Brain-like computing demystifies H_2O

WATER GUARDS ITS SECRETS WELL, BUT NATURE'S METHOD FOR LEARNING HAS BROKEN THROUGH TO SOME OF THEM, WRITES **S ANANTHANARAYANAN**

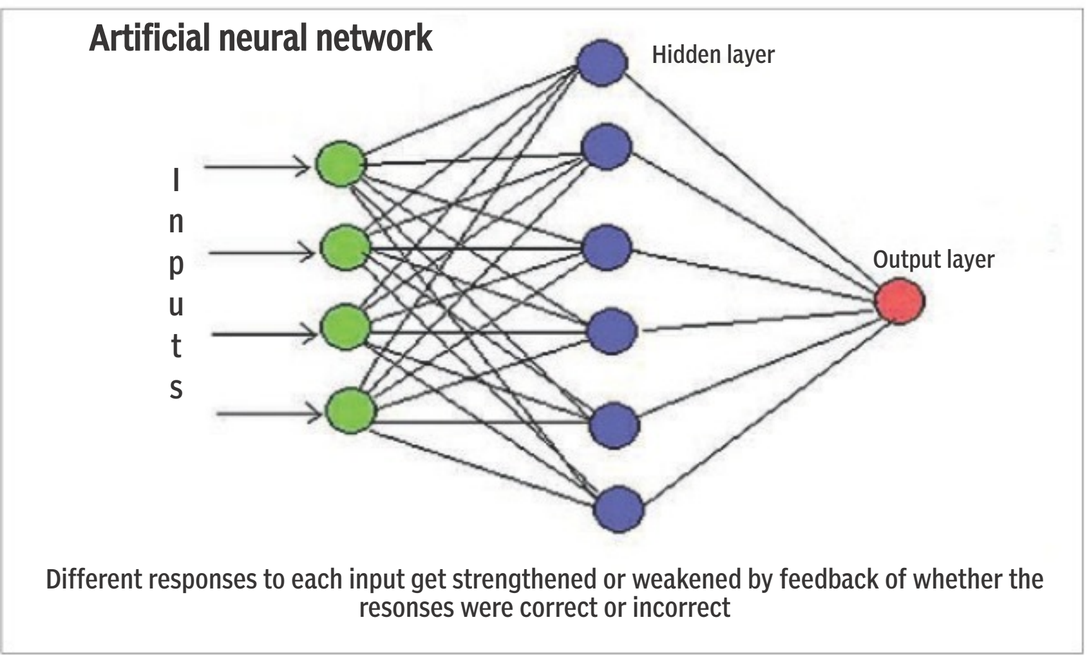
Water, on which all of life depends and which covers the larger part of the earth's surface, is one of the least understood substances. It is the best solvent known, neither acid nor alkaline, and it is uniquely suitable for carbon-based life and also for a host of industrial uses. But it has properties that are basically different from other substances, and are rightly described as anomalies.

Understanding these peculiarities would be possible if we did an "ab initio" study of the forces between the atoms and molecules of water, using the rules of quantum mechanics, which is the mechanics of very small distances. Matter at very small dimensions behaves differently from matter in bulk and we now have methods to calculate how interactions at these dimensions should be.

The trouble is that the computations to get solutions of reasonable accuracy are time-consuming, to the point of being impractical. Tobias Morawietz, Andreas Singraber, Christoph Dellago and Jörg Behler of the Chair for Theoretical Chemistry, Rurh University and the Faculty of Physics, University of Vienna, have used an alternative — a laboratory imitation of the way a natural system, like the brain, would approach a problem. They describe the exercise in their paper in the *Proceedings of the National Academy of Sciences* and report confirmation of the belief that it is a set of weak forces other than electric attraction or repulsion that lead to the peculiar properties of water.

The reason substances occupy volume is that their component parts, the molecules, are in agitation. As warmer substances are in a state of greater agitation, warmer things occupy more space, and things expand when warmed. Conversely, they contract when cooled.

