Thomas D. Albright

Thomas D. Albright at the Indian Institute of Science, Bangalore on 22 October 2011.

Vastusāmye chittabhedāttayorvibhaktaḥ panthāḥ

Sage Patanjali

Many years ago, the Indian sage Patanjali in one of his 196 *yoga sutras* (above) put forth a theory of perception that has been explained as follows[1]: '… Even though the object is one, its perception becomes different according to the difference of the *chitta* (individual consciousness which includes the conscious, subconscious and unconscious levels of mind). The same object is perceived differently at different times because of the difference in the mental condition or the instrument of cognition ....' Other *sutras* indicate that when we experience objects, our mind comes in contact with them through the sense organs. When next there is a similar contact, memory of the past experience arises if the experience is not allowed to escape from the mind[1].

Research in more recent years on the operation of the brain has shown that, 'If a previously encountered search display is seen again, the search process operates more quickly even though the searcher has no ability at all to recognise that the display has been seen before. Implicit memory processes, which may be called tacit knowledge, are increasingly recognised as playing an important role in the control of behavior'[2].

The work of Thomas D. Albright is related to the above concepts. He studies the neural structures and events underlying the perception of motion, form and colour, and those involved in the interactions between top-down signals that reflect visual memories and bottom-up signals that convey retinal image content. The findings of his group provide insights into the brain mechanisms that underlie the natural human tendency to see what we expect to see ... (http://salk.edu/faculty/albright.html)[3].

Albright is currently Professor and Director and Conrad T. Prebys Chair in Vision Research at the Vision Center Laboratory, Salk Institute for Biological Studies, California (http://www.vcl.salk.edu/). In recognition of his contributions to the field, Albright has been elected to the US National Academy of Sciences, the American Academy of Arts and Sciences, and the American Association for the Advancement of Science. He also holds a DST-IISc Centenary Chair Professorship[4].

Albright spoke to *Current Science* when he visited the Indian Institute of Science (IISc), Bangalore this October.

Is this your second trip to India?

I have been to India many times. I came here first in 1983, almost 30 years ago now, and travelled all over the north of the country. I was young and had just gotten my Ph D. I came to a conference organized by the National Brain Research Centre (NBRC) in Delhi in 2003 and eventually became a Member of the Scientific Advisory Committee for the NBRC. I have come back every year for those meetings, which is great for me because I fell in love with India in 1983.

How do you find the differences in culture and research facilities in India compared to the US?

Well, things have changed a lot recently. When I was here last summer I went on a lecture tour to several institutions, including the Tata Institute in Mumbai, Indian Institute of Chemical Biology in Calcutta and Jiwaji University in Gwalior, and the research facilities in general now are first rate.

It has improved?

Greatly! This is in part because the Government has much more money now. When I was here in 1983, I was so enchanted by India and briefly considered spending a year here as a postdoctoral fellow. My goal was, not so much to further my career, but to get the life experience of spending a year in India. I looked into it and the answer I got was: 'Well, there is no neuroscience!' There were some neurosurgeons who were practising neuroscience at that point, but there was no basic research in neuroscience. Then there was no money. And if there was any money, it wasn't going to go to an American; it would be dedicated to an Indian pursuing that line of research.

I came away realizing that India had no neuroscience research community. It made sense because this was a developing country – still is a developing country – and the priorities for India 30 years ago were very different; it was bridge and road building, and infectious diseases. A basic research programme in neuroscience – that as a priority hadn't been recognized; plus, the country was poor. Now, with the economy growing by leaps and bounds, there is money to fund basic research in neuroscience.

The cultural differences are extreme. I came here, I thought, well informed. I had read every book I could find about India and had seen pictures of things … But when I got off the plane in Calcutta, it was a shock! India is so different on so many different dimensions from life in America. There are many places in Indian society where there is a sensory overload and experiences like you would never find in America.

I have travelled in other places. I have travelled in Western Europe which is a lot like America, except it is older. I have travelled in South America … . But India is the most different place I have ever been to, in a very good way. It is a complicated place to travel, but I just embraced it. It somehow appealed to me, still does, though India today is very different from 30 years ago.

What are your responsibilities as a DST–IISc Centenary Professor?

I am doing my best to interact with the neuroscientific community here. There are some faculty in the Centre for Neuroscience I have known for a long time – Vijayalakshmi Ravindranath, Aditya Murthy and Shyamala Mani. Last summer I got to know S. P. Arun and tomorrow (23 October), I am helping him with an experiment related to the study of visual perceptual experience and object

recognition that is being done in the Centre. I view the Centenary Professorship as a means to offer my experience to a growing neuroscience community, as an opportunity to connect and collaborate with top Indian neuroscientists, and as a chance to meet students. India is full of brilliant students who are like sponges, they want to learn; and this is an exciting field, neuroscience. I hope that someday these students will come and work in my laboratory!

