CTSConnections

Building research teams of the future to improve human health • 2016 • Volume 6, Issue 2

A passion for applied research: College of Engineering Dean Jennifer Sinclair Curtis inspires others

TO SOMEONE WHO DOES NOT KNOW the field, particle flow may seem like a pretty dry and esoteric subject. But spending a few minutes with Jennifer Sinclair Curtis, Dean of the UC Davis College of Engineering, whether one-on-one or in a large lecture hall, is an engaging experience.

Her career has been devoted to studying the behavior of granular materials in different environments. Picture a uniform mixture of various sized pebbles being fed through a large funnel. As they flow through the narrow opening, a natural segregation of the particles by size occurs. This is an undesirable trait for materials in many situations because uniformity is lost during the process.

This can be a problem, for example, in mining and agricultural operations. But it also has consequences in just about every field imaginable, including space exploration and even medicine. How can a pharmaceutical company manufacture a drug consisting of a mixture of particles of different shapes, sizes, and densities so that every tablet has an identical composition? How does one develop an inhaler for an aerosolized medication to ensure that the desired dose is delivered through the airways to the target area?

An internationally renowned researcher, Curtis has co-authored more than 100 publications and earned numerous national and international awards for her pioneering research in developing and validating models for predicting the behavior of particleladen and gas-solid flows.

"Modeling tools has interested me throughout my career," said Curtis, who received her Ph.D. in chemical engineering from Princeton University in 1989. "The list of practical problems in the field of particle flow is endless, and each project I have worked on has had its own challenges."

A new home at UC Davis

Curtis joined the UC Davis community just one year ago, previously serving



Jennifer Sinclair Curtis, Dean of the UC Davis College of Engineering

DIRECTOR'S MESSAGE

Lars Berglund, M.D., Ph.D.

An innovation game changer becomes law

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THE 21^{sr} CENTURY CURES ACT IS NOW LAW. This bill has been a multi-year effort and passed with a wide majority in both houses of Congress. On December 13, 2016, President Obama signed a bipartisan bill that provides the NIH with \$4.8 billion in new funding over 10 years. These additional funds will help advance the Precision Medicine Initiative to drive research into the genetic, lifestyle and environmental variations of disease; bolster the "Cancer Moonshot" initiative; and invest in the BRAIN initiative to improve our understanding of diseases like Alzheimer's. These are all areas of research in which the CTSC is providing assistance to researchers at the UC Davis School of Medicine.

There are 10,000 known diseases or conditions for which only 500 have treatments or cures. While the pace of scientific advancement has been impressive over the last 20 years, translating discovery into new FDA-approved treatments has proven difficult.

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as Associate Dean for Research at the University of Florida College of Engineering, and prior to that as a member of the faculty at Lafayette College, Carnegie Mellon University, the University of Arizona and Purdue University.

The collaborative atmosphere – widespread throughout the UC Davis campus and permeating through all levels of undergraduate and graduate students, as well as faculty – was striking. She noticed it when she came to interview, and her impression deepened over time. "The level of interdisciplinary collaboration at UC Davis is really unique for an institution of this size," she said. "The consequence of this is that creativity and out-of-thebox thinking are really encouraged, leading to the development of truly cutting-edge products."

As dean, she values the role of fostering the matchmaking process: bringing together researchers from other colleges, supporting proposals and helping to obtain grants, and nurturing relationships with other academic institutions and industry. "Providing support and making connections is really what the CTSC is all about," she added. "This is a tremendously valuable program available to UC Davis researchers."

Curtis sees challenges ahead for research, as more students come up through the pipeline but funding resources become scarcer. In addition, there is an increasing degree of research compliance oversight without funding for academic institutions to support these new requirements.

A rewarding career

Curtis reminisces about her highly varied career in applied research. A high point – both figuratively and literally – was the research she conducted for NASA.

