept at the time. The idea of using DNA as a medicine was exciting." His time at MIT was followed by a year of postdoctoral research at the Salk Institute with Fred Gage.

Armed with a new view on the use of chemical engineering principles in working with stem cells, Schaffer joined the CBE faculty at Berkeley in 1999. His research is focused on engineering stem cell and gene therapeutic approaches for neuroregeneration. His research includes the mechanistic investigation of stem cell control, as well as molecular evolution and the engineering of viral gene delivery vehicles. One of his major research outcomes has been the development of delivery vehicles based on the adeno-associated virus, an approach which has achieved success in clinical trials for several rare diseases, including hemophilia.

Schaffer has developed exceptional skill in the art of successful translational science, guiding his lab's research into beneficial applications. In an astoundingly short time, he has created three startups that create a bridge from his lab's research to the marketplace. He observes, "My goal is to have a positive impact on health. These companies can create and run trials that allow the research to be useful."

In 2010, he co-founded his first company, Valitor, with fellow UC Berkeley professor Kevin Healy, to develop a new generation of biotechnology drugs to precisely target diseased tissue. Two years later, he co-founded 4D Molecular Therapeutics (4DMT) with David Kirn *(B.A. '85, Physiology; M.D. '90, UCSF)*, Theresa Janke *(B.S., '96, UCSB)*, and Melissa Kotterman *(Ph.D. '13, ChemE)*. Last fall, 4DMT raised $90M in Series B financing. The company intends to use the funds to advance its Therapeutic Vector Evolution platform and a pipeline of next-generation AAV gene therapeutics. Kirn, who is Chairman and CEO of 4DMT, says, "The Therapeutic Vector Evolution platform has the potential to overcome the delivery and immunology challenges that currently face the field of gene therapy. The platform could ultimately unlock the full potential of gene therapy."

Schaffer met Kirn during an event at QB3, the UC Berkeley hub for innovation and entrepreneurship in the life sciences. Getting to know each other, they determined they had a lot in common. Kirn, a biotechnology entrepreneur and physician-scientist, had already generated a number of startups along with doing consulting on clinical development programs. Schaffer comments, "Working with David has been wonderful. I've been able to come up-to-speed on the business side of developing startups along with working with him on clinical trials."

Melissa Kotterman, 4DMT's first hire and current V.P. of Discovery and Engineering, had prior experience with Schaffer as a graduate student in his lab. She had worked on the company's gene therapy technology while in the Schaffer group. She says, "I think it is very rare for a graduate student to have a direct opportunity, so quickly out of graduate school, to see their research really be translated, able to help patients in a really, really, rapid way."

In 2016, Schaffer, Kirn, Janke, Kotterman and others created a third startup, IGNITE Immunotherapy. IGNITE's focus is to further the discovery, engineering, and optimization of proprietary oncolytic vaccine products for IV administration. IGNITE has established a promising partnership with Pfizer in the area of intravenous oncolytic cancer vaccines. The companies are currently working together on cancer immunotherapy combination studies.

In our recent interview, Schaffer discussed how he manages both his lab and multiple startups: "My lab is always going to be my priority, but that said, being able to work with companies has really benefited the lab in a couple of ways. It has taught me about the next steps of drug development, and that has helped the way that I shape the research in our lab. And it has also really motivated the people in the lab — I can say that, for the first time, something a graduate student created a few years ago is in a human clinical trial."

When asked what advice he has for up-and-coming young entrepreneurial scientists, he comments, "It's important to learn across fields. You need to figure out how to 'speak' both science and business. You can consider a multi-disciplinary approach, which could mean taking classes outside your major or doing research across fields. UC Berkeley recognizes the need for such training and now offers simultaneous degree programs that allow students to study both science and business, but nothing can replace the hands-on experience of starting a new company."

MICHAEL BARNES

# MARTIN MULVIHILL: THE GREEN ENTREPRENEUR

Martin Mulvihill *(Ph.D. '09, Chem)* is co-founder of Safer Made, a seed-stage venture capital fund he started with Adrian Horotan in 2016, focusing on green chemistry startups. Safer Made invests in companies and technologies that reduce people's exposure to toxic chemicals. Mulvihill has also directly developed technologies that help provide access to clean drinking water via the detection of arsenic.

In a recent editorial on CALmatters, Mulvihill and co-author Gina Solomon proclaimed, "Healthy chemistry is California's future. Consumers are demanding products that are safe for families and for the environment. Retailers and product manufacturers are asking their suppliers tough questions about chemical ingredients."