Over the summer, I organized a workshop here with Murthy[5]. We had 50 of the best and brightest students from all over the country come to that workshop and it was a huge success. I recruited about ten faculty presenters from America … there was one imminent scientist who came from Italy. The students got a lot out of it.

You are here this time only for three days in Bangalore?

Well, I was in Delhi for the Scientific Advisory Committee meeting of the NBRC. I would stay longer, but unfortunately I have to go to another meeting in Paris next week. So this time, I am just doing this experimental procedure tomorrow with Arun and on Monday (24 October), I'll probably talk to some of the scientists here and I have a lecture at 4 O'clock.

But you'll be coming back often?

Yes.

What is your current research on?

In the experiments that we do, the subjects are monkeys. Monkeys are used for these procedures because they see the world pretty much the same way that we do and their brains are organized in a way that is very similar to ours. There is a long tradition of using the Rhesus monkey, in particular, as an animal model for understanding the brain bases of visual perception. In fact, Torsten Wiesel was one of the first to use those techniques[6], and the kind of work that I do is very much following in the tradition that he established.

How far can you extrapolate these studies to humans?

Well, the major differences between the brains of Rhesus monkeys and humans are two. One is they don't have language. Much of the way that I perceive the world is influenced by language. I can use linguistic means to remember things in my environment. So I can in part have a pictorial memory. For example, when I look at this little park area here I will have a visual image of it in my mind, but I will also remember how it is constructed in a verbal conceptual way. That facilitates my ability to remember what this space looked like if I was trying to remember it. Or if there was somebody I met and I was trying to remember him, I might use verbal description of the person in order to help conjure his image in my mind's eye. So language makes a difference. In that sense, monkeys probably do see the world a little bit differently from us.

Another thing that differs between us and monkeys is – this is just an anatomical difference but has implications – that we have a greatly elaborated frontal lobe, which is a part of the cerebral cortex. There are parts of that elaborated frontal lobe that are involved in decision-making, planning and executive control (a monitoring system to make sure all your actions are coordinated and scheduled). People with damage to the frontal lobe have a difficult time making decisions, in particular making decisions based on the emotional consequences of those decisions. So, there is probably a difference there. You could extrapolate from that and say: 'Well, monkeys probably aren't as good in planning for the future as we are'. I can plan and make up whole scenarios for the rest of my life and – although we don't really know – it is probable that a Rhesus monkey doesn't make those kinds of plans. A Rhesus monkey is probably thinking at most about what it is going to do in the next hour or two.

But I don't think these differences have much of an influence on low-level things like sensory processing, which is what I study.

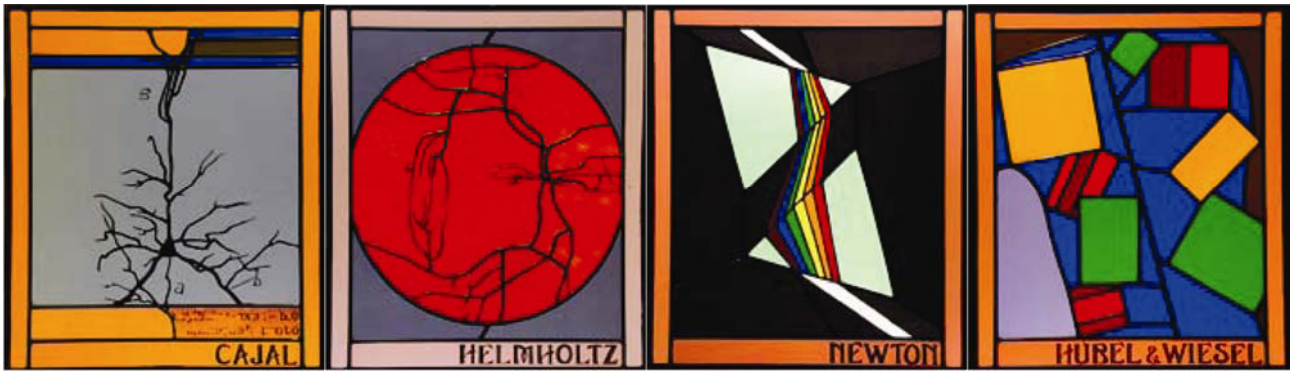
How has the field progressed over the years? How has our understanding improved?