Water in the liquid state also behaves in this way when it is reasonably warm. But when it is cooled to just about four degrees Celsius, it starts to expand on cooling, in place of contracting. This goes on till it freezes as ice, at which point it expands by a whole nine per cent. When ice has formed, it behaves like a normal solid and contracts when cooled, till it is exceedingly cold, at -203° Celsius, when it starts expanding again.



Different responses to each input get strengthened or weakened by feedback of whether the resonses were correct or incorrect

A partial explanation for this anomaly has been that the manner in which the molecules of water arrange themselves when they cool below four degrees Celsius, or form ice, is not so close together as when they were warmer, or in the form of water. To explain the anomaly as "because of more space being taken", of course, is only a re-statement of the anomaly and not an explanation. Better reasoning has been that in water, there are not only the electric attraction or repulsion between charged particles, but also weak forces, known as *van der Waals* forces, which arise from pairs of separated charges, charges in motion, etc, and come into play. Because of two hydrogen atoms connected to one oxygen atom, and the shape, in the form of a V, for stability, the water molecule is not symmetrical and also acts like a pair of charges. The interplay of the forces, and the specific ratio of the masses of the atoms in water result in the sum total of forces crossing a tipping point at about four degrees Celsius and again on freezing.

This conjecture has been based on computer-aided simulations of actual forces at play, from the starting point of quantum mechanical computation of the forces arising from the atomic structure and arriving at the forces on the molecules of water in bulk. Such simulations, however, are feasible only to short time scales and small systems, the *PNAS* paper says, and are of restricted utility.

Neural networks

A more efficient, if not exact, and very powerful method of computation is that used by natural systems, like the brain. Unlike the digital computer, which manipulates actual numbers and needs to process each input in a programmed way, the neural network is one that arrives at the answer based on the random and simultaneous treatment of each input at different nodes. The working is not a method of computation, but a method of managing the random process, with successful operations becoming more likely to be repeated and unsuccessful ones less likely.

A task like recognising numbers written by hand, for instance, is the simplest possible for a human. But the same task for a computer involves taking in the inputs from the thousands of light sensitive cells in the retina, matching their distribution, one by one, based on yes/no comparison with a library of data and deciding what the image looks like as a result of millions of computations and comparisons. The task would be not only a huge computation job, it may even be neither possible nor reliable.

The brain, on the other hand, does not process the data in the same, serial way. The neurons, or brain cells that receive different inputs, first put out random outputs to other neurons, all at the same time. If the results, which are fed back, are successful, there are changes along the various sequences of cells, which make the same sequences more likely if the input is repeated. Or less likely, if the result is unsuccessful. Learning, in this way, takes place thousands of times, with different variations of the inputs that lead to the same successful outputs. The system thus gets equipped with a network of neuron paths, each of which will respond independently with a given net result for a number of nearly similar sets of inputs. The system is then able to generate nearly the same output for variations of a set of inputs, even when some were partly not encountered before, and with great speed. A digital computer, on the other hand, would be hard put to tell even reasonably matching data as representing the same shape as it would need to make a serial comparison of very large numbers of complete input sets with some reference library.

The same consideration would apply to teaching a computer to play chess, for instance. With 32 pieces and 64 squares, the theoretically possible moves are a very large number, and so are the possible moves of the opponent. The number of possible positions after even a few moves is hence an impossibly large number and even a powerful computer that works in this "brute force" method may miss the correct move in a given position. But the human mind takes in the whole board at once, ignores moves that it can recognise as unimportant and sees patterns that represent "strong" positions, in a manner that it would be difficult to programme a computer to do. The brain is able to do this because it does not work like the computer but employs networks of nerve cells whose choices, based on inputs, have been programmed by experience and where outputs can be generated even with partial data.

Artificial neural networks are computer programmes that simulate the brain by creating layers of nodes that receive inputs from one layer and send outputs to the next, with "learning" taking place with software-based "strengthening" of successful responses. The number of such nodes possible even in a large assemblage of computers cannot compare with the number of neurons in the brain, but such networks are able to deal with problems that would be out of the reach of the normal, serial computer programmes.