> "Healthy chemistry is California's future. Consumers are demanding products that are safe for families and for the environment."
> —MARTIN MULVIHILL, 2019

Mulvihill has always followed his passion, although it wasn't clear at first that it was chemistry. "I hated chemistry in high school," he says with energy. "It wasn't until I went to Reed College that I discovered I really loved chemistry! I have alumna Maggie Geselbracht *(Ph.D. '91, Chem)* to thank. She introduced me to the magic of inorganic chemistry. What I found compelling was that basic learning and research is really fun. It's a way of seeing the world with a molecular set of rules that lends insight into our day-to-day lives. To not know about chemistry is like seeing coffee, but not the caffeine."

He decided to pursue his Ph.D. at Berkeley with professors of chemistry John Arnold and Peidong Yang. He notes, "I was very fortunate to have them as advisors. John provided me freedom and support, while Peidong gave me structure and opportunity.

"A major opportunity that opened for me at Berkeley was my introduction to green chemistry. I had invited John Warner, considered the father of the green chemistry movement, to come and lecture. We went to dinner afterwards with professors Rich Mathies (who was dean at the time), Matt Francis, and John Arnold. The UC Berkeley green chemistry program was born that evening. Berkeley was the first 'Tier 1' university in the country to start such a program."

In 2010, the Center for Green Chemistry at Berkeley became a reality, with a focus on education. Mulvihill recalls, "Originally we called the program 'Chemists for Peace.' We even had cups made with blended peace and atom symbols. There were four or five members," he laughs. "The name just wasn't capturing the purpose. In a fundamental shift of focus, we changed it to the 'Berkeley Center for Green Chemistry' (BCGC) because it was more accessible. It was still the same concept: connecting chemistry to society, inspired by John Warner's principles of preventing pollution, designing safer chemicals and using better energy management."

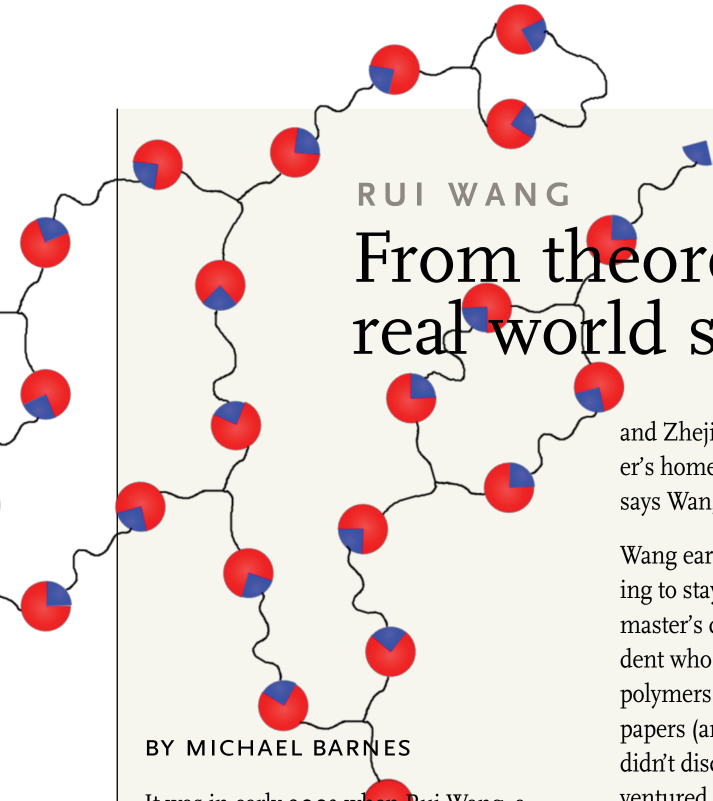
He continues, "I learned some very important things about raising funds while working on writing grants for the BCGC. For one, early grants are intended to be catalysts. Generally, the expectation is that the dollars you receive will generate more dollars toward a project. You often need to find matching funds from other sources, so you wind up writing multiple grants to fund one project or program."

Thus, it wasn't much of a leap for Mulvihill to go from executive director of the green chemistry program at Berkeley to founding Safer Made in order to give fledgling green startups their first funds and make a wider commercial impact. Says Mulvihill, "The proof is in the direction the markets are moving. Consumer brands that differentiate as green are winning in the marketplace, and not in small numbers. If you take the organic food business as an example, over the last ten years there have been $42 billion in acquisitions of organic startups, much of it by mainstream companies."

Consumer trends are driving change in how chemistry research is working with the marketplace. Mulvihill notes that some key trends currently include:

- **CLEAN PRODUCT LABELS** — consumers are now preferentially buying products that have the fewest items listed and are "pronounceable."
- **DIFFERENTIATED PACKAGING** — packages that are compostable and truly recyclable are winning the war for shelf space in stores.
- **BACTERIA** — about 100 trillion good bacteria live in and on our bodies. Many of these bacteria reside in our gut, helping our bodies break down food and absorb nutrients. Consumers are looking for new and better ways to live in harmony with bacteria and thrive.

