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The Brain and Mind

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Professor M.G.K. Menon, President of the Institute, Professor S.K. Pal, Director of the Institute, members of the faculty, distinguished guests, and students and staff of the Institute:

It is a particular privilege for me to address the 43rd Convocation of the Indian Statistical Institute. I offer my warmest congratulations to the students who are receiving their degrees today. Your degrees represent the culmination of considerable effort on your part, as well as on the part of your teachers and your families and loved ones. They too deserve our congratulations, and our gratitude.

The ISI has a special place in the intellectual history of interdisciplinary research and education not only in India but also in the world. The foresight of P.C. Mahalanobis was to recognize that the practice of science starts with measurements, and extends through the analysis of data to the extraction of concepts that form the intellectual foundations of a field. This scientific method can be applied to a range of phenomena, which may seem superficially disparate but are united conceptually.

I am privileged to work in a new field, Neuroscience, which is being transformed by this method. Neuroscience is a quintessentially interdisciplinary field, for it relies for its advances on fields as diverse as biology, physics, chemistry, mathematics, psychology, engineering and even the social sciences. Today, I hope to share with you some of the insights that our field has derived into the workings of the brain and the mind. It is always tempting to claim a great deal for a field, but neuroscience holds particular lessons for understanding the role of change in nature, and the nature of change itself.

The human brain

The human brain is the most complex machine in the universe. It has 100 billion (or 10**11) neurons. Neurons convey information via electrical spikes, and each neuron interconnects with hundreds of other neurons via, on average, 10 thousand (or 10**4) connections or synapses. Thus, the brain has about a thousand trillion (or 10**15) synapses - this staggering number of connections is one reason for the complexity of brain processing. Another is the precision of wiring between neurons in order to make networks and modules. Neurons are not simply interconnected with any and all other neurons; rather, they make precise connections with a subset of cells and form networks that process information. Pathways that convey information and networks that process them are at the core of the brain's function, for they transform simple inputs to make complex outputs, often via nonlinear operations. Complexity and nonlinearity are the essence of higher brain functions, and of the mind.

For millennia, humans have reflected on the brain and mind. The brain has routinely been compared to the most advanced machine of the age – to a clock, to an engine, and today to a computer. But these comparisons have limited value except as metaphor. There are many ways in which a present-day computer far outstrips the brain. A computer, for example, can multiply two large numbers faster than we can read out even a small part of one number. But there are a few ways in which the human brain is well ahead of our most advanced computers, and is likely to remain so for quite some time. These pertain to the means by which we derive meaning from the world, and are perhaps best exemplified by two phenomenal capacities of the human mind. One of these is language – it is nothing short of a miracle that the sounds I am uttering at a steady stream are being understood by you (I hope) as conveying some meaning. Another is vision – the fact that we can recognize objects and scenes from the pattern of light that comes into our eyes, and that we can often do so in a few tens of milliseconds, at a single glance.

The mission of Neuroscience and Cognitive Science is to understand how we do this, and in general to understand the rules by which the brain works and how it gives rise to the mind. Until recently, the study of the mind was considered to be the realm of philosophy alone. Under the sway of behaviorism, the mind was not even considered an important subject of study; all operations of the mind were considered to arise from a black box that learnt to produce an output when conditioned by reward. However, the rise of cognitive science as a field has transformed this view. We now know that the mind has specific domains of operation, such as language, vision and memory. While these domains partially overlap and interdigitate, they also arise from specific brain modules that have specific inputs, networks, and outputs. And perhaps most importantly, the brain and mind can be considered to process information and carry out computations – that is, logical operations on inputs in order to produce outputs that exemplify our human capacities. Thus, almost every sentence we utter is new and unique in some way – we have in our brains the capacity to string together words in ways that make sense, and we can do so in an infinite variety of ways. Even something as automatic as vision involves recognition of patterns and images that we have almost never encountered before in exactly the same way – yet we see effortlessly. All this is possible because we have in our brains not the details of every possible sentence or image, but the rules of how to construct infinite numbers of sentences from finite words, and interpret infinite images from finite views. These rules are the embodiment of how the brain creates the mind, and thus of cognition.

Brain wiring and brain function

How is it that the brain, comprised of 1 kg of matter, possesses these capacities, yet our most advanced computers do not? The answer lies in understanding how the brain is wired. Someone has to wire a computer and program it. But the brain wires itself.

The brain's wiring consists fundamentally of laying down pathways of information flow and networks of information processing. Brain wiring is carried out by processes that are derived from the genome, but the information for this wiring is not entirely contained within the genome itself. Rather, the brain develops by a progressive sequence of steps that each involve an interplay between genetic programs and environmental influences.

