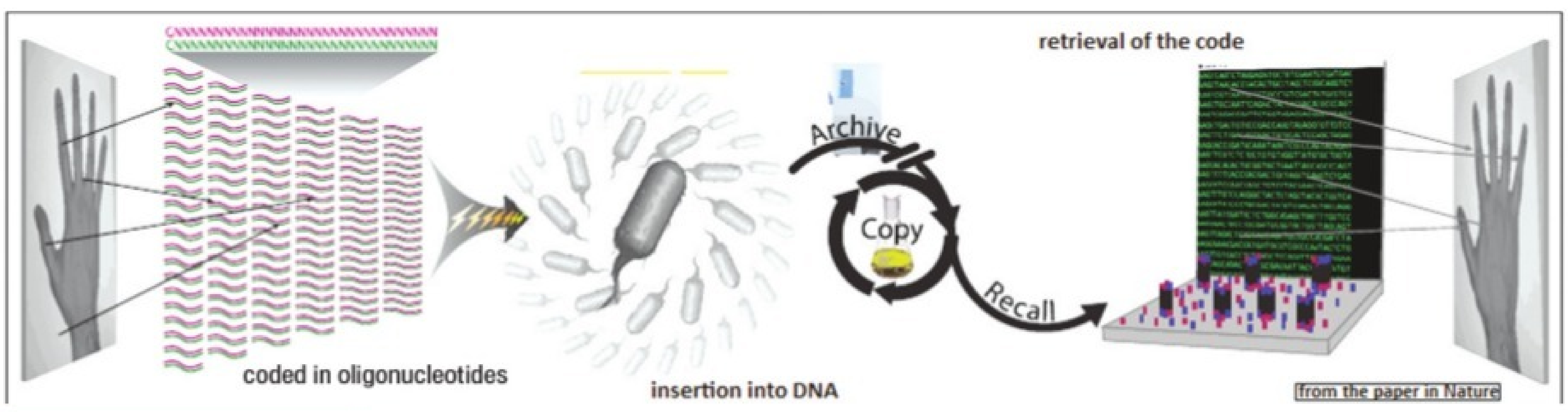
Creating cellular records

Safe storage of large information sets within DNA in living cells has become practical



S ANANTHANARAYANAN

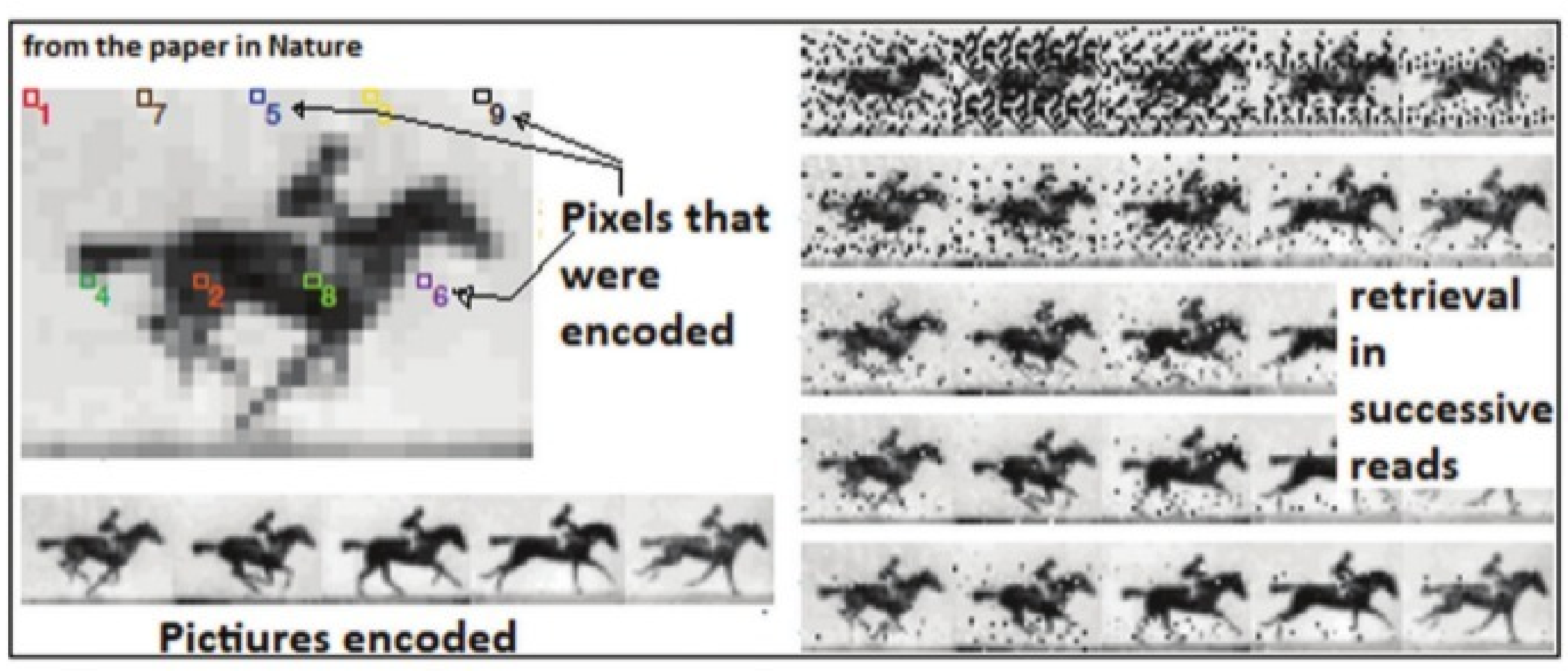
In the days when information was written down and letters of the alphabet had to be recognised by the eye, records could not be packed closer than what could be easily seen. But in the era of computers, devices can detect “0s” and “1s” that are written very close together. Data that is converted to the “0” and “1”, or the binary form, can hence be stored in great quantity, in media like magnetic tape, hard disks or pen drives.