One of the biggest risks of a moon landing is the debris kicked up by the exhaust from the rocket as it approaches the surface. The resulting plume of rocks and dust can cause fatal damage to the spacecraft. Curtis became an expert on lunar and Martian soil models to help predict cratering and particle scatter during launches and landings. In 2010, her research group was selected to conduct experiments on the reduced gravity airplane, also known as the "vomit comet," Curtis said with a laugh. But looking back, Curtis said without hesitation that the greatest reward of her career has been fostering the interest and careers of others. She has garnered numerous awards for teaching and mentoring. A colleague from Carnegie-Mellon University remembers that Curtis was "the strongest and most popular teacher in the department, and received the highest scores on student evaluations. This is especially noteworthy because she was teaching core courses like Mathematics for Chemical Engineers and Heat and Mass Transfer."

In many of the places she has lived, Curtis developed and taught summer courses for junior high and high school girls in underprivileged neighborhoods. She found this experience particularly rewarding because it encouraged these students to consider a career in engineering. "Training students and young faculty, and nurturing their careers are really what I love best," said Curtis. "I look forward to more opportunities in this direction as Dean of the College of Engineering and working hand-inhand with the CTSC." §

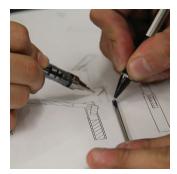
DIRECTOR'S MESSAGE continued from page 1

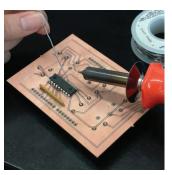
The Cures Act will advance new therapies by:

- Modernizing clinical trials and removing barriers to increased research capabilities.
- Putting patients at the center of the regulatory review process.
- Supporting broader, more collaborative development of biomarkers to assess efficacy.
- Streamlining regulations to provide more clarity and consistency for innovators.
- Incentivizing the development of drugs for pediatric diseases.
- Investing in science and next generation investigators. This Act reiterates the importance of clinical and

translational science by providing more flexibility on the use of funding, removing restrictions on the conduct of phase IIb-III clinical trials, and supporting the pursuit of innovative approaches to major challenges that have potential for leading to breakthrough discovery. Further, the Cures Act will improve delivery of new therapies to the right patients by ensuring electronic health record systems are interoperable and capitalize on the benefits of a learning healthcare system while observing privacy protection. This Act will also address mental health and substance abuse issues with grant making, improved communication, targeted efforts to reach patients in need, and strengthening the workforce of those who serve those in need.

Sweeping legislation of this nature, ensconced in some 1,000 pages of text, demonstrates strong support for the research community. By addressing many aspects of the national biomedical research enterprise, this Act serves as a foundation for the ongoing effort to innovate and translate discovery into cures and aligns perfectly with the mission of the CTSC. §









CTSC champions innovative design in engineering capstone projects

WHEN CRISTINA DAVIS, professor of Mechanical and Aerospace Engineering, College of Engineering (COE), arrived at UC Davis in 2005, she worked closely with her colleagues in the Department of Biomedical Engineering - Professors Angelique Louie and Anthony Passerini - to create a series of project-based senior design courses that would challenge and inspire their students. These courses, a COE requirement for graduation, help students blend the knowledge they acquire through 4 years of coursework with hands-on experience designing and building device prototypes in collaboration with faculty mentors.

The main objective of the course is for students to develop a functional device prototype – ideally one that has been tested to determine if the device met its established performance specifications and is practical for development for the intended application. Through the development process and close mentoring by engineering faculty, students learn how to work in teams, follow a defined design process, and are responsible for creating progress reports, documenting functional requirements, and generating manufacturing plans.

In order to bring a broad selection of project ideas to the senior capstone students, engineering faculty require access to a reliable source of project proposals, along with subject-matter experts who are willing to be involved in the project and serve as faculty mentors. Following a conversation with School of Medicine (SOM) faculty in the CTSC, Davis and her research partner, Nicholas Kenyon, professor in the Department of Internal Medicine, developed a proposal to tap into a new source of project ideas. They envisioned using CTSC resources to connect SOM faculty mentors with engineering faculty mentors and students to collaborate on focused medical engineering projects.

