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Supporting groundbreaking neuromodulation research:

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In their words: A Q&A with previous *Science* & PINS Prize winners

We spoke with all previous prizewinners to learn what has changed since they won their Science *& PINS Prize for Neuromodulation.*

What has happened in your research career since winning the *Science* & PINS Prize for Neuromodulation?

Bozhi Tian: We have expanded our neuromodulation work to include cardiac and microbial modulation, using similar devices and material platforms to those we developed for neuromodulation. At the same time, I also feel more confident in exploring new areas of research, such as soft matter dynamics.

Nir Grossman: My team continues to develop the prize-winning temporal interference (TI) brain stimulation strategy and its applications.

Guosong Hong: We have continued our research in sono-optogenetics, which was described in my prize essay. Specifically, we have expanded the toolbox of ultrasound-responsive mechanoluminescent nanoparticles by developing a palette of these materials with different colors.

Raag Airan: My lab and academic effort have grown substantially. We are making steady progress toward clinical translation of our nanotechnology for ultrasound-mediated targeted drug delivery to the brain, and are fortunate to be funded by the NIH [U.S. National Institutes of Health] BRAIN and HEAL Initiatives to pursue first-in-human trials of this technology.

Shuo Chen: I receive emails from families of patients with neurological diseases who are eagerly awaiting next-generation deep brain stimulation (DBS) technologies. I am now doing a postdoc in both a computational and an experimental lab in New York. Although my research is still a long way from clinical applications, I feel encouraged about its prospects.

Aryn Gittis: We are currently finishing up an exciting follow-up study, where we build upon the discoveries described in my PINS essay to develop a DBS protocol that can be rapidly translated to humans, that provides sustained therapeutic benefits in a preclinical mouse model of Parkinson's disease (PD).

Do you think that winning this prize helped your career? If so, how?

Viviana Gradinaru: I am a physicist-turned-neuroscientist and engineer of proteins and viruses, motivated by a desire to understand the brain and to improve human health. Since winning, I cofounded (and serve on the board of directors of) a company based on the science described in my essay. Capsida Biotherapeutics is a fully integrated adeno-associated virus (AAV) engineering and gene therapy company. I hope it can provide better solutions for brain disease.

Grossman: The prize helped establish our brain stimulation strategy's credibility and exposure among the neuroscientific community.

Hong: This prize significantly increased the visibility of our research. As an early-career investigator, [I find] it is often a struggle to get visibility for my research. Since winning, I have received invitations to speak at prestigious conferences and institutions, and have received several early-career awards to support my team's research in this area.

About the *Science* & PINS Prize for Neuromodulation

The prize is awarded for innovative research that modulates neural activity through physical (electrical, magnetic, optical) stimulation of targeted sites in the nervous system with implications for translational medicine. Established in 2016, the prize is administered by *Science* and *Science Translational Medicine* and awarded annually for outstanding research as described in a 1,500-word essay based on research performed in the past 3 years.

The winner of the *Science* & PINS Prize for Neuromodulation is awarded USD 25,000 and has their essay published in *Science*. The Grand Prize essay and that of the runner-up are also published on *Science* Online. The award is announced and presented at a ceremony in September each year. PINS also provides financial support to help the Grand Prize winner attend the ceremony.

BIOGRAPHIES

2021 GRAND PRIZE WINNER

Stanisa Raspopovic is an assistant professor of neuroengineering at ETH Zurich. His research is focused on the design of neuroprosthetics for treatment of neurologically disabled persons. In particular, he develops mechatronic systems that interface the environment with the nervous system.

2021 FINALIST

Weijian Yang is an assistant professor of electrical and computer engineering at the University of California, Davis. His research group aims to develop advanced optical methods and neurotechnologies to interrogate and modulate brain activity.

Airan: Certainly! The exposure really propelled my career forward. It was incredibly helpful to share the essay with an interested collaborator or potential funder. In addition, meeting Meaghan Creed [the Grand Prize winner in 2017] that year and discussing potential collaborations was incredibly stimulating (pun intended)—we're still trying to figure out how best to combine our systems.

Chen: Definitely. Most importantly, more people in the scientific community get to see my work, as well as the importance of the research that my colleagues and I are doing. This presents more collaboration opportunities with scientists from various fields, including physicists, chemists, and engineers, in addition to a higher likelihood of securing research funding.

Gittis: It made my work visible to a larger audience and has helped me to make connections with neurosurgeons who are interested in translating our findings to benefit humans.

Why do you think it's important to support early-career scientists through funding and awards?

Tian: Beyond helping early-career scientists gain more visibility and support their labs better, it is also a way to help them attract more students and postdocs, giving them opportunities to improve their leadership skills. Without enough funding or awards for early-career scientists, their ability to support their team's career development is limited.