Mulvihill's message is an exciting one. Future-thinking chemistry and smart product design can really change what happens to our planet and to us. So next time you are in the store, be sure to flip over the package and read the label!



RUI WANG

# From theoretical models to real world solutions

BY MICHAEL BARNES

It was in early 2003 when Rui Wang, a third-year undergraduate from Zhejiang University in Hangzhou, China, first came to the College of Chemistry. Wang was spending two months as a visiting chemical engineering student at UC Davis. Intrigued by the College's reputation and its unique structure, he made an appointment with chemical engineering professor Jeff Reimer, and stopped by to talk.

Wang didn't know it then, but his career would become intertwined with that of the college's Chemical and Biomolecular Engineering department, and 16 years later, he would return to Berkeley as the department's newest faculty member. Just like the polymer networks that he studies, Wang's life has had many interconnected strands that led him here to an office in Gilman Hall and a joint appointment with fellow theorists in the Pitzer Center for Theoretical Chemistry.

Wang was born in 1981 in Chengdu, the capital of Sichuan province, a growing regional commercial center with a thriving electronics industry. His father was a factory manager and his mother a nurse. He attended high school there, and when it was time to pick a university, he chose the prestigious Zhejiang University in Hangzhou, about 100 miles southwest of Shanghai. "Zhejiang University is one of China's best, and Zhejiang Province is near my mother's hometown, which also appealed to me," says Wang.

Wang earned his ChemE B.S. in 2005, electing to stay on at Zhejiang University for his master's degree. He was an outstanding student who studied techniques for producing polymers, winning awards for his research papers (and later his thesis). However, he didn't discover his scientific passion until he ventured to McMaster University in Ontario, Canada, for a six-month visitor's position in 2007. There he studied with An-Chang Shi, a theorist in polymer physics.

Wang comments, "It was at McMaster that I first read the writings of Pierre-Gilles de Gennes (1932-2007), who won the Nobel Prize in Physics in 1991. I was so impressed with the breadth of his thinking that I decided to switch from polymer chemistry to working on soft-matter physics."

De Gennes, who has been called "the Isaac Newton of our time," was a postdoc at Berkeley with physicist Charles Kittel in 1959. Wang states, "De Gennes had an amazing ability to spot common features in patterns of order, or lack of it, in a variety of physical systems, from magnets, liquid crystals to polymers, and to describe general rules for how these systems move from order to disorder and back."

Wang went on to complete his M.S. in 2008 and traveled to Pasadena to begin work on his chemical engineering Ph.D. at Caltech. He wrote several theoretical studies of polymers, membranes and charged interfaces with his Ph.D. adviser, Zhen-Gang Wang.

While at Caltech, he met then postdoc, Bradley Olsen, who had received his Berkeley ChemE Ph.D. in the lab of Rachel Segalman in 2007. Olsen moved on to MIT to start his own research group, and Wang became one of his postdocs in 2015. He was the first theorist in Olsen's group. During his time at MIT, Wang began to study polymer networks and devise theoretical models of how defects in these networks affect their characteristics. He then worked with several experimentalists to verify the predictions of his models.

Wang states, "Theory and experiments are not opposites or substitutes. Theoreticians and experimentalists need to work together to explore the boundaries of scientific knowledge. At MIT, I often worked on theoretical problems as the only theoretician in a research group of experimentalists."

Wang's research involves refining theoretical models of polymer networks to accurately predict their characteristics based on the number and type of defects in the network. Unlike crystals or metal-organic frameworks, polymer networks are connected in random patterns without any spatial order. Different defects in the network are inevitable and can cause tremendous changes in the nature of the polymer.

In his research, Wang has rigorously quantified the number of the varieties of defects and their impacts on the topology, mechanical response and percolation of polymer networks. For example, a polymer link, instead of connecting to a nearby junction, might loop back to its original junction. Or two or more links might join in an irregular way as a "double bridge" that disrupts the regular pattern of the network.

Like his role model, Nobel Laureate de Gennes, Wang was looking for fundamental principles that spanned more than one type of system. Says Wang, "Beyond polymer networks, cyclic defects that suppress the spread of information also exist in many other networks. Good examples are routing loops in computer networks and acquaintance clusters in social networks. Understanding and controlling cyclic defects is critical to many forms of network science and engineering."

In January 2019, Wang joined the faculty of the Department of Chemical and Biomolecular Engineering (CBE). He is also a member of the Pitzer Center for Theoretical Chemistry, the world's leading group of theoretical chemists. For the first time in his career, Wang will be surrounded by like-minded theorists.