Davis and Kenyon approached Lars Berglund, principal investigator and director of the CTSC, with their new program plan. Berglund agreed that the new program would be an excellent way to create an environment where physicians and other healthcare professionals could co-create medical devices to improve human health. The program would also align well with the CTSC's overarching mission to build research teams of the future. Mechanical and biomedical engineering students would have the opportunity to use their skills to develop prototypes of biomedical devices that serve a critical need. Beginning in 2008, the CTSC's Pilot Translational and Clinical Studies Program initiated an annual call to solicit project proposals from clinicians and provided some financial support for selected projects.

For engineering faculty, the project entails a year-long process. After project ideas are collected, a committee comprised of COE and SOM faculty selects 5 to 8 proposals that merit CTSC support. Projects must be feasible and not likely to exceed two quarters of development work. Students and projects are matched, and students are trained in a prototyping laboratory prior to beginning actual project work. When project work begins, engineering faculty members mentor the trainees through the entire process of design toward a functional prototype.

To date, the CTSC has sponsored 64 projects and included 58 School of Medicine faculty mentors and 282 senior design capstone students who produced 35 abstracts, 5 patent disclosures, and several peer-reviewed publications. In addition, preliminary data gleaned from projects were used to support federal grant proposals and further development work for the prototypes. The UC Davis COE-CTSC-SOM capstone senior design course collaboration highlights that effective translational teams can be formed very early in the training experience.

In addition, students report an increased interest in biomedical entrepreneurship after developing a prototype of a medical device in the course. Abundant opportunities to present their work at a variety of university, regional and national events – including a TEDx talk at UC Davis – have also resulted from this program.

The capstone collaboration earned national attention in 2013 when Davis and Kenyon were recognized as finalists for the Association of American Medical

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VentRight – a portable "expert" to deliver correct ventilation

A PARAMEDIC ARRIVES AT THE SCENE of a crash and rushes a child into the awaiting ambulance. The child's breathing is labored, so she quickly places a bag-valve mask over the child's mouth and nose to assist in ventilation. How fast should she squeeze the bag, how deep should the breaths be?

According to M. Austin Johnson, assistant professor of emergency medicine, the answer has no simple formula, although that is what is usually relied upon during an emergency. Changes in blood oxygen, CO_2 , and pH levels affect the amount of ventilation needed – factors difficult to assess in the heat of the moment. In pediatric patients, this becomes more complex, since both ventilation rate as well as breath size are both age/height dependent.

"Over- or underventilating a critically injured patient can contribute to a poor outcome," said Johnson. "What if we could distill the expertise of doctors into a device to guide providers to optimize ventilation out in the field?"

Johnson first had the idea of a "smart" ventilation monitor device when working in Peru as a medical student. Healthcare workers often had primitive ventilator equipment and only basic training, and family members often manually ventilated children for hours due to mechanical ventilator shortages.

Johnson submitted his idea of a device to overcome this limitation as a CTSC Capstone project in 2014, and a team of students set to work. Their goals were to devise a device to monitor the ventilation rate being delivered in a bag-valve mask, and based on respiratory measures, set off an alarm if the user was inappropriately ventilating the patient. The device was to include adjustable settings for infants and children of various sizes, simplifying the ventilation of critically ill children.

Jason Adams, a UC Davis Health physician and assistant professor



Drs. Adams and Johnson (holding VentRight) were supported by award 5 K12 HL108964-02, from the National Heart, Lung, and Blood Institute.

of Pulmonary and Critical Care medicine, immediately saw the potential applications of such a device not only in ambulances but in the emergency department, operating room, and intensive care unit when patients are placed on mechanical ventilators. Adams joined the team, contributing additional expertise in diagnostic and decision support algorithm development for the device. "A portable add-on device for existing ventilator systems that can inform a user how to deliver optimum ventilation can have enormous benefit across the continuum of critical care," said Adams.