Grossman: High-profile international awards such as the *Science* & PINS Prize for *Neuromodulation* help to grow a scientific culture of excellence by setting the standard and providing role models for future scientists.

Stanisa Raspopovic: In science, and especially neuromodulation, experimental setups and equipment are expensive. Without sufficient funding, it is impossible to perform cutting-edge research. Awards for early-career scientists are really important to motivate them to remain resilient and persistent while pursuing long-term research goals.

Hong: Being an early-career scientist requires juggling multiple tasks. Funding and awards help alleviate some of these burdens and help them focus more on advising their students and starting new research projects.

Airan: Funding early-career scientists has a high return on investment. At that point in our careers, we're scrimping and saving and seeking out any amount of research dollars, looking for any avenue to get our message and vision out there. Almost any amount of funding or chance for exposure is hugely beneficial and has an exponential impact.

Weijian Yang: Early-career scientists typically have many bold ideas that offer high reward if successful. However, compared with senior scientists, early-career scientists have fewer preliminary results or resources as part of their research proposals. This could disproportionately place them in an unfavorable position when trying to secure funding. Recognizing their capabilities and funding their bold ideas is extremely helpful to accelerate their careers.

What are you most proud of in the research that you've done?

Meaghan Creed: My research has focused on understanding how activity and plasticity within basal ganglia circuits leads to behavioral changes in models of neurological and psychiatric disorders, and on using DBS to modulate circuit function. I am most proud of my trainees, who are continuing to build on this foundation by asking creative questions and are sincerely motivated to improve the lives of patients with their research.

SCIENCE-PINS PRIZE FOR NEUROMODULATION

SCIENCE-PINS

Grossman: I am most proud of discovering the temporal interference neuromodulation strategy that addresses the long-standing challenge of noninvasive focal DBS. Its discovery has opened up new therapeutic frontiers and provided new insights into the mechanisms by which physical fields modulate neural cells.

Raspopovic: We showed that by using meticulously designed neural implants and our stimulation strategy, it is possible to restore close-to-natural sensations from missing limbs to amputees. Neurally integrated prosthesis for lower-limb amputees reduced neuropathic pain and cognitive load, and reduced metabolic consumption during movements. This is a first step toward achieving a long-term amelioration of health and quality of life. I am also very proud to see the smiles of our patients, who demonstrate unique dedication and altruism for the development of novel solutions for disabilities.

Hong: I am most proud of the concept of sono-optogenetics described in my essay. The ability to convert one modality (sound) into another (light) leverages the deep-tissue penetration ability of ultrasound and the energy of photons to control cellular activity in vivo via light-sensitive proteins such as opsins.

Airan: The feedback from the scientific community has been incredibly positive and gratifying. I've received words of encouragement about my vision for enabling targeted drug delivery to the brain as a means to modulate its activity for neuropsychiatric applications. People want to see us succeed.

Yang: I am most proud of the two-photon holographic microscopes that I developed. They include the simultaneous multiplane two-photon microscope to image neural activity and the two-photon holographic microscope to modulate neural activity. Using these microscopes, we investigated the causal link of neuronal circuit activity and behavior, and demonstrated efficient approaches to modulate behavior.

Gradinaru: I am most proud of the scientists I trained, who are now making their contribution in academia and industry alike.

How do you think your research can help move your field forward?

Tian: Our latest unpublished work (which was mostly done by my former postdoc and my graduate student) suggests that nongenetic biological modulation with light intensity similar to that used for optogenetics is possible. This latest advancement pushes our neuromodulation technology closer to clinical application.

Gradinaru: As a neurotechnologist, I have developed methods that enable functional and anatomical access to the vertebrate nervous system, such as tools for readout and control of neural activity, tissue clearing and imaging, and gene-delivery vectors. I have used my mastery of distinct fields—neuroscience, protein engineering, and data science—to overcome some of the biggest challenges in optogenetics and gene delivery, developing microbial opsins that are tolerated by mammalian cells and viral capsids capable of crossing the blood–brain barrier in adult mammals.

Grossman: Aberrant neural activity plays a critical role in numerous brain disorders. By discovering a strategy to focally control the aberrant neural activities that underpin the pathologies and/or symptoms of these conditions, we may transform the lives of millions of people who suffer from debilitating brain disorders.

BIOGRAPHIES

2020 GRAND PRIZE WINNER

Viviana Gradinaru is a professor of neuroscience and biological engineering at the California Institute of Technology (Caltech), and cofounder and board member of Capsida Biotherapeutics, a fully integrated AAV engineering and gene therapy company.