This view has antecedents. The physicist Erwin Schrodinger, in his 1944 book 'What is life' published before the discovery of the structure of DNA, pointed out the necessity of a crystalline genetic material in living organisms that would form the template for reproduction. The biologist Sydney Brenner has pointed out that the defining feature of a living organism is its ability to clone or recreate itself from its genetic code. We add that the brain wires itself from coded instructions that are open to and interpret extrinsic information, and this is in fact central to understanding human cognition and biological intelligence.

The earliest events in brain development consist of neurons being born and migrating to the right place. Subsequently, cells in one region of the brain extend axons or wires that link that region with another. Thus the eyes project to visual centers deep in the brain, and connections from there project to the visual cortex. These projections are highly specific – there are hardly any mistakes tolerated during such pathway development – and evolution has set up a large number of genes that orchestrate this specificity.

The human genome project has transformed our ways of mapping genomic sequences and identifying genes, and has turned biology into an information science. Of the approximately 20,000 genes that comprise the human genome, about 80% are expressed in the brain. Different genes are expressed in different parts of the developing nervous system, and at different times. Sometimes the same gene is expressed in different brain regions, and sometimes a gene stays on for variable durations in different regions, but rarely is a gene turned off and then on again in the same region. Each gene thus has a unique function in space and time in the developing brain, but one that is influenced by context.

One of the most remarkable discoveries of recent years is that genes can be regulated in a large number of ways. They can be turned off and on by critical control elements, including epigenetic mechanisms in the genome and small pieces of RNA. And not only what protein a gene makes but also how much it makes is influenced by a host of factors inside and outside the genome.

Pathways in the brain bring information but networks process them. The formation of networks must require more information than even allowed by combinatorial combination of genes, due to the sheer complexity in the number of synapses involved. This information is derived from the environment, or from the world. The principal way by which the brain knows about the world is by the pattern of electrical activity in brain pathways. Another major finding of recent years is that electrical activity can have a huge influence on gene expression. Furthermore, evolution has produced specific mechanisms that extract the details of information and use it to wire the brain. These include receptors at synapses and channels on neurons that are exquisitely sensitive to the quantity, or amount, and quality, or timing, of electrical spikes. Plasticity is fundamental for the formation of networks, and the brain encodes rules of plasticity through multiple mechanisms.

The debate between nature and nurture thus seems outmoded to a neuroscientist like me – we now know that there is no such thing as a gene that acts in isolation and that every gene needs an environment, whether the environment is the presence of molecules made by other genes, signals generated internally within the developing nervous system, or electrical activity transduced from the external world. At the same time, brain wiring itself is carried out by molecules that are made by genes. Rather than ask about nature versus nurture, it is more useful to probe the integration of nature and nurture, and even more, to the nature of nurture – that is, what are the kinds of environmental influences that can impact genes and developmental mechanisms at specific time points of brain development.

The nature of such environmental influences is a matter of active investigation. At the earliest stages, such as during developing of long-range pathways, merely the presence of certain molecules or signals may be sufficient. Later on, such as during development of cortical networks, the influence of the environment may be instructive, so that the specific pattern of signals or of electrical activity shapes brain networks and function.

Rewiring the brain

My laboratory studies plasticity during brain development and in adulthood. Some years ago, my students and I did an experiment to demonstrate the phenomenal capacity of change in the developing brain. Vision starts with the eyes but is created in the brain. Normally, information from the eyes is conveyed by specific pathways to visual brain centers and processed there. Networks in the visual cortex extract information from the visual image, such as the orientation of line segments that outline objects, and thus set up the elements of vision. We asked whether a very different part of the brain, such as the auditory or hearing cortex, would also create similar networks if it was driven by visual information. We thus rewired the brain in very young animals, by inducing projections from the eye to target the auditory centers of the brain. We discovered that by adulthood the auditory cortex was transformed by visual input. It developed networks that extracted the orientation of line segments, and had many other features of the visual cortex. Rewired animals were even able to use their auditory cortex to see.

In complementary natural experiments, it is known that humans who are born congenitally deaf due to an unfortunate genetic defect undergo rewiring of their auditory cortex so that it processes vision. Similarly, humans with congenital blindness have novel functions in their visual cortex: it responds to and processes hearing or touch. Indeed, one reason for the heightened sensory capacities of people deaf or blind from birth is the fact that a larger extent of cortex is devoted to other sensory modalities.

These discoveries demonstrate the profound influence of the external world in shaping brain networks. Mechanisms of plasticity operate during development as a means of utilizing information from the world. Specific pathways convey information required for plasticity, and plasticity sharpens the specificity of networks that process the information.