The concept of a theoretical chemical engineer may seem like a contradiction, but it is actually part of the tradition of the College. An early practitioner of this approach was CBE professor John Prausnitz, who came to Berkeley in 1955 and began working with physical chemists. He laid the theoretical foundation for the use of molecular thermodynamics in gas separation techniques. Emeritus professor Prausnitz has characterized this work as seeking the "future practical." His success earned him the 2003 National Medal of Science.

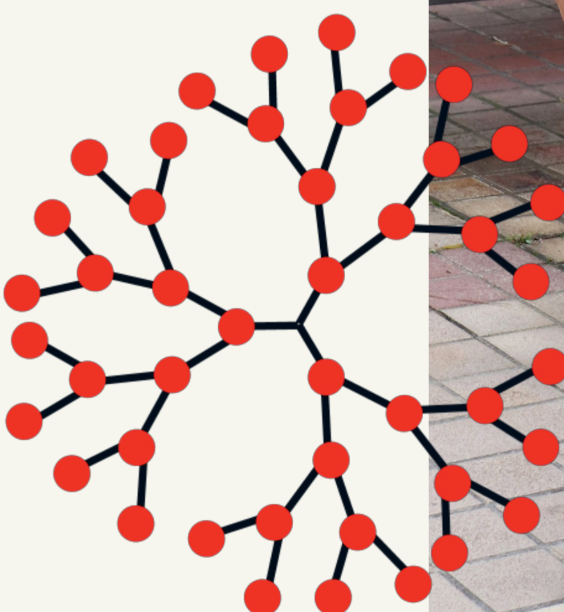
Both the problems that chemical engineers must help solve, and the tools available to them, have evolved dramatically during the last few decades. The classical problems of unit operations and process engineering have become more tractable. Meanwhile, emerging problems in energy storage and biomaterials, just to name a few, are now at the forefront of the tasks that engage chemical engineers.

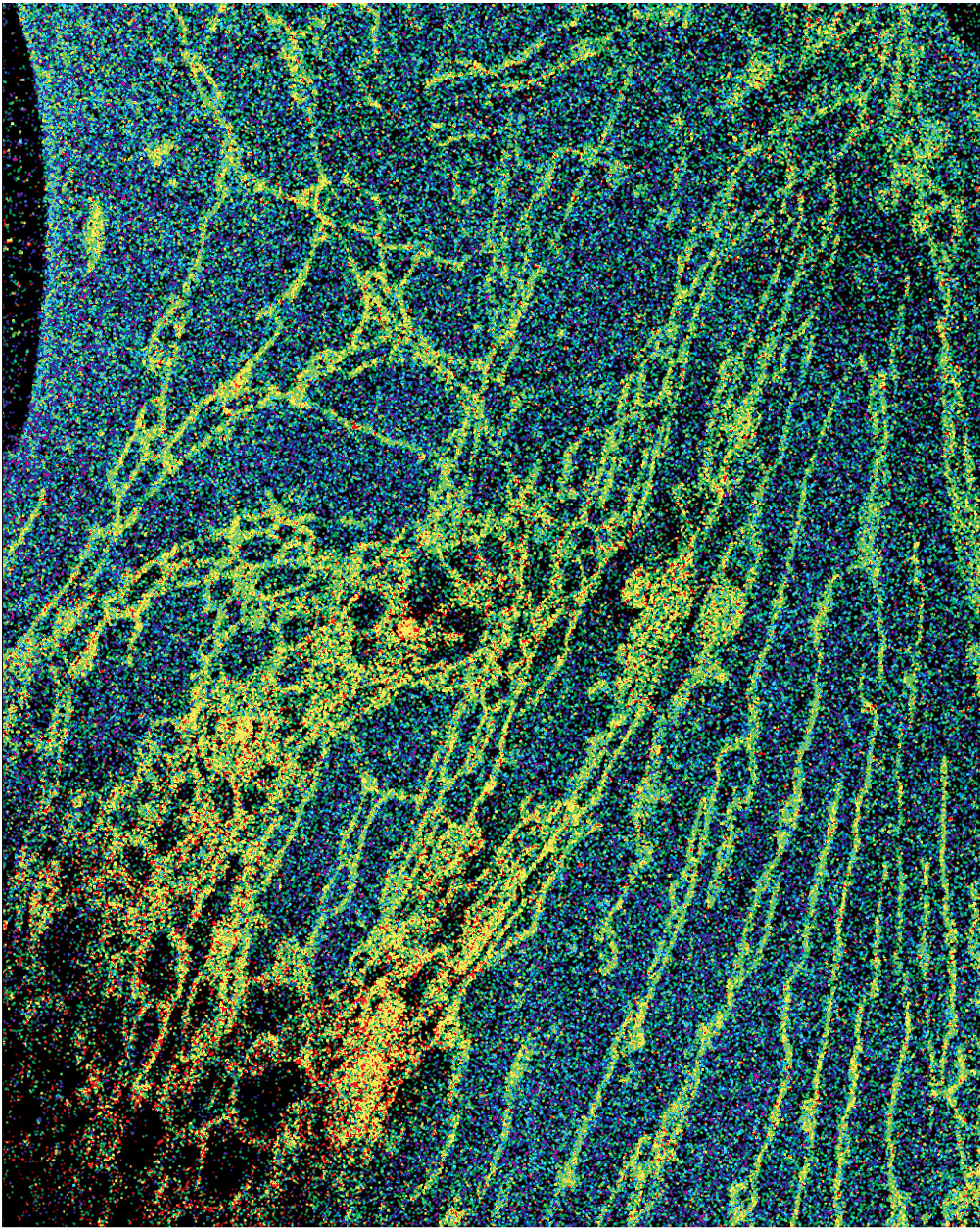
Asks Wang, "How can we realize the social benefits of energy storage and biomedical materials? These are fundamental challenges, and we need to apply new scientific principles to serve engineering problems. Modern chemical engineering has become an increasingly molecular-based discipline, and the number of unknowns is too large to explore in an ad hoc fashion with experiments alone. Theory can help suggest which experiments, out of the hundreds that could be conducted, will lead to the right path.

