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Q & A

Pawan Sinha

Pawan Sinha is a professor of vision and computational neuroscience in the Department of Brain and Cognitive Sciences at MIT. He received his undergraduate degree in computer science from the Indian Institute of Technology, New Delhi and his Masters and doctoral degrees from the Department of Computer Science at MIT. Pawan is a recipient of the Pisart Vision Award from the Lighthouse Guild, the inaugural Asia Game Changers Award, the Presidential Early Career Award for Scientists and Engineers (the US Government's highest award for young scientists), the Alfred P. Sloan Foundation Fellowship in Neuroscience, the John Merck Scholars Award for research on developmental disorders, the Troland Award from the National Academies, the Oberdorfer Award from the ARVO Foundation, and the Distinguished Alumnus Award from IIT Delhi. Pawan was named a Global Indus Technovator, and was also inducted into the Guinness Book of World Records for creating the world's smallest reproduction of a printed book.

What brought you into the field of vision research? My interest in art. Inspired by my sister, I started drawing and painting from an early age. I was especially fond of doing portraits. The results often left me puzzled; why did some portraits capture likeness so well while others, that seemed to have taken just as much of my effort, did not? I used to wonder about what crucial information needed to be included in a drawing for it to be a faithful rendition. This, of course, is very close to the question a vision scientist would ask: what information from an image does the brain extract in order to recognize an object? So, my interest in vision had an early genesis, but my actual journey to being a vision scientist was a little circuitous. I majored in computer science and then went to the University of California at Berkeley with a plan to do a PhD in high-performance CPU design. But, my heart was not in it; every hour spent tweaking VLSI chip layouts seemed like drudgery.

As luck would have it, Donald Glaser (who had won a physics Nobel Prize for inventing the bubble chamber) had become interested in vision and was offering a free-form course exploring various topics in the field. I loved it and followed up with courses from Karen DeValois, Jitendra Malik, Corey Goodman and Frank Werblin, all amazing teachers. I knew then that this was the field I wanted to be in. A year later, I transferred to the AI Lab at MIT to work on computational vision.

(By the way, two of the portraits that I had done in elementary school, and that turned out reasonably well, were of the Soviet Union's Premier Leonid Brezhnev and the UK's Queen Elizabeth. I mailed them the pictures and got back a box full of books and stamps from Moscow and a nice letter from Balmoral Castle. Talk about encouragement.)

Which problems in vision do you think are the most fascinating? There are numerous open problems in vision. Several years ago, I had reached out to about 60 leading visual neuroscientists and asked them to list the most significant open questions. I pored over the lists I got back and was amazed by the diversity of challenges still in front of us. There were several overlaps across the lists too. I call the top 17 of these the 'Hilbert Problems in Vision', after the list that David Hilbert had proposed to mathematicians over a century ago. The problems span low-level neural mechanisms to high-level computations implemented across multiple sites of the brain. It is fair to say that there is still much to be discovered about vision.

Of the many interesting challenges in vision, the two that fascinate me the most are the principles behind robust object recognition and object discovery. By 'discovery' I mean the process by which the brain is able to analyse complex natural visual inputs and find, in a largely unsupervised manner, subsets of features that constitute distinct objects (or, more colloquially, how the brain puts together the visual world). Considering the vast amounts of data and the robustness of performance, this is an absolutely amazing accomplishment.

Photograph by Ed Quinn.

I would like to understand the computational underpinnings of this process and also any biological constraints it is subject to, such as those related to neural plasticity.

With machine vision systems now performing almost on par with humans, do you think that the study of human vision will soon be considered a quixotic quest, of academic interest but superfluous from the practical perspective? Undoubtedly, great advances have been made in machine vision over the past several years, but claims that machine vision systems are at the threshold of, or already exceed, human capabilities are somewhat over-wrought. Face recognition is a case in point. Beginning around the mid 2000s, we started seeing headlines heralding machine systems that were supposedly better than humans. But, these claims are typically based on constrained test-sets, for example images with reasonably good resolution where the faces are largely frontal. Getting high performance on such images is no mean feat, but one has to be cautious in extrapolating from this accomplishment to broader claims. Indeed, in our testing, systems that show good performance on one set of test data are often dramatically compromised by small excursions beyond the test set parameters. For instance, 'adversarial images' also demonstrate that small changes to

an image can unexpectedly change the classification labels produced by deep nets. Human performance, by contrast, is robust across many such changes. All of this is to say that it is perhaps premature for machine vision to declare victory over its biological counterpart. A study of the latter has much to offer in terms of insights for how to construct a robust vision system.