2020 FINALIST

Guosong Hong is an assistant professor of materials science and engineering and an institute scholar of the Wu Tsai Neurosciences Institute at Stanford University.

BIOGRAPHIES

2019 GRAND PRIZE WINNER

Shuo Chen is a postdoctoral fellow at New York University School of Medicine. His research interests include minimally invasive methods to record and manipulate brain activity and how long-term memory is formed, stored, and recalled.

2019 FINALIST

Bozhi Tian is a professor in the chemistry department at the University of Chicago. His research focuses on bioelectronics, subcellular biophysics, and chemical dynamics at the soft-hard interfaces.

Raspopovic: My research moves from a basic understanding (via laboratory and animal experiments) to in-silico computational models and then to meaningful clinical validation through purposely developed demonstrators. I think that this framework, which I have implemented in peripheral somatosensory nerves for amputee applications, can be extended to a range of other neuromodulation approaches (such as vagus nerve stimulation).

Hong: I hope that my work can allow researchers in different fields to deliver light into the desired locations and depths of a living organism via minimally invasive ultrasound. This ability may enable a wide array of new possibilities for in vivo manipulation and interrogation.

Creed: The ultimate goal of my research program is to optimize neuromodulation therapies for disorders of reward processing, specifically for affective symptoms of comorbid chronic pain and substance use disorders. Our work would provide general strategies that could bridge the gap between our rapidly growing understanding of the neural circuit mechanisms underlying specific symptoms of chronic pain and substance use disorders and tangible neuromodulation therapies for these disorders. Developing neuromodulation protocols to treat symptoms of these disorders would increase treatment options for patients, while an improved understanding of the neurobiology underlying specific symptoms may help predict and optimize patient responses to different therapeutic strategies.

Airan: By enabling targeted drug delivery to specific brain regions and limiting drug exposure outside of those targets, we can enable a platform of better clinical therapies, as well as a better understanding of how these drugs yield their varied neuropsychopharmacologic effects.

Chen: My research aims to develop novel molecular actuators to enable precise, effective modulation of neural activity by transcranial stimuli. When combined with progress in physical approaches for brain stimulation, this work may have the potential to promote both fundamental research about how the brain works and the development of remote DBS therapies.

Gittis: I hope that our findings will lead to improved DBS protocols that can improve the therapeutic benefits of DBS, especially in late-stage PD patients. Our overall goal is to find strategies to actually repair circuit function in disease, rather than simply masking disease symptoms.

What do you love most about doing research? What gets you up and into the lab every day?

Grossman: I am excited by the challenge of inventing transformative neuromodulation technologies and motivated by the potential to help millions of people worldwide with debilitating brain disorders.

Tian: First, exploration, and second, mentoring. I have had a lot of setbacks and I learn and improve myself in this process. I also like to interact with my mentees, especially when I see good things happen for them.

Creed: I still really, really enjoy recording neurons and being at the rig helping students and postdocs tackle new or difficult experiments. I also love doing deep dives into the literature while helping plan the next experimental steps, and being in the lab when those experiments come to fruition.

Raspopovic: I love seeing the benefit of my work helping individuals with disabilities. Patients rarely get the best solution, because industry does not see a profit in developing expensive technology to solve their specific problems. We work hard to fill this gap. Importantly, I enjoy every day in the amazing environment of my young and talented collaborators, whose creativity and ambition are propelling our efforts.

Hong: I am always fascinated by the depth and breadth of nature. I strongly believe that the ultimate key to understanding biology lies in physics, yet only a small fraction of physical discoveries have been used to develop tools for biology research. I hope to leverage unexploited physics to facilitate biologists—especially neurobiologists—in their research.

Airan: I get to think creatively about a problem at hand, work hard with a motivated team, and utilize random bits of knowledge, and the end result has an honest chance of alleviating suffering for neurologic and psychiatric patients. Both the fun of working on these problems and the importance of the impact we could have are incredibly motivating. That, and lots of coffee.

Yang: I work at the interface between engineering and neuroscience. I enjoy the "aha" moments, such as sudden insights for new engineering inventions or new scientific discoveries. I enjoy how my research findings could benefit human society. I also enjoy working with my students, from whom I often learn new concepts.

Chen: I feel very peaceful when I am doing research. I love to concentrate on solving long-standing questions. Nothing is comparable to the moment when a new finding is made at the bench or a new idea has come up from communication with a colleague.

Gittis: I am endlessly fascinated by the brain and its ability to change and adapt when challenged by new experiences or disease. For every problem in the brain, there is a biological solution; we just need to know how to look.