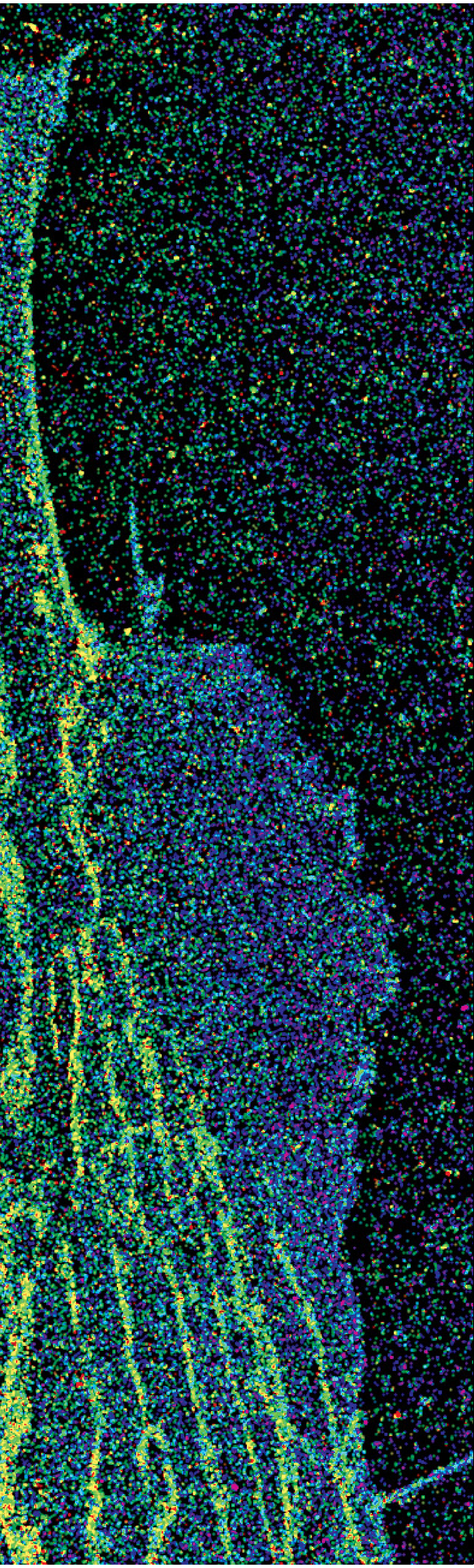
"It's my hope that we'll make the discoveries necessary to allow us to rationally design new materials from the molecular level. Major improvements in materials—electrolytes for safer batteries and electric vehicles, synthetic tissues to repair damaged organs, membranes for purifying drinking water, intelligent soft particles for sensors and actuators—will require molecular-level theory. Without new approaches we can't design new materials. And without new materials we can't touch society's important problems.

"For me," concludes Wang, "Berkeley is the best place for this work for four reasons. First is the department's tradition of theoretically sophisticated chemical engineering. Second is the Pitzer Center with its strong group of theorists interested in a variety of research areas in physical chemistry. Third is that I can collaborate with the world-leading experimentalists in polymer and soft materials. Fourth is that at Berkeley I will be able to work with the best students."

The College of Chemistry welcomes Wang and wishes him the best in his pursuit of the future practical.







# The super-microscopic world of Ke Xu

When Assistant Professor of Chemistry Ke Xu finished his Ph.D. on superconductors, he decided to work in a different research field that is also "super:" super-resolution microscopy, a name collectively given to a variety of rising new microscopy techniques that achieve nanometer-scale spatial resolutions with light.