Mankind has long had an interest in how the brain works and there is natural human curiosity about how we see, think and remember. There have been many significant developments in the field of neuroscience over the past 150 years or so. In the field of visual neuroscience, one of the most important developments in the past half-century was the work of David Hubel and Torsten Wiesel[6] (see Box 1). They, along with colleague Stephen Kuffler, completely transformed the way we think about how vision works. They were able to physiologically demonstrate the properties of cells in the visual system and that then gave insights into how information is transformed from the point where light enters the eye up to the subsequent stages in the visual cortex.

We are able to recognize complex objects. How does that happen? There must be some complex representations in the cortex, a collection of cells or a cell that will be activated when I look at those palm trees over there or if I look at a person's face. The original approach that Hubel and Wiesel took was to look at how cells in the cortex represent the patterns of light cast upon the back surface of the eye – a surface known as the retina. However, what you see is not determined solely by the image on the retina. It is determined to a great degree by what you've seen before, by the things stored in your visual memory. This is something that my laboratory has worked on recently and we've made great strides in understanding how prior experiences are represented in the visual cortex.

In simple terms, the goal of vision is to identify what physical attributes of the world in front of us cause the retinal images received by the visual system. This is an extremely difficult problem because much of the visual information in the retinal image is noisy and ambiguous. In addition, biological vision is confronted with the so-called 'inverse problem of optics', which states that there simply isn't enough information in the retinal image for you to uniquely identify what gave rise to that image. The only way we can possibly solve this problem is by taking into account other sources of information, such as the things that we've seen before. For example, that palm tree casts a particular image on my retinae. I recognize it as a palm tree because I have seen them before and know implicitly what the relationship is between the image and the real-world stimulus that caused that image. So we have signals ascending into the visual cortex from the retina, and at the same time, signals descending from the memory store – these signals collaborate to generate our perceptual

Box 1. On the pictures found on the laboratory webpage of Albright.



There is an interesting history to these pictures. I was hired at the Salk Institute by Simon LeVay, who was a student of David Hubel and Torsten Wiesel. Simon was highly respected, a very skilled neuroanatomist, a real scholar and intellectual. A friend of Simon's made these stained glass panels for him. Simon's plan was to build a Centre for Vision Research at the Salk Institute. Vision research is generally considered today as one of the leading areas of systems neuroscience, and the hope is that if we understand how vision works, we can understand lots of other things about the brain. So the Salk Institute decided to focus on the visual system, in part because of the successes of Hubel and Wiesel. Simon was the first person who was part of that vision research group and I was the second. His plan was to mount these panels in the laboratory, signifying that this was the Vision Research Centre. When Simon left the Institute, for personal reasons, he left the panels behind and I asked him if I could have them. So now they are mounted in a window in my office.

They represent important figures in the history of vision research. Ramón y Cajal was one of the great neuroanatomists in the late 19th century, early 20th century. He was the first person to demonstrate clearly the morphology and architecture of neurons in many areas of the brain. The picture is meant to represent a neuron.

Hermann von Helmholtz was a German physicist and physiologist. He had a lot of insights into the way the visual system worked. A brilliant man! This was in the mid-19th century, around 1850 or so. One of the things Helmholtz invented was the fundus camera, which enables you to look through the pupil and see the retinal surface at the back of the eye. The picture is a depiction of what you would see using the fundus camera. The lines are meant to represent the blood vessels that are coming into the retina. The point on the right is where the blood vessels enter the back of the eye and is called the optic disc. It creates a blind spot because you have no photoreceptors at that location. This image is iconic of a physiological approach to understanding vision.

Isaac Newton was among the first to understand the physics of light. He discovered that white light is composed of multiple wavelengths of light, which can be separated using a prism. In the picture, you can see how the light is expanded as it comes out of the prism; the white light turns into multiple colours. The last panel iconically depicts the contributions of David Hubel and Torsten Wiesel, who transformed our understanding of vision in the middle of the 20th century with their discoveries of the ways in which visual information is encoded by cells in the visual cortex.

So, these images are iconic; they symbolize heroes in the field of neuroscience, and more particularly, in the field of visual neuroscience.

experiences of the world. These experiences are, in effect, our best hypotheses about the likely causes of the images cast upon the retinae.

There is a concept in ancient Indian texts that our present perceptions and actions are coloured by our past experiences and memories ...

It is a simple idea. I don't profess to have developed this idea. What I have brought to the table is an understanding of how it is implemented by the brain. You can find elements of this idea in philosophical and psychological discussions back into history from multiple traditions. I love learning about the history of things, especially ideas about the brain and perception and behaviour. Modern neuroscience is a very young field, but interest in how the brain works goes back centuries, millennia. I think it is useful and inspiring in some cases to know something about that history.