Even those, however, are proving insufficient, as the data needs of applications have become very large. Another difficulty with the existing forms of storage is that records degrade with age or need to be transferred to new media when there are changes in technology.

Being able to store data in the DNA of cells has hence been viewed as a solution made to order. This is because the DNA molecule has both great capacity and is exceedingly hardy. We know DNA last long because DNA from scraps of once living tissue, which are discovered in archaeological remains, is intact for analysis!

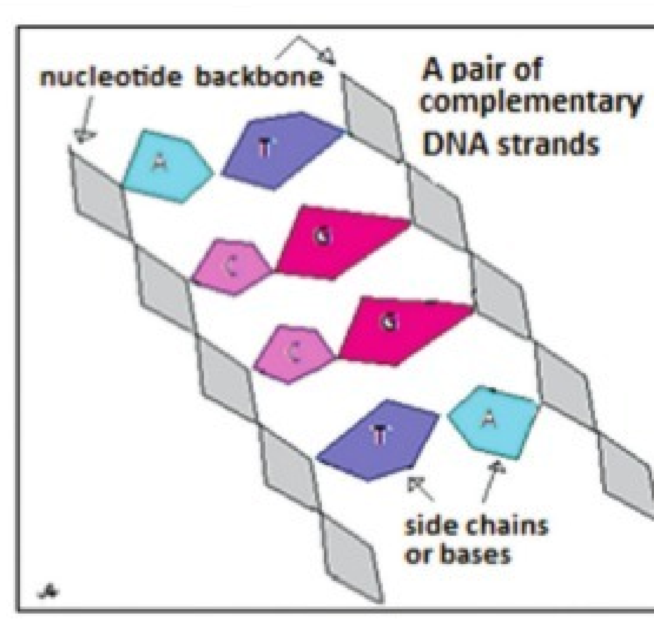
Seth L Shipman, Jeff Nivala, Jeffrey D Macklis and George M Church from Harvard Medical School and Harvard University report in the journal, Nature, that they have scaled up a method of using native, biological tools to insert encoded data, which has been recorded in a synthetic molecule, into the DNA of living cells. In a proof of principle demonstration, a movie clip of a galloping horse has been secured in a single living cell.

Shipman and colleagues explain in the paper that the trick involves two steps. The first is to encode the information in the form of a sequence of units like the ones found in the DNA molecule. And the second step is to snip the DNA molecule at a specified place, to insert the sequence that has the information.



These DNA-like portions that are inserted into DNA are molecules that are built in the same way. Hence, like DNA, they consist of a chain or backbone of units, called nucleotides or bases, as shown in the picture, with “side chains” of four kinds of molecular groups along the length of the DNA backbone. The DNA, and the shorter variety, which are called oligonucleotides, carries information as coded by the sequence of the four kinds of side chain groups. These groups have the names, C, G, A and T and in the DNA, groups of three consecutive bases, each with one of four forms of side chain, code for 20 amino acids, which are the building blocks of proteins. Series of triads thus code for series of amino acids and hence for different proteins.