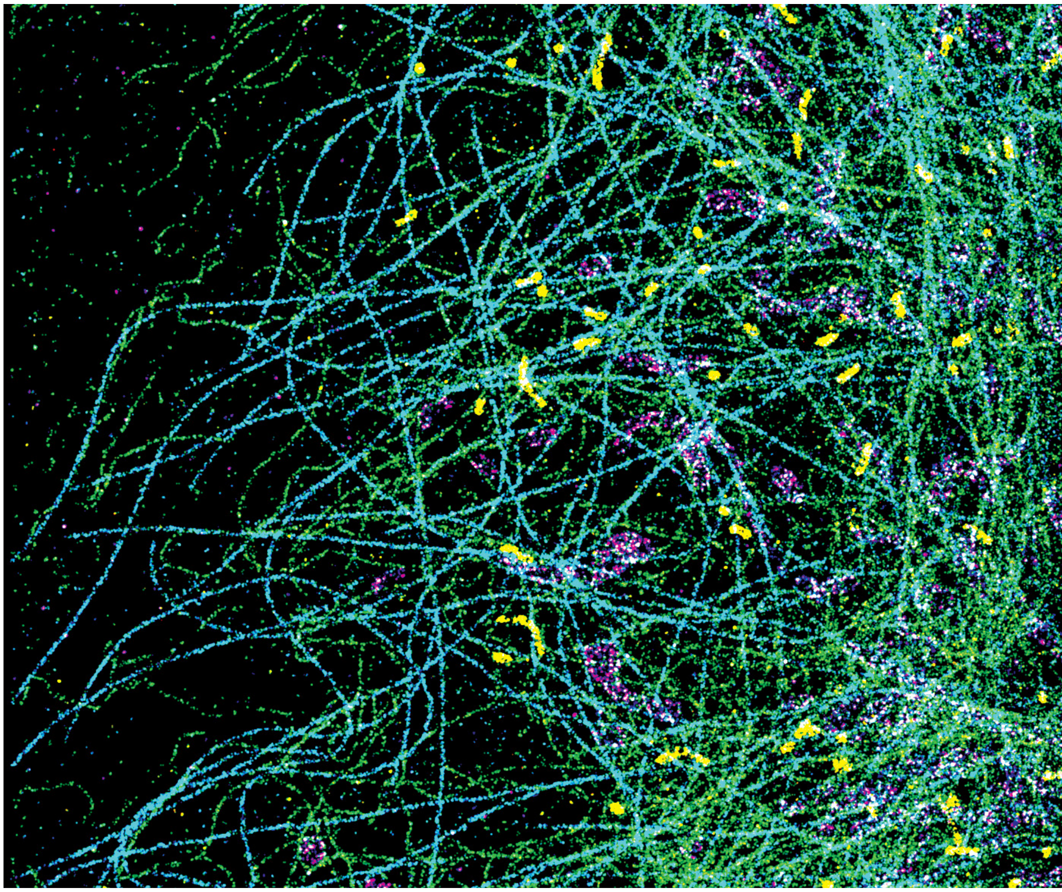
Xu, a Chan-Zuckerberg Biohub investigator, is pushing the frontiers of super-resolution microscopy to enable the probing of functional parameters — including pH, chemical polarity, and molecule diffusivity — at the nanometer scale. To achieve this, his lab is adding novel dimensions, including the spectral (color) dimension of single molecules, to move beyond traditional 3D spatial dimensions.

The results are visually beautiful, and unveil insightful nanometer-scale spatial variations in chemical compositions and physical properties for both live mammalian cells and chemical systems.

**Spectrally resolved, polarity-sensing super-resolution image of the membranes in a mammalian fibroblast cell**
(MOON ET AL. 2017)

• Nile Red, a solvatochromic dye that changes color (spectrum) based on local chemical polarity, is used in this spectrally resolved super-resolution study, which labeled all the membranes of the cell. • Each detected single molecule is color-coded according to its spectrum peak position, on a continuous scale of 612-648 nm. • Spectral resolution shows polarity differences between organelle and plasma membranes in the living cell; such differences are due to a disparity in cholesterol levels.