There was a lot of interest in the 19th century although they didn't have the tools that we have today, they couldn't do the experiments that we can do today. But they raised similar questions and had similar insights. I think it is useful and appropriate and insightful to know how we got to this point partly because in this field we are trying to understand who we are, what our experiences are and why we perceive the world the way we do. It is likely that mankind has always wanted to know the answer to that.

The knowledge of our brain cells is sometimes not reflected in our behaviour?

That's right. If I look outside in the morning and see that the sky is cloudy and rain is likely, the rational thing to do as I go out the door would be to take the umbrella. But I may or may not take the

umbrella. I know what the right thing to do is, but as I'm walking past the umbrella stand I might be thinking about what I had for breakfast, I might be scratching my head, or maybe I just don't care if I get wet. So there are many reasons why we don't do the right thing or the rational thing, that we don't act upon the knowledge that we have.

The study that we did was about identifying neuronal representations of knowledge and recognizing that there are knowledge-based signals in our brains that can be dissociated from behaviour. We could show that there was a neural correlate, a pattern of neural activity that represented the right thing to do. But in many cases, our experimental subject (monkey) didn't do that thing. Who knows why he didn't do it? You can conceptualize this in the form of a flowchart: information about the right thing to do originates on one side of the chart, and our actions propagate on the other side of the chart. Between these two processes is a decision centre, which has multiple sources of noise coming into it, factors that ultimately influence whether the incoming information leads to the correct action.

We never know why we don't do certain things?

No, we can find out why we don't. It is easy to come up with a hypothesis about why you didn't do something that you knew you should do. But at the time, who knows the real reason why?

So we can't be sure?

I wouldn't say we can't be sure. I think we can confabulate a lot about the reasons we do things, after the fact. A general principle of human existence is that we try to make stories out of our lives. This is important for having a coherent sense of oneself, to look at the track we've followed through our lives and have it make sense to us. As people get older, they tend to (though this is not a conscious process) make aspects of their life conform to one another and that involves, I think, a tweaking of reality or personal history. For example, you might remember something that happened 20 years ago in a way that is consistent with the sort of person you are now, that can somehow justify the person you are now.

What are the contributions of neuroscience to other fields?

I am a member of an organization called the Academy of Neuroscience for Architecture (ANFA; http://www.anfarch.org/). The organization operates on the premise that if we know enough about the brain, then we ought to be able to use that information to guide the design and construction of human environments such as habitats and spaces for learning and working. Good architects have an intuition about what makes people feel good about the space they are in, makes people work efficiently in certain spaces and what facilitates learning, and they implement these (typically implicitly). But one of the goals of ANFA is to derive some foundational principles from neuroscience that can be used to guide architecture. This cross-disciplinary bridge that we are trying to build is at a very early stage. ANFA was founded about ten years ago and up to this point, it has largely involved a lot of interesting conversations between neuroscientists and architects. Our hope is that at some point the field of neuroscience will be in a position to inform architecture in both broad and specific ways.

There are similar ideas that apply to forms of art, for example. In my lecture on Monday, I will speak about how an understanding of visual memory gives us some insights into how we perceive art. In most art created in the last 150 years or so, we can see a big move away from realism, at least in the West. A major non-realist movement is that known as Impressionism, which originated in France in the late 19th century. The goal of the impressionist painters was to not provide all of the realistic details but just to provide an impression, with the assumption that viewers would fill in the blanks based on their own experiences. So the experience is richer by virtue of drawing the viewer into the process.

The other part of my talk is about criminal justice. One thing that I tend to do when thinking about vision and our understanding of how the brain gives rise to vision is to consider how that knowledge bears on an understanding of common-place visual experiences. There are lots of things we do on a regular basis in which we depend very heavily upon vision without even being aware of it. An example of that is forensic fingerprint analysis, which has been around for about 125 years. It is considered the Gold Standard of forensic evidence in criminal proceedings. It really boils down to a person making a visual comparison between fingerprints that are stored in some database (which are of high quality and obtained under optimal conditions) with those taken from the crime scene (which are noisy, incomplete and ambiguous). Forensic fingerprint analysis is an example of what is known as a binary visual classification problem. It is the same type of problem as finding your luggage on the luggage trailer or tracing your car in a parking lot. You are trying to compare one stimulus with another that is either there at that moment or that you have in your memory. In the case of forensic fingerprint analysis, the problem has significant weaknesses that can be readily understood by consideration of the ways in which vision works. This type of understanding leads to the conclusion that there have been thousands of people inappropriately incarcerated based on flawed conclusions drawn from visual analysis of forensic fingerprints. An appreciation of how memory influences visual processing has great relevance to our understanding of this problem and its implications for justice in society.