Just as the DNA codes for proteins, the shorter oligonucleotides can code digital information. In computers, groups of eight “bits” or binary units, code for 2^8=256 characters. In DNA, a group of three bases, which can take four forms each, can have 4^3=64 forms (but only 20 amino acids are coded, as some acids have alternate codes, for safety). Oligonucleotides, which have the same structure, can hence be used to form codes to represent strings of text characters, numbers or pixel values. In practice, it is found that more than three consecutive bases with the same side chain create instability in oligonucleotides. The side chain, G, is hence reserved to break series of more than three identical bases and only the remaining three side chains are there for coding.



The human DNA contains about three billion bases. However, only about 1.5 per cent of the bases form triads to code for amino acids and proteins.

The rest of the bases are used for “regulation” or as “spacers”, as in CRISPR and the function of much of the DNA is yet to be understood

The Harvard paper describes a scheme of coding in the synthesised segments, where the pixels in an image of a hand, as shown in the picture, are represented by the side chains along the length of bases. As there is a limit to the length of segments, coding is done over more than one set of synthetic bases. To identify which pixels a segment represents, a part of the segment is used for identification. After this and other overheads, only 28 bases were left in the segments for coding pixels.

The second step in the process was to insert the set of oligonucleotides into the DNA of a living cell. This was done with the help of a feature of real cells, which has been perfected for artificial manipulation of the DNA. The mechanism by which cells gain immunity against virus attacks is that when a virus attacks a cell, the cell copies signature portions of the viral DNA into a portion of its own DNA. This part of the cell DNA, called CRISPR for Clusters of Regularly Interspaced Short Palindromic Repeats, is not used for the cell's normal functions. But if the virus should attack again, the cell's defences have a copy of unique parts of the virus DNA. Another part of the cell DNA, called CAS genes, for CRISPR Associated genes, now use this information to go out and snip, or divide, the viral DNA at the place identified.

This method, native to cells, was then turned around to cut the DNA of a cell itself, at specific places. The cut ends would then spontaneously join, and in the process, there could be repair of defective DNA or the insertion of a portion to add to the genes that are present in normal DNA. The method, called CRISPR-CAS9, has taken genetic engineering by storm and has set in motion great new work and advances in the field.

The Harvard group made use of CRISPR-CAS9 to insert the panel of oligonucleotides, which had been fashioned to record digital data, into the DNA of living cells. The DNA would then be efficiently replicated, in the process of cell division, and preserved, with economy and security! There are now efficient methods of reading the sequence of side chains along the length of the bases of DNA. These techniques enable the information coded in the inserted segments to be read, or retrieved, for use.

That the technique works was demonstrated by recording a panel of pictures of a galloping horse, by Eadweard Muybridge, a celebrated 19th century photographer of people and animals in motion. The pictures, as shown, could be recorded and retrieved with good preservation of quality, and displaying the pictures in succession created a motion picture of the horse in action — all recorded inside the DNA of a living cell!

The writer can be contacted at response@simplescience.in

In the grand scheme of things

Many scientists say there's no purpose to life but a theoretical study suggests there could actually be a point to all of this

MICHAEL E PRICE

Does humanity exist to serve some ultimate, transcendent purpose? Conventional scientific wisdom says no.

As physicist Lawrence Krauss puts it in his latest book, *The Greatest Story Ever Told...So Far*, our evolution on this planet is just a “cosmic accident”. If you believe otherwise, many would accuse you of suffering from some kind of religious delusion. I don't think this view of life is necessarily correct. Despite that, my worldview is entirely naturalistic — it doesn't rely on invoking any supernatural powers. And I usually do agree with conventional scientific wisdom!

However, I know of one possible mechanism by which life could, in fact, be endowed with a natural purpose. The idea, just published in the journal, *Complexity*, is highly speculative but worth considering.

In biological natural selection, genes' ability to replicate themselves depends on how well they can encode traits that permit organisms to outreproduce other members of their own species. Such traits — for example, camouflage to avoid predators or eyes to enable vision — are adaptations to the environment, as opposed to traits that are just by-products of adaptations or random genetic noise. Clearly, the purpose of these adaptations is to solve difficult problems, like seeing, digesting or thinking.