IMAGE SIZE: 29x26 μm



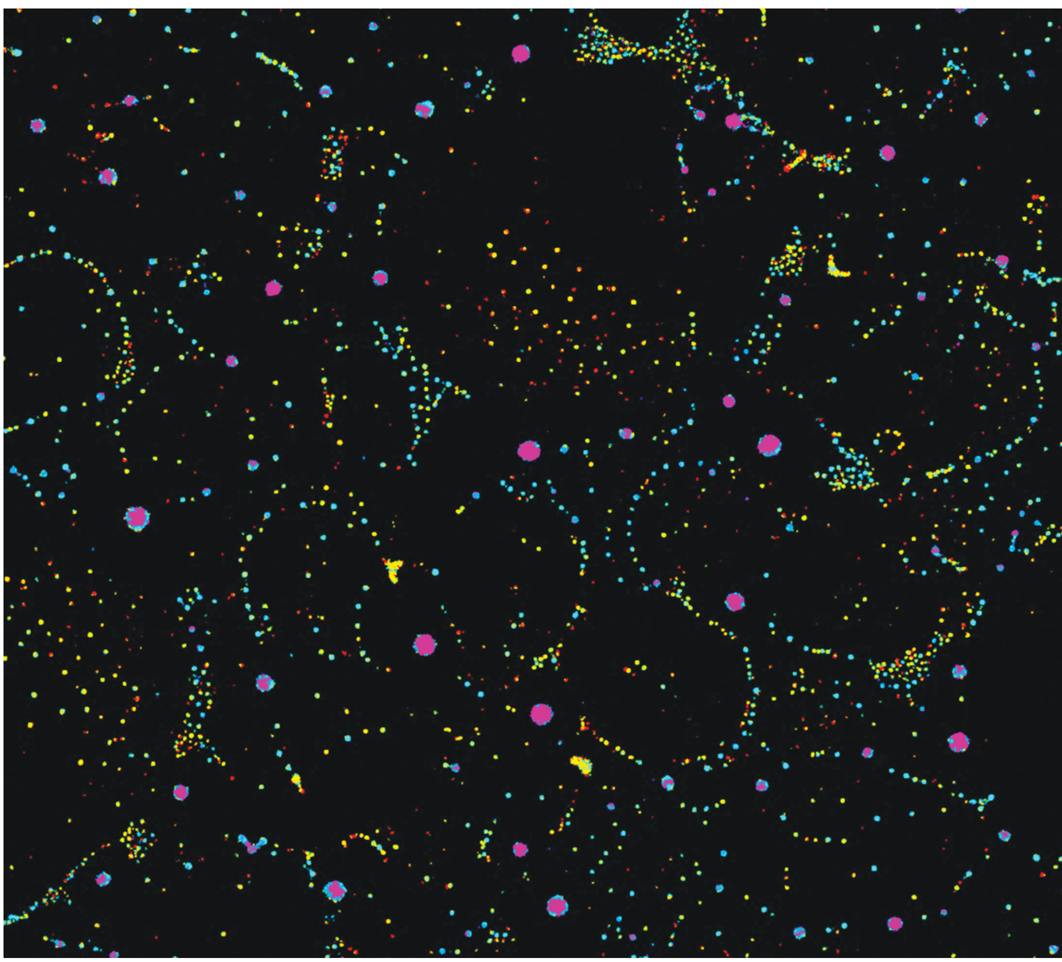
## Spectrally resolved, multicolor super-resolution image of a mammalian fibroblast cell

( ZHANG ET AL. 2015)

• Four far-red dyes, with slight differences in emission spectrum, were used to label the four different intracellular structures. • The colors represent the measured spectral peak positions of individual molecules on a continuous scale (676-720 nm in wavelength). • The four major colors showed up due to the four dyes used. • The colors highlight the following — magenta: mitochondria, cyan: microtubules, green: vimentin filaments, and yellow: peroxisomes.

IMAGE SIZE: 22x18 μm





## Spectrally resolved, polarity-sensing super-resolution image of microscopic organic droplets on a glass surface

( XIANG ET AL. 2018 )