The five-student team worked for six months on the multidisciplinary project, which combined the areas of emergency medicine, computer science, and electrical and mechanical engineering.

Student Justin Koos found the experience invaluable, especially for learning to work effectively in a team. "Everyone had their own area of expertise, and we needed good communication to ensure that all parts came together into a working whole," he said.

The team made great progress during the course, according to Johnson, and their final prototype won the award for Outstanding Clinical Impact at the UC Davis Biomedical Symposium.

Koos graduated soon after, but continued to work with Johnson and Adams to develop the device. They have made use of the UC Davis Center for Virtual Care to experiment with mannequins and ventilation machines as well as the TEAM lab at the College of Engineering to 3D print new prototypes.

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Audion – a stethoscope for the hearing impaired

WHEN MICHAEL MCCLOUD, a geriatrician with a busy clinical practice, developed hearing loss, he adapted by getting a behind-the-ear hearing aid. But while he could once again listen with ease to his patient's words, listening to their heart and lungs was another matter.

"To accommodate the ear pieces on the stethoscope, I had to take out my hearing aids, use the stethoscope, then pop my hearing aids back in. It was a very inconvenient process," said McCloud, a physician who served as clinical professor of medicine at UC Davis until recently retiring to pursue interests outside the university.

He began to search for options available to hearing-impaired clinicians. What he found was disappointing. Neither traditional stethoscopes nor the electronically amplified audio-enhanced stethoscopes he found could be used comfortably with a hearing aid. Most hearing aids, he explained, have a tiny plastic tube that runs from the device into the ear canal. Jamming standard stethoscope earbuds into the ear canal with the tube in place is uncomfortable and damages the tube over time, requiring frequent replacement.

The choice remained to either wear his hearing aid or use a stethoscope at any given time. When he contacted a stethoscope manufacturer, thinking he

VentRight from page 4

Johnson, Adams, and Koos have since filed two patents surrounding the device, and they are currently seeking funders in industry and government to allow them to fine-tune the system – now called VentRight – and prepare it for FDA approval. Their goals for the device have expanded to include adult



Audion replacement ear tips for stethoscopes.

was overlooking something that was surely available, he was met with a disinterested shrug.

Not giving up, he submitted the idea of a hearing aid-compatible stethoscope as a CTSC-COE Senior Design Capstone project. The project was selected, and a team of engineering students set to work, with McCloud serving as their clinical advisor. The results were outstanding, said McCloud, who enjoyed being a part of the process as much as trying out the final prototypes. "The students were creative and energetic, always thinking outside the box," said McCloud. "It was exciting to watch them develop their ideas, from searching to what was already patented to using a 3-D printer to develop model designs."

patient populations, greatly expanding the potential number of patients who could benefit from this technology.

According to Johnson, the team continues to work to develop this technology to be sufficiently inexpensive and portable so that it can be used in multiple care settings; from rural prehospital environments to state-ofthe-art intensive care units. Johnson and Adams also have not forgotten

Mentored by Biomedical Engineering Professor Anthony Passerini, the team came up with interesting and viable options during the 5.5-month-long COE Senior Design Capstone course. The resulting device is a modified ear tip that replaces the standard ear tip on any stethoscope. It features a strategically placed cutout to allow the hearing aid tube to avoid contact with the device. An optional electronic add-on provides additional amplification and filtering to improve sound quality. Designed to mitigate the effects of hearing loss instead of simply redirecting sound, the device allows personalized settings according to the user's auditory needs.

Kenneth Chang, a student member of the Audion team, recalls the experience as formative. "The course allowed us to apply everything we learned in engineering to a real-world problem," he said. "When I went for a job interview and talked about the course, my interviewer said, 'Oh – you know exactly what we do!""