Because organisms are bundles of complex adaptations, they are the most improbably complex things in the universe. And improbable complexity is, in fact, the hallmark of natural selection — the fundamental way in which we recognise that a trait actually is an adaptation.

This makes them improbably low in “entropy”, which is the degree of disorder in a physical system. A basic law of physics is that entropy tends to always be increasing so that systems become more disordered, known as the “second law of thermodynamics”.

It's because of this law that you can crack an egg and mix it all together to make an omelette (making it more disordered), but you can't turn the omelette neatly back into an egg with shell, white and yolk (making it more ordered).

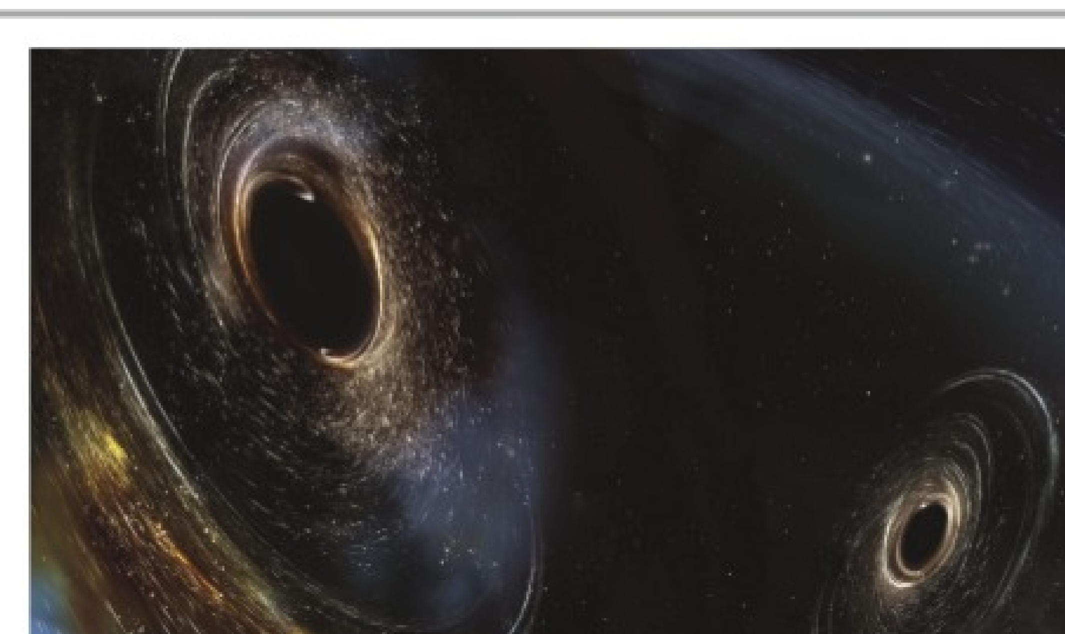
Because natural selection is the process that “designs” organisms -- incrementally organising random, disordered matter into complex, functional organs — it is the most powerful anti-entropic process that we know of. Without the incremental changes that natural selection allows, the only way a complex adaptation like a mammalian eye could come into existence would be as the result of random chance. And the likelihood of that is extremely low.

Biological natural selection explains how adaptations have purpose (to facilitate survival and reproduction), and why organisms behave purposefully. It does not explain, however, how life in general could have any transcendent purpose. To figure out the point of our existence, we require a higher-order explanation, like the one I describe.

My higher-order explanation is based on cosmologist Lee Smolin's theory of cosmological natural selection. Smolin founded his theory on the increasingly popular view that our universe exists in an innumerably vast population of replicating universes — a multiverse. Many physicists put stock in the idea of there being a multiverse, because its existence is predicted by eternal inflation, our most promising model of universe origins.

Smolin reasoned that in a multiverse, universes that were better at reproducing would become more common. He proposed that they could be created from existing black holes. And if black holes are how universes reproduce, then cosmological natural selection would favour universes that contained more black holes. In this theory, life is simply the accidental by-product of processes “designed” by selection to produce black holes.

Smolin's theory has considerable intuitive appeal. It seems analogous to Darwin's selection theory. And black holes do seem to be likely candidates to give birth to new universes. A black hole is an infinitely small concentration of space-time, matter and energy — a singularity. And it's exactly this type of phenomenon we believe the Big Bang started from.