Where do you see yourself in 5 or 10 years? What would you like to accomplish? What future plans do you have?

Grossman: In the next decade, I aspire to develop our TI stimulation strategy into a disruptive brain stimulation technology widely used by the neuroscientific community to discover neuromodulatory targets, and used by clinicians to treat brain disorders in which neuromodulatory targets were established.

Raspopovic: I see myself working in neurotechnology and helping to transfer our research outcomes to viable solutions for the wider population. I see myself creating new spinoffs that improve the quality of life of people with neurological disabilities.

Hong: I hope to be able to fully develop the sono-optogenetics approach in my lab, thus making it a widely accessible and useful tool for anyone who needs a noninvasive light source in vivo.

Airan: My main goal is to successfully clinically translate our system for targeted drug delivery and see it through first-in-human trials. I also want to extend this platform beyond small molecule drugs to encompass larger therapeutic compounds, and develop and clinically translate other forms of ultrasound-mediated drug delivery that we are working on. There's also the whole tenure clock thing that I should probably be more attentive to!

Creed: I hope to continue building on work from our lab, and to provide rationally designed neuromodulation protocols to treat affective symptoms of chronic pain that could ultimately be applied in clinical trials.

Yang: We are still limited by what we can use to fully investigate how the brain works, and I aim to develop advanced imaging and interventional tools, and to investigate functional organization and plasticity of neural circuits and understand how behaviors emerge from neuronal activities.

BIOGRAPHIES

2018 GRAND PRIZE WINNER

Nir Grossman is an assistant professor at Imperial College London and a fellow of the UK Dementia Research Institute. His team develops neuromodulatory interventions for people with neurodegenerative diseases.

2018 FINALIST

Aryn Gittis is an associate professor of biological sciences at Carnegie Mellon University. Her research seeks to understand how neural circuits in the basal ganglia are organized and function to shape movement in health and disease.

BIOGRAPHIES

2017 GRAND PRIZE WINNER

Meaghan C. Creed is an assistant professor and principal investigator at Washington University Pain Center at Washington University School of Medicine in St. Louis, where her research focuses on understanding how plasticity in the ventral basal ganglia mediates behaviors such as reward-seeking, risk tolerance, and hedonic valuation of rewards.

2017 FINALIST

Raag Airan is an assistant professor of radiology (neuroradiology) at Stanford University, a clinically active neuroradiologist, and director of a laboratory developing and clinically translating ultrasound-based therapeutic strategies for the nervous system.

Chen: I hope to run my own independent research lab at a prominent institution in the near future. Two major goals for me in the long run would be to cultivate next-generation neuroscientists and to tackle seminal challenges regarding noninvasive brain stimulation and the neural mechanisms behind long-term memory.

How do you balance your work and personal life?

Hong: I work off my stress by exercising: I run and do strength training on a daily basis and find physical exercise the best way to improve my energy, motivation, and happiness.

Airan: My brilliant wife (who is the managing partner for her law firm's office) and I have two kids. Especially through the pandemic, it's been tough to get our scientific, clinical, legal, and managerial responsibilities done while also making sure the kids are well fed, well enriched, and well educated, without just parking them in front of screens and toys. For the most part we're making it work by taking it day-by-day or even hour-by-hour, recognizing that the days are long but the years are short—and that mama and papa need an occasional break too!

Chen: I don't intentionally keep a work–life balance, as I enjoy my time both in and out of the lab by doing things that truly interest and inspire me. In my time out of the lab, I gain most happiness from activities such as going to an artist's solo exhibition or visiting a historical city for cultural inspiration.

Gittis: I am fortunate to have a supportive group of friends, coworkers, and family, especially my husband, who is the one who keeps the household on track.

Do you have any suggestions for other young researchers interested in submitting a prize entry in the future?

Creed: Communicate why *you* are excited about your research, to emphasize the elements that make your body of work unique and the vision you have for the future impact of your work beyond the immediate technical findings.

Tian: Try to find a unique aspect of your work and tell a good story. There are important lessons beyond the science that you will discover through your writing process!

Gittis: Writing the essay was a great experience. Even if you don't win, explaining your research in concise, accessible language is an important exercise that will improve your writing and presentation skills.

Grossman: Radical innovation requires a clear, transformative goal; questioning common scientific assumptions; a systematic trial-and-error plan; and the courage to fail.

Raspopovic: Go for it!

Hong: My suggestion is the three "i's": Find an important question, design an innovative solution, and tell an interesting story.

Airan: If your research at all applies for the award, submit an application. You lose every grant or award you don't apply for. I wasn't sure if my own work applied to the mission of this award but was encouraged by my postdoc advisor to submit. I'm certainly glad I did!