Chang has since graduated and was hired as an engineer in a medical device start-up company. McCloud is hoping that eventually the project will lead to a marketed product, so that one day hearing-impaired clinicians will have the option that he needed. §

where this idea originally came from, as both physicians are dedicated to ensuring this technology makes it back to health care settings in developing countries. "We are creating a device that lets anyone become an expert in ventilation," said Johnson. "We're grateful for the Senior Design Course Capstone project that allowed this dream to hopefully soon become a reality." §

VisionFinder – a portable vision tool inspired by a global need

WHILE MOST OF THE IDEAS FOR MEDICAL DEVICE PROJECTS for the COE Senior Design Capstone course are submitted to the CTSC by physicians, sometimes suggestions are proposed by community groups, or individuals, as in the case of Rose Hong Truong, a biomedical engineering student at UC Davis.

When Truong was a freshman, she spent a quarter abroad in Ecuador. There she met a group of medical students from other universities who had set up a makeshift clinic. One patient, an elderly man who had walked miles through the rain forest to get a pair of eyeglasses, left empty-handed. Though the clinic had plenty of glasses, they had no way of testing the man's vision to determine his prescription.

The experience of the visually-impaired man haunted Truong after she returned to UC Davis. During her senior year, Truong conceived of a way to help patients in similar circumstances get access to basic eye care. She proposed a portable eye-examination tool as her capstone project in the Biomedical Engineering Senior Design course in 2015.

With CTSC support, Truong and three of her classmates set out to develop a device that would work like a phoropter, the instrument used by optometrists to determine a patient's prescription for corrective lenses.



Student Rose Hong Truong demonstrates use of VisionFinder.

While a full-size phoropter is too large and heavy to be portable, Truong's device, called the VisionFinder, is light, portable, non-electric, and resembles the classic View-Master toy. A standard phoropter can cost thousands of dollars, but Truong and team were able to develop their plastic prototype for about \$80.

VisionFinder has gained attention beyond the College of Engineering. The VisionFinder prototype won the \$3000 Poverty Alleviation Award during the Graduate School of Management's 2015 *Big Bang! Business Competition*. Truong was invited to speak about the device at the 2015 TEDx talk at UC Davis.

Truong praised Anthony Passerini, professor in the Department of Biomedical Engineering for his role in mentoring and coaching the student team. "He understands the design process deeply. The project wouldn't have excelled without his guidance, high expectations, and incredible patience for our group," said Truong.

After graduation, Truong accepted a position as product manager at Flex's Innovation Labs. She credits the VisionFinder project for educating her in how to evaluate an opportunity through benchmarks and thorough client assessments, and how to create specifications that meet the most design criteria with minimal trade-offs. Jackie Lim, a VisionFinder team member, is currently enrolled in an optometry school. Lim was interested in optometry before participating in the project, and working on VisionFinder cemented her decision to pursue that career.

Just as the students have moved on, so has the development of VisionFinder. Truong reports that VisionFinder is pending a second design iteration to incorporate new features. Someday, perhaps visually impaired patients in developing nations will not have to leave a medical clinic without eyeglasses for lack of a prescription.

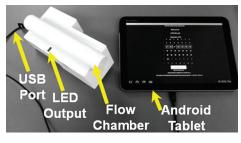
Cody Kitaura & University News contributed content for this article

Sequel to a successful collaboration

TEN YEARS INTO THEIR COLLABORATION, Cristina Davis and Nicholas Kenyon continue to benefit from the Capstone program (see story on page 3). Together they comentored a four-student team through the design and production of a firstgeneration lung function monitoring device to measure peak expiratory flow rates (PEFRs) - the maximum speed of a person's exhalation. The students developed a novel approach that simplified the data collection and dissemination process, and used a modified cell phone as a mobile platform interface. The end result was a convenient, accurate, and portable PEFR device that patients could use anytime, anywhere.