The authors of the *PNAS* paper hence devised algorithms to create a matrix of nodes that would receive inputs and whose connections would get strengthened when they arrived at valid results. Using this model, different forms of dynamics of water molecules could be tried out and the model was able to correctly work out the actual expansion/contraction behaviour, the density change on freezing and even electrical properties of water. The exercise hence succeeds in showing that it is the balance of van der Waals forces and the forces of asymmetric water molecules that act to bring about the celebrated anomalies.

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MICROSCOPIC MUTANTS

TAPAN KUMAR MAITRA CHRONICLES THE STUDIES THAT LED TO THE IDENTIFICATION OF MOLECULES CONTROLLING THE CELL CYCLE

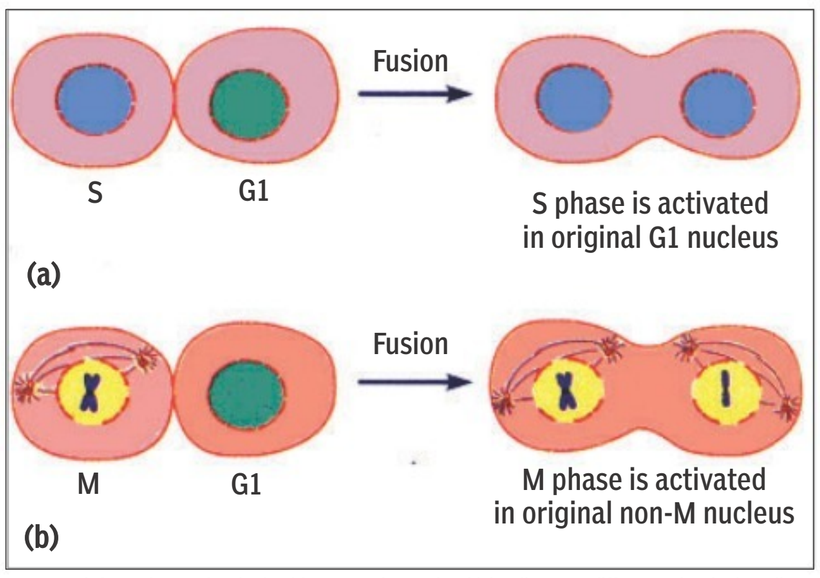
T\The first hints concerning the identity of the molecules that drive progression through the cell cycle came from fusion experiments carried out in the early 1970s. In some of the earliest studies, two cultured mammalian cells in different phases of the cell cycle were fused to form a single entity with two nuclei called a heterokaryon. As indicates, if one of the original cells is in S-phase and the other is in Gl, the latter nucleus in the heterokaryon quickly initiates DNA synthesis, even if it would not normally have reached the S-phase until many hours later. Such observations indicate that S-phase cells contain one or more molecules that trigger progression from Gl into S. The controlling molecules are not simply the enzymes involved in DNA replication, since they can be present in high concentration in cells that do not enter the S-phase.

Fusion experiments have also been performed in which cells undergoing mitosis are fused with inter-phase cells in Gl, S, or G2. After fusion, the nucleus of such cells is immediately driven into the early stages of mitosis — including chromatin condensation into visible chromosomes — spindle formation and fragmentation of the nuclear envelope. If the inter phase cell had been in Gl, the condensed chromosomes will be unduplicated.

Cell fusion evidence for the role of cytoplasmic chemical signals in cell cycle regulation suggested that specific molecules present in the cytoplasm are responsible for driving cells from Gl into S-phase and from G2 into mitosis. Progress in identifying these cell cycle control molecules was greatly facilitated by genetic studies of yeasts. Because they are single-celled organisms that can be readily grown and studied under defined laboratory conditions, yeasts are particularly convenient model organisms for investigating the genes involved in cell cycle control.