Even if we were to accept the premise that machine vision systems are now close to humans in capability, there are a few factors that make a study of the biological visual processes a very worthwhile undertaking. First, to understand, and eventually intervene in, visual disorders, we must necessarily study their biological roots. Why are prosopagnosics unable to extract identity signals from faces? Why are some children with autism attracted to spinning parts of objects? Why does amblyopia cause acuity loss? These are questions of great import for millions of people, and their answers lie in understanding the functional architecture of biological vision. Second, biological vision systems are remarkably versatile. They excel not just in dealing with a few object classes, but several. Machine vision systems would benefit from knowing what kinds of representations and algorithms their biological counterparts use to achieve this versatility. Third, biological vision systems are mostly self-taught and reach their impressive capabilities with quite limited experience. A few exposures to a toy is all it takes for a young child to recognize it subsequently under very different viewing conditions. State-of-the-art machine vision systems, by contrast, need massive numbers of training images. A study of biological systems can reveal strategies for more efficient object discovery, a topic of great interest to my lab.

How is your lab studying the problem of visual object discovery? My students and I have had a unique opportunity to study this problem. I use the word 'unique' because we are able to couple our scientific investigations with a humanitarian mission. We screen children in remote parts of rural India to find those who were born blind, but can be treated. We provide free sight surgeries to these children. The onset of sight is transformative for the lives of children and their families. It is also an incredible opportunity to investigate the very initial stages of object discovery. We conduct behavioral as well as neuroimaging studies and are able to glimpse the rapid changes occurring in the children's visual abilities and their brains. The results also provide guidance for the computational modeling work we undertake back at MIT. We call this overall effort 'Project Prakash' (http://www.ProjectPrakash.org) after the Sanskrit word for luminous energy.

How has the field at large responded to Project Prakash? Very positively. I started Project Prakash a few years before I came up for tenure. I must confess that I was a little worried about how this project would be seen by my departmental colleagues and the neuroscience community at large. As the project got underway and we started getting results demonstrating visual plasticity late into childhood and even early adulthood, the response from other researchers was enthusiastically positive. The sincerity and unanimity of this reaction was such that I felt, and feel, that Project Prakash is not just an effort from my lab, but an enterprise shared across the entire community. We all take pride in its progress and help move it further, along both the humanitarian and scientific avenues.

What is next for Project Prakash? Although it is now 10 years old, it feels as if Project Prakash has really just scratched the surface of scientific possibilities. In the coming years, we plan to treat many more children and address new research questions. In our work so far, we have primarily gathered evidence showing that visual skills can be acquired late in the developmental timeline. The natural next step is to ask *how* this happens. We intend to undertake densely sampled longitudinal psychophysical and neuroimaging studies to be able to correlate the timelines of behavioral and neural changes. Additionally, we shall develop computational models of visual learning guided by our empirical data. To accomplish these goals, we have started work on creating a 'Prakash Center for Children'. Not only will this center provide medical care and undertake scientific research, it will also formulate and deliver specialized educational programs for newly sighted children so as to maximize their ability to lead independent adult lives. It is an ambitious goal, but given the goodwill for Project Prakash, I am convinced that it will happen.

Some years ago, a picture of your then infant son wearing a camera on his forehead appeared on the front page of* The New York Times*: what was that about? For researchers interested in brain development, the birth of a child is a doubly remarkable event, eliciting not only the joy of becoming a parent, but also the awe of witnessing one of nature's most impressive learning systems. I was no different. I had many studies planned for Darius even before he was born. One of them was simply to observe the world from his perspective. The goal was to guide the design of a machine vision system that could take in naturalistic input and autonomously discover the objects therein (the challenge of object discovery I alluded to earlier). To this end, I placed a small webcam on Darius' forehead — with its optics modified to mimic some of the known limitations of the infant visual system — and recorded short clips of the world from his point of view. It was very interesting to see how the endogenous and exogenous constraints of Darius' biology and environment highlighted and/or simplified the nature of visual input his brain had to deal with. A reporter from *The New York Times* happened to be at a talk I was giving where I had included a picture of Darius with the webcam. She requested a copy and had it accompany an article about scientists whose children also sometimes act as their scientific subjects. The article appeared in a Sunday edition of the *Times*, which also happened to be the one that coincided with Barack Obama's inauguration. I got a flood of email that day, mostly positive, but also some from well-meaning people who felt that I was exposing Darius to grave dangers. It was quite an experience.

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Darius, who is now 10 years old, loves to show the *Times* article to his friends. He enjoys coming to MIT whenever his school schedule lets him. But, other than a few scattered experiments, he has not really participated in any significant studies of visual development in my lab. The primary reason is that for the kinds of questions I am interested in — the early stages of visual learning — he is simply too old. In fact, even a year-old baby is probably too mature for these studies in terms of his or her visual capabilities. Visual skills develop so rapidly that we really need to study them right from the moment of eye opening. This is part of the reason I am so drawn to Project Prakash.