What do you expect in the future in this field?

The future is bright. Today I can tell you a lot about how individual cells in the cortex are correlated with perception or visual memory or cognition. But I don't know a lot about how that happens, about the nature of the wiring or the brain's computational strategies that lead to the observable neuronal correlates of perception. Part of the problem is that these circuits are so fine and so densely packed into the brain that it is very difficult to see what is connected to what, and synapses themselves are microscopic. There are a variety of new techniques, however, mostly originating from the fields of genetics and molecular biology, that will enable us to tease apart the circuitry to be able to understand these mechanisms.

These techniques are fairly advanced when using on animals for which it is easier to make genetic manipulations, particularly mice. You can grow new generations of mice in a few weeks. You would like to be able to do those genetic manipulations on monkeys as they have a

much richer repertoire of visually guided behaviours and visual perceptual experiences, but their generational time (several years) makes it impractical. But you can use viruses as tools to introduce genes of interest; take out all the bad stuff from the virus and put in particular genes that will, for example, alter the behaviour of particular classes of cells in the visual system.

There is a new technique available called optogenetics. This is an ingenious technique and has been around only for 5 or 6 years. The technique is based on the use of light-sensitive protein molecules (known as opsins), which are derived from pond algae. The genes that encode for these opsin molecules have been identified and can be loaded into a viral vector, which can in turn be injected into the brain. The opsin gene will then be expressed in the infected host cells, and the opsin molecule gets implanted in the cell membrane. This molecule acts as a light gated valve through which ions can flow into the cell. If you shine light on the cell, it will open up a little window on the membrane and ions will go into the cell and change its membrane potential, which will change the ability of that cell to have action potentials (electrical events that carry the information by neurons). So you can turn cells on and off in the brain by shining light on them, and the beauty of it is that light is very easy to control in space and time. Lasers with microscopic beams of light zap particular cells in the brain with precise temporal control and influence what the cells are doing. From this, you can infer how those cells contribute to the circuits that underlie visual perception. These are techniques that are just coming on-line now and will make a huge difference in our ability to understand what the cellular mechanisms of perception and behaviour and cognition are.

From the study of mice, can you extrapolate to humans?

Mice are valuable in this research endeavour in part because you can easily do these genetic manipulations because their generational time is so short. Monkeys are important because they perceive, interact with and think about the world in a way that is very similar to us. If you try to study vision in a mouse, you can learn a lot about the basic aspects of visual function. But if I want to know, for example, how visual memory influences my ability to recognize a face, I am not going to get very far with a mouse; I can easily do that in a primate because this is a general feature of primate behaviour.

If you want to understand how a circuit works and if you believe the circuit is evolutionarily conserved – for example, we might conclude that the same neuronal circuit exists in a mouse and a primate for early visual processing – then there are many advantages to the use of molecular-genetic tools for investigation of the circuitry in a mouse. It is a much bigger deal to work with monkeys. Nonetheless, there are many things you can only understand by studying a monkey. So we have this two-pronged approach – using mice because there are basic things we can more easily understand in them in that they are a lot easier to handle with genetic manipulations, and using primates because they have a much richer behavioural, perceptual and cognitive repertoire.

1. Saraswati, S. S., *Four Chapters on Freedom: Commentary on the Yoga Sutras of Patanjali*, Yoga Publications Trust, Bihar, 1976.
2. Findlay, J., In *Thinking About Almost Everything: New Ideas to Light Up Minds* (eds Amin, A. and O' Neill, M.), Profile Books Ltd, London, 2010, pp. 138–139.
3. Albright, T. D., Lecture delivered at IISc, Bangalore on 24 October 2011 entitled 'Art, Magic and Criminal Justice in the Age of Neuroscience'.
4. Ten DST–IISc Centenary Chair Professorships have been established by DST at IISc to 'attract world class researchers to visit the Indian Institute of Science in particular and India in general to conduct collaborative research and initiate cutting edge research and development at the Institute' (http://www.iisc.ernet.in/news/iiscdstprof.pdf?riisc=6e9ea4a2f9e27975eab8e7031737ff82). Other current awardees are: Venkatraman Ramakrishnan (MRC Laboratory of Molecular Biology, Cambridge), Uriel Frisch (CNRS, Observatoire de Nice, France), P. M. Ajayan (Rice University, Houston) and Bruno Riccò (Università di Bologna, Bologna – Partita, Italy).
5. 'Brain and Cognition Workshop' held at and organized by the Centre for Neuroscience, IISc, during 5−14 July 2011.
6. Monto, G., *Curr. Sci.*, 2011, **100**, 154–156.

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