Working with the budding yeast Saccharomyces cerevisiae, geneticist Leland Hartwell pioneered the development of techniques for identifying yeast mutants that are "stuck" at some point in the cell cycle. It might be expected that most such mutants would be difficult or impossible to study because their blocked cell cycle would prevent them from reproducing. But Hartwell overcame this potential obstacle with a powerful strategy — the use of temperature-sensitive mutants. It is a type of mutation whose harmful effects are apparent only at temperatures above the normal range for the organism. Therefore, yeast carrying a temperature-sensitive mutation can be successfully grown at a lower ("permissive") temperature, even though their cell cycles would be blocked at higher temperatures. Presumably the protein encoded by the mutated cell cycle gene is close enough to the normal gene product to function at the lower temperature while the increased thermal energy at higher temperatures disrupts its active conformation (the molecular shape needed for function) more readily than that of the normal protein.

Using this approach, Hartwell and his colleagues identified many genes involved in the cell cycle of S cere-visiae and established where in the cycle their products operate. Predictably, it turned out that some of these genes produce DNA replication proteins but others seemed to function in cell cycle regulation.



Important information can be obtained from experiments in which cells at two different points in the cell cycle are induced to fuse, forming a single cell with two nuclei, a heterokaryon. Cell fusion can be brought about by any of several methods, including the addition of certain viruses or polyethylene glycol, or the application of a brief electrical pulse, which causes plasma membranes to destabilize momentarily (electroporation). If cells in S phase and Gl phase(a) are fused, DNA synthesis begins in the original Gl nucleus, suggesting that a substance that activates S phase is present in the S phase cell. If a cell in M phase (b) is fused with one in any other phase, the latter cell immediately enters mitosis. If the cell was in Gl, the condensed chromosomes that appear have not replicated and therefore are analogous to a single chromatid.

A breakthrough discovery was made by Paul Nurse, who carried out similar research with the fission yeast Schizosaccharomyces pombe. He identified a gene called cdc2, whose activity is needed for initiating mitosis — that is, for moving cells through the G2-M transition. The cdc2 — the acronym stands for cell division — cycle gene was soon found to have counterparts in all eukaryotic cells studied. When the properties of the protein produced by the cdc2 gene were examined, it was discovered to be a protein kinase — an enzyme, which catalyses the transfer of a phosphate group from ATP to other target proteins. This discovery opened the door to unravelling the mysteries of the cell cycle.

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No cheating here

BEING MONOGAMOUS ON A LONELY MOUNTAIN CRAG MAY BE EASY, BUT BIRDS OF PREY STAY TRUE EVEN AFTER MOVING TO CHICAGO, SAYS **IAN JOHNSTON**

Sex in the animal kingdom often seems to lack any sign of romance whatsoever. In fact, it can be really quite nasty: just ask a female mallard duck or a male redback spider. However, a new study suggests that peregrine falcons could be champions of true love, with a far greater sense of "to love and to cherish, till death us do part" than most humans.

Peregrines are known to mate for life when they are in their natural habitat on isolated cliffs, far away from other pairs – and temptation. But, quite reasonably, researchers hypothesised that the birds of prey would be more promiscuous when nesting among the 50 or so birds that live on the skyscrapers and bridges of Chicago.

How wrong they were.

After carrying out DNA tests on the birds and their eggs, they found just one brood out of 35 in which the chicks were fathered by a different bird. But they believe that this happened because a female peregrine was widowed and found a new mate who then helped her raise her former partner's chicks.

John Bates, associate curator of birds at The Field Museum of Natural History in Chicago, who took part in the research, said, "Peregrine falcons that now live in the Chicago region are living in very different conditions than you'd normally see for these birds, so we wondered if the falcons' mating habits had changed too.

"They're in much closer proximity to each other than they'd be in a more rural environment, and we thought they might be more promiscuous with more potential mates nearby. Each spring this population also has migratory peregrines passing through on their way to all parts of Canada, so we didn't know what we were going to find. But it turns out that almost all of the mated pairs in the city remain monogamous through the years."

Peregrines, which can reach speeds of 110 mph as they swoop down on their prey, came close to extinction in the USA in the 1960s as the now-banned pesticide


Peregrine falcons -- champions of true love.

DDT caused the shells of their eggs to thin. But they have since made a comeback, particularly in Chicago, where 90 per cent of the breeding pairs in the Midwest nest on buildings and bridges in the city.