Many disorders of brain development have their roots in mechanisms of plasticity. In the US and Europe, there is increasing awareness of a disorder known as autism, in which there are profound deficits in social interaction and communication, and exaggeration of restricted and repetitive behaviors. My laboratory also studies the mechanisms of autism, mainly using animal models in which we try and capture certain key elements of the disorder. One of the disorders we study is Rett Syndrome, which is a rare but devastating subset of autism in which a single gene called MeCP2 is mutated. Rett Syndrome strikes 1 in about 10,000 girls. Because the gene is on the X chromosome, and boys have 1 X and 1 Y chromosome, boys do not survive a deletion of one copy; in contrast, girls have 2 X chromosomes and survive due to a functioning copy of the gene on their other X chromosome. The early development of the brain occurs normally, but by 2 years of age the girls begin to show the effects of the disorder. They develop serious deficits in movement, speech and cognition, and the quality of their life is drastically limited for the duration of their lives.

It was discovered some years ago that the MeCP2 gene regulates transcription; that is, it influences the function and effectiveness of many other genes. We and others discovered that mice in which the gene is removed recapitulated several aspects of the disorder (as best as can be measured in a mouse). Importantly, synapses in the cortex showed too much plasticity and stayed immature for a prolonged period of time. Based on these findings, we have proposed a therapeutic for the disorder – a molecule that makes synapses mature rapidly – and we hope that the therapy enters clinical trials soon. Other subsets of autism are likely due to too little plasticity, and neuroscientists are working actively to discover the synaptic mechanisms underlying different subsets along with appropriate therapies.

These approaches represent the first steps in understanding brain disorders in a rational, mechanistic way. As we discover how the brain is wired and how it works, we can understand its function and disorders in much the same way that we understand the function and disorders of other organs of the body. My hope is that neuroscience will thus remove the stigma associated with brain disorders. There are concrete physical reasons why the brain works and why it sometimes does not work, even if its product, the mind, is not a physical entity. And the mind also has specific rules and mechanisms that can be specified and understood.

Plasticity and statistics

Mechanisms of plasticity are prominent not only in the developing brain but also persist into adulthood as mechanisms of learning and memory. Plasticity gives rise to the tremendous dynamics and flexibility of the brain, regardless of age, and underlies our ability to learn, remember, adapt, change, view things in context, understand speech, and make sense of visual images. Our brain starts with a scaffold of connections that anchor the rules of cognition, then continually sharpens its networks and updates its cognitive programs.

As an Electrical Engineer who studies the brain, I have always been impressed by the breadth of intellectual inquiry represented at the Indian Statistical Institute. The activities of ISI, initiated by P.C. Mahalanobis and nurtured by generations of its leaders, span the range and even the aspirations of the human mind. Indeed, the function of the brain is deeply intertwined with statistics. Statistics as the act of analyzing measurements, assigning probabilities, and making predictions describes well many components of cognition. The precision of brain wiring derives from the ability of brain cells to make millions of synapses and shape them according to the statistics of the input. The brain extracts information about regularities in the world and encodes them via changes in synaptic strength and the construction of networks that are the best-estimate match to incoming information. From the imprecision of millions of synapses that are not precisely specified as to location and strength arises the precision of brain function.

Plasticity of synapses implies that information transmission and coding are inherently statistical – our neurons compute average rates of firing summed over time intervals of tens and hundreds of milliseconds in order to code and decode information. Such mechanisms may seem terribly imprecise. Yet information transfer and transformation is highly precise, due to pooling over thousands of neurons and millions of synapses for even the simplest tasks. Statistical processing is at the core of brain wiring as well as of brain computations and cognition.

Conclusion

I have outlined here some of the key emerging concepts that underlie the field of neuroscience and cognitive science. For the first time, we are able to pose answerable questions and make measurements that can prove or disprove hypotheses. We are beginning to get a glimpse of what it is to know ourselves. We know more about the brain in the past 25 or 30 years than we have known in all of human history before that. Neuroscience is truly a field as old as most of you are.

But lots of questions remain to be answered. The hardest questions in our field pertain to the products of the human mind: how does the mind create culture, what are the sources of creativity and humanism, what are the roots of power in society, even a question appropriate for our times: what makes human beings greedy?

Some argue that the actions and behaviors of humans are innate or hard-wired into our brains, that social and economic systems are the way they are because there can be no other way. But that answer belies the deepest truth about our brain and mind, that it is shaped by change, and formed by an inseparable confluence of innateness and experience. While neuroscientists have the hubris of a new and expanding field, I believe the answers to many of the deepest questions about our place in the world will come from the work of thoughtful social scientists.

Above all, the goal of our field, as of all science and technology, must be to improve the human condition and be a force for social justice. Too often, the fruits of scientific research seem obscure to common people or even antithetical to their interests. The capacity of the human mind to change is itself a potent force that requires vigilance, for it can be used for good or for evil.

So at this time in your lives, I urge you to explore the world, perhaps even with some degree of imprecision, for imprecision is not the enemy of precision but rather the route to precision and direction. As you choose your areas of endeavor, I also urge you to think about the world and its rules, and of making it a better place. As a famous philosopher once said: 'Philosophers have only interpreted the world; the point, however, is to change it.' We have the means at our disposal, in our very brains.

Thank you.

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