Guidelines developed by the National Asthma Education and Prevention Program's Third Expert Panel Report, which is widely used by health care professionals, recommend the use of monitoring plans based on PEFRs to better identify warning signals of worsening asthma symptoms in patients. Consequently, this new device represented an important advance in care. The engineering student team and their faculty mentors coauthored an account of this work titled, "Coupled mobile phone platform with peak flow meter enables real-time lung function assessment," in the IEEE Sensors Journal in 2012*.

When Professor Jean-Pierre Delplanque (Mechanical and Aerospace Engineering) and two graduate students – Alice Kwan and Alexander Fung – joined the project, the team acquired the skills to build the next generation prototype. Through a CTSC Highly Innovative Award pilot project, Delplanque and colleagues were able to design and build a mobile phone-based spirometer that more accurately measured lung function and



Portable spirometer and breath analysis device.

automatically recorded information from the application (date, time, GPS location, spirometry data). Former UC Davis pulmonary fellow, Dr. Laren Tan, conducted an IRB-approved clinical study to test this device in patients with asthma and chronic obstructive pulmonary disease (COPD).

This work addressed a technology gap that has existed for portable monitoring systems to perform these functions while continuously logging data. Ultimately, this undertaking led to a National Institutes of Health (NIH) National Institute of Biomedical Imaging and Bioengineering (NIBIB)funded project to develop wearable diagnostic health monitoring sensors for children with asthma to improve their daily quality of life. And the work continues. Building on the original Capstone Design team project, Professors Davis, Kenyon, and Delplanque plan to combine four major functions in a single packaged system worn by the user that will: (1) measure routine portable spirometry and pulmonary lung function, (2) identify exhaled breath oxylipin biomarkers, (3) monitor environmental chemicals, and (4) log patient symptoms and drug dosages. Together these data will allow the team to more fully understand pediatric asthma in a way that has never been possible before.

In this one example, the Capstone Design project resulted in mentored students, a peer reviewed publication, two grants, and a medical device that provides significant improvement in patient care. Now that is a proud legacy!

*IEEE Sensors Journal article is found at http://bit.ly/2h68jry The collaborative research of Professors Davis and Kenyon was highlighted in the Fall 2011 edition of CTSC Connections. http://bit.ly/2jwcYH9



Patient demonstrates the portable spirometer and breath analysis device.



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CTSC Capstone projects Continued from page 3

Colleges (AAMC) Award for Innovative Institutional Partnerships in Research and Research-Focused Training.

For Berglund, the success of this program has far exceeded expectations. "Through this program, the CTSC fulfills its mission in an innovative and exciting way," said Berglund. "What makes the program so rewarding is that we sponsor projects with direct health significance, projects with community collaborators – such as Easter Seals, and projects that continue to be developed after the senior design course has ended." §

Contact Dr. Nicholas Kenyon (njkenyon@ucdavis.edu) if you would like to share your idea for a project.

Citing the CTSC grant

 \mathbf{W} ith new funding (July 2016) for the CTSC come new grant numbers. Please use the new number - UL1 TR001860 - when acknowledging the main CTSC grant in publications, posters, presentations, etc. Investigators are required to cite the CTSC grant in all publications that result from any support received from the CTSC, including use of CTSC services (such as biostatistics, biomedical informatics, clinical trials resources, etc.) or resources (such as the CTSC Clinical Research Center) or direct funding (such as pilot grant awards). In addition, these investigators must ensure that their peer-reviewed publications are uploaded to PubMed Central, as mandated by the NIH. To help investigators comply with NIH Public Access Policy, the CTSC has expanded its services. Staff will help with every stage of the process, including determining journal copyright polices, contacting publishers on your behalf, uploading your article to the NIH Manuscript Submission system, and providing one-on-one assistance. We aim to make it as painless as possible for you to comply with NIH Public Access Policy. Visit the CTSC at http://www.ucdmc.ucdavis.edu/ctsc/audience/investigators/ctsc publication_citing.html/ to access the resources we have prepared for you.



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