That prompted the researchers to look into whether "sex in the city" was different to the habits of the birds' country cousins. "Whenever you have animals living in habitats that have been influenced by human development, you have to wonder how the animals' life histories will be altered," Dr Bates said.

"It's important to do studies like this one to see how birds are adapting to living in human environments, so that we can monitor changes through time."

THE INDEPENDENT

PLUS POINTS

Robots in space

What if an army of robots could assemble a large space-based modular telescope that would help astronomers on earth see things much clearly in dark space?

Nicolas Lee and his colleagues from the California Institute of Technology and the National Aeronautics and Space Administration's Jet Propulsion Laboratory have described a design to build the Robotically Assembled Modular Space Telescope. The design focuses primarily on a robotic system to perform tasks in which astronaut fatigue would be a problem.

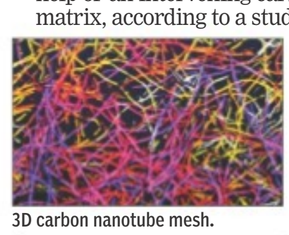
"Our goal is to address the principal technical challenges associated with such an architecture so that future concept studies addressing a particular science driver can consider robotically assembled telescopes in space," the authors wrote in a paper that appeared in the *Journal of Astronomical Telescopes, Instruments and Systems*.

The main features of their proposed architecture include a mirror built with a modular structure, a robot to put the telescope together and provide ongoing servicing and advanced metrology technologies to support the assembly and operation of the telescope. An optional feature is the potential ability to fly the unassembled components of the telescope in formation. The system architecture is scalable to a variety of telescope sizes and would not be limited to particular optical designs.

"A robotic system of assembly, upgrade, repair and resupply offers the possibility of very long useful lifetimes of space telescopes of all kinds," said Harley Thronson, senior scientist for Advanced Astrophysics Concepts at Nasa's Goddard Space Flight Center.

Reconnecting neurons

Sections of spinal tissue placed one to two millimetres apart in a culture dish can reconnect their neurons with the help of an intervening carbon nanotube matrix, according to a study published on 15 July in *Science Advances*. The 3-D matrix is also well tolerated when inserted into rat brains, the authors reported.


3D carbon nanotube mesh.

"The important thing about the paper is that, for the first time, it shows that a three-dimensional scaffold of the carbon nanotubes can really improve the connection between two networks in the spinal cord . . . in comparison with 2-D nanotubes or other 3-D networks," said neuroscientist Jürg Streit of the University of Bern, Switzerland, who was not involved in the study.

Immediately after a spinal cord injury, "there will be a scar that will physically block any kind of reconnection of the (original) fibers", explained neurophysiologist Fabio Benfenati of the Italian Institute of Technology in Genova, who also did not participate in the study. But researchers believe they might be able to circumvent such lesions. The idea is to induce the neurons next to the scar to make new connections and take "sort of a detour… to reach the target", said Benefanti.

A variety of approaches to encourage spinal neurons to regrow are therefore being investigated. One such method is to provide a scaffold between the separated spinal sections to encourage the cells to connect. Laura Ballerini of the International School for Advanced Studies in Trieste, Italy, who led the new research, believes carbon nanotubes might be a suitable scaffolding material because neurons seem to like growing on it. "This material has always proven to be extraordinarily good for growing neurons and improving their ability to reconnect," she said.

THE SCIENTIST

Genome kits

Direct-to-consumer genomics firm 23andMe is offering its spit-to-sequence kits to researchers for $199. Study volunteers can then join the company's ancestry database and receive information on carrier status for diseases. Duke University's Ahmad Hariri, who has used the product for his research since 2009, gave The Verge a rave review. "It's allowed us to maintain the highest quality of genotyping research without any need or necessity to have our own laboratory and our own staff," he said.

While the service may ease the handling of the sample and analysis — 23andMe can process kits sent directly to study participants and then give researchers raw genotyping data online — some balked at the price. Dan Arking of Johns Hopkins University told The Verge he typically spent $40-50 per sample for similar services through research consortiums that order in bulk.