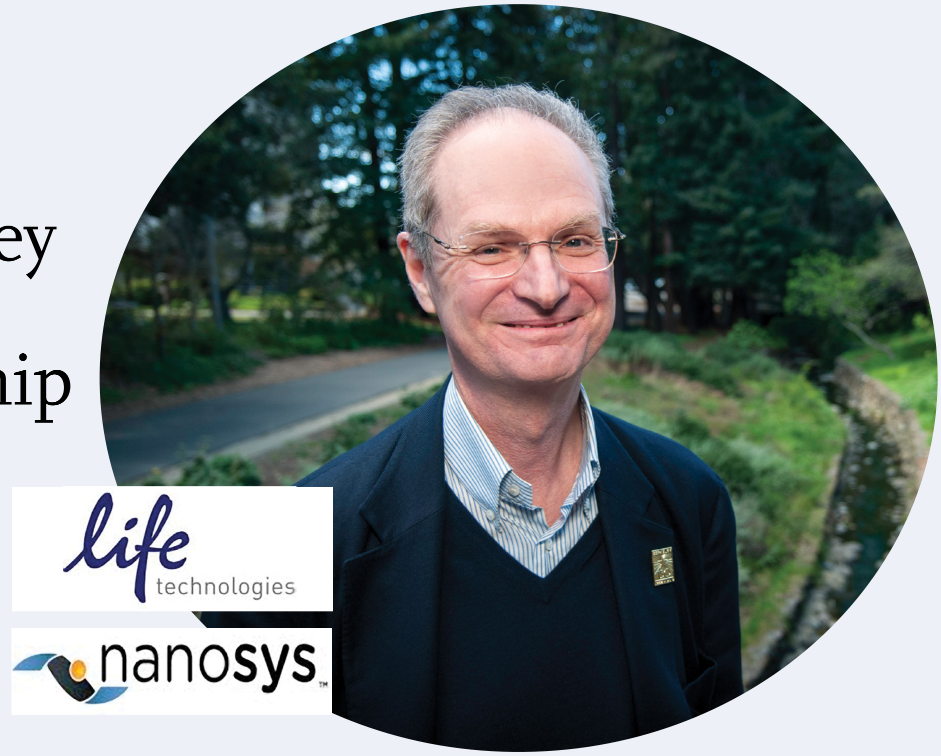
• For this image trichloroethylene (TCE) and chloroform spontaneously demixed on a glass surface to form adlayer nanodroplets of different compositions. • Nile Red, a solvatochromic dye that changes color (spectrum) based on local chemical polarity, is used in this spectrally resolved super-resolution study. • Each detected single molecule is color-coded according to its spectrum peak position, on a continuous scale of 620-638 nm. • A palette of different colors and nanoscale structures was found for the adsorbed organic droplets, thus revealing unexpectedly rich structural and compositional behaviors of surface adlayers at the nanoscale.

IMAGE SIZE: 14x12 μm

• • • NOTE: more images, and research details, are available at catalyst.berkeley.edu

PAUL ALIVISATOS

# Reflection on a scholar's journey in the world of entrepreneurship




From the time I was a graduate student at Berkeley in the early 1980s, I always wanted to find a way for the fundamental research I was part of to also find a practical use. This follows from the broader ethos of Berkeley, where scholarship is brought to bear on changing the world in many different ways, and has guided me in my choices over the years. It is one of several factors that led me to a postdoctoral position at Bell Labs, and a strong motivation for my choice to work on tiny crystals in the first place, at a time when this was not a recognizable subject for my field. At that time there were many debates among academic colleagues in my discipline at Berkeley about the relative merits of basic and applied research, which were generally viewed as quite distinct from each other. At Bell Labs I sensed that the community had a more nuanced and refined concept in which these two could ideally be seamlessly integrated, one always enhancing the other and often morphing unexpectedly between them. It has always been my personal goal to work in this way.

I have personally been involved in the creation of three companies, Quantum Dot Corporation, Nanosys, Inc, and Solexant, Inc. Each was a wonderful adventure that followed from our team's very foundational research in nanomaterials. Quantum Dot is now part of a large biotech company, and the products that were first designed at that company are widely used today in medical bio-imaging. Solexant didn't work out as well, as we had misjudged the nature of the opportunity in solar. Nanosys has been the most fun of all, as the materials we developed continue to have more and more impact in diverse areas, especially in wide color gamut energy efficient displays that are now widely available commercially. I am viewing this document as I write it on a Quantum Dot display that is just beautiful.

In all three cases, my engagement in the world of entrepreneurship did not just follow research in the lab. It in fact greatly enriched my academic work. Once a company sets to developing a technology that has been first demonstrated at a base level in a university, the focus narrows, and the pace quickens remarkably. In all three cases, it was not long before I could see that these companies surpassed anything that a university lab could do, my lab or even, I believe, those of my outstanding colleagues elsewhere. That has thrust me into periods of introspection, where I was forced early on to consider how to adapt to a changing reality. This can be hard, as it means changing directions, or even walking away from some potential publications which are still possible in the academic world, but which are no longer at the cutting edge of technology. I suspect many of my more entrepreneurial colleagues will recognize this situation. In the end, it has prompted me to move along towards the questions that are best suited to an academic group, while also providing me invaluable context for the possibilities of my work.

As an academic scholar, a deep commitment to patient scholarship and careful foundational work is essential. Still, entrepreneurship has been an invaluable aid to my intellectual renewal, and it has helped me be at the forefront of new directions in my field. I still am looking for an opportunity for another foray into entrepreneurship with excitement. I have learned a lot from all my prior experiences, and I think that next time, if I am careful, I can go even further in realizing my career-long dream of participating in the full journey wherein my foundational academic research reaches out to make an important positive difference in this world.

Catalyst

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## ChemX Conference

**Saturday September 21, 2019**
**1:00pm to 5:00pm**
**Chemistry Plaza**

This year's Conference offers opportunities to hear talks by star faculty and alumni, attend corporate and industry networking hubs, and view graduate student research projects while sipping drinks and noshing on appetizers!

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