At the risk of sounding mawkish, I do want to say that although Darius is no longer a study participant for me, there is a very significant way in which he has impacted how I think about my work. Having him has made real for me the nebulous theoretical notion of parental love. I now understand the intense affection every parent must feel for their child and, by extension, the agony if he or she is in distress. This has given me a renewed appreciation for our field's mission of understanding typical and atypical brain development, and our obligation to succeed.

Do you still draw and paint? Yes, and I now have collaborators! Given how important and enjoyable art has been for me, I have tried to introduce it to others. Darius and I often paint together and we try to find new art techniques. My students and I have used some of these techniques in 'UnrulyArt', a hands-on art initiative directed towards children with different types of sensory, motoric or cognitive challenges. We have conducted several UnrulyArt sessions in New Delhi with Project Prakash children and in Boston with children who have autism. These have been exceptionally joyful experiences for everyone involved. We recently had an exhibition of some UnrulyArt pieces in Princeton University. Just like science, art has greatly enriched my life. I know that it will forever be a part of me.

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Quick guide

Tensins

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What are tensins? Tensins are a group of proteins that typically reside at a specialized cell–matrix junction called the focal adhesion. The tensin family has four members in mammals (tensin-1, tensin-2, tensin-3, and cten; Figure 1A), but only one in *Caenorhabditis elegans* or *Drosophila melanogaster*. Tensin-1, -2, and -3 are larger proteins of 170–220 kDa. In contrast, cten is a smaller, 80 kDa protein, but is included in the family because it localizes to focal adhesions and also contains the Src homology 2 and phosphotyrosine-binding (SH2–PTB) tandem domain that is unique to the tensin family.

What are focal adhesions? Focal adhesions are transmembrane junctions that connect the extracellular matrix with the actin cytoskeleton. These structures allow cells to communicate with their outside environment and respond appropriately, leading to numerous cellular activities, such as cell attachment, migration, proliferation, and gene expression. Focal adhesions are formed around a transmembrane core of an $\alpha\beta$ integrin heterodimer; the extracellular region of this heterodimer binds to a component of the extracellular matrix, and its cytoplasmic tail is the site for anchoring the actin cytoskeleton and adaptor proteins to the plasma membrane.

How was the first tensin discovered? In the 1980s and 1990s, researchers were searching for the 'protein X' that could anchor actin filaments to focal adhesion sites, thus maintaining the 'tension' (how tensin was named) between the cytoskeleton and plasma membrane. Tensin, specifically tensin-1, was first cloned by screening a chicken expression library using an antibody raised against a pool of polypeptides that had been shown to bind to actin and reduce its polymerization rate. Given that the antibody also labeled focal adhesion sites in cells, the antigen for the antibody was expected to be an actin-binding protein that localizes to focal adhesions. It was later demonstrated that tensin-1 interacts with the barbed (i.e. growing) ends of actin filaments and crosslinks these filaments, while its PTB domain binds to the β integrin tail. Thus, tensin-1 molecules directly connect actin filaments to integrin receptors. Not surprisingly, later studies identified additional molecules that are able to bridge actin filaments to integrins.

What are the cellular functions of tensins? Being focal adhesion residents, it is not surprising that tensins contribute to the processes of cell attachment, migration, and proliferation, since these are major functions of focal adhesions. Tensins regulate these functions through interactions with relevant molecules (Figure 1B). In addition to binding to the actin cytoskeleton and integrins, tensins regulate the Rho family of GTPases, such as RhoA and Rac1, through interactions with GTPase-activating proteins (such as DLC1) or guanine nucleotide exchange factors (such as DOCK5), which respectively downregulate and upregulate Rho GTPase activity. These GTPases play critical roles in cytoskeletal dynamics, cell movement, and organelle biogenesis. The SH2 domains of tensins recruit numerous tyrosine-phosphorylated signaling proteins, including Src, Fak, p130Cas, paxillin, c-Met, EGFR, c-Cbl, and Axl, and function as signaling hubs. Another interesting function of tensin-1 is its ability to regulate the internalization of ligand-bound integrins by controlling their centripetal movement, positioning them for Arf4-dependent endocytosis. Intriguingly, the highly homologous tensin-1, -2, and -3 proteins do not always have similar regulatory roles in the same processes; for example, tensin-1 promotes and tensin-3 suppresses cell migration. The reason for the functional discrepancy is currently unknown, but it may relate to each tensin's unique spatiotemporal localization and binding partners.

How about their biological functions? These functions have been revealed largely by studies of knockout mice. Tensin-1 is essential for maintaining normal renal function, since knockout mice establish histologically normal kidneys but eventually develop cysts and die from renal failure. Additionally, loss of tensin-1 markedly reduces the processes of skeletal muscle regeneration and angiogenesis. Tensin-2 mutant mice also