Life, more than black holes (in picture), could be a mechanism of universe reproduction

In one glaring aspect, however, Smolin's theory falls short of being analogous to Darwin's. It does not predict that the most improbably complex feature of our universe will be the one most likely to be an adaptation produced by cosmological natural selection — because that least entropic feature is life, rather than black holes.

Smolin does identify life as the least entropic known thing. His theory, however, does not make the connection between entropy and selection. That is, it doesn't acknowledge that, just as improbably low entropy is the hallmark of selection operating at the biological level, this is likely to be true at the cosmological level as well.

If life is, in fact, the universe's reproductive system, the implication is that sufficiently evolved intelligence could acquire the ability to create new cosmic environments. In order to be habitable, these baby universes would need to replicate the physical laws of the life form's native universe. Cosmologists expect that in billions of years, our universe will cease being habitable. By that point, however, life could conceivably have become intelligent enough to produce new life-supporting universes, perhaps by civilisations “building” something similar to black holes.

However, scientists currently lack the methods to test the idea conclusively. A start would be to discover that there are indeed other universes — something that astronomers are currently looking for.

A basic prediction it does make, however, is that human technological progress is likely to continue into the vastly distant future. If cosmological selection “designed” life to use its technology for universe reproduction, then it seems reasonable to expect that life will succeed in this regard — just as you'd expect an eye produced by biological selection to actually succeed in seeing.

That doesn't mean that unceasing technological progress is guaranteed — after all, we could use our technology to destroy ourselves. Nevertheless we can reasonably expect humanity — or whatever it evolves into — to be sticking around for a long, long time.

It's not a new idea to propose in general terms that life might constitute a mechanism for cosmological evolution; good histories of this idea are already published. The new aspect of my research is that it spells out exactly why life — as the least entropic known thing in the universe — is more likely than black holes (or anything else) to be a mechanism of universe reproduction. I hope others will continue to explore this idea.

The writer is a senior lecturer in psychology and director at the Centre for Culture and Evolution, Brunel University, London

The Independent

PLUS POINTS

Picking up a language

Two-year-old Summer Tan spends her afternoons watching English cartoons and reading Chinese storybooks with her mother. Exposed to both languages, the energetic tot effortlessly switches between English and Mandarin when she speaks.

Science says she stands to benefit from this ability. Bilingual infants such as Summer are able to learn a third language more easily, a study by National University of Singapore researchers has found. They are able to differentiate between words from an unknown foreign language, unlike their monolingual counterparts. “That suggests that the window on further language acquisition had started to close on monolingual children but was very much open for the bilingual children,” said associate professor Leher Singh from the NUS department of psychology.

During the nine-month study, infants who were solely exposed to English and those who knew English and Mandarin were exposed to the southern African language, Ndebele. In one experiment, the 40 infants were shown an image and at the same time read a Ndebele word. After that, they were shown the same image but this time a different word was read out to them. The bilingual children detected the change in sound while the monolingual children did not. The conclusion was made using a method that tracks the time that they spent looking at an object on a computer screen while the word was read out to them. More fixation time when the tone changed reflects a surprised response, indicating that they were sensitive to the differences.

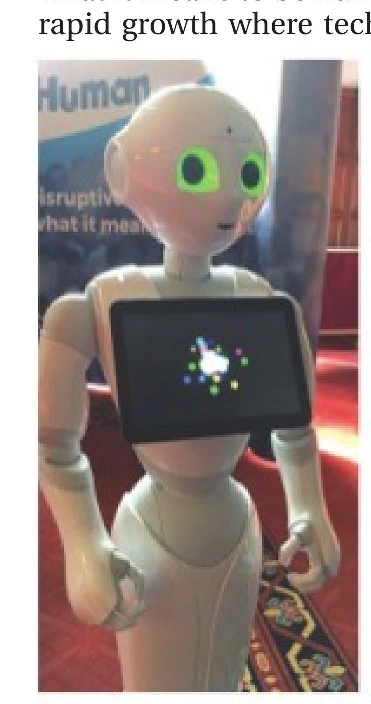
The finding, published in the scientific journal *Child Development*, further supports the theory that exposing children to two languages at the same time has cognitive benefits.

The straits times/ann

What makes us human?

A new ground-breaking institute at the University of Sheffield was launched recently at Sheffield Town Hall by robots and BBC Radio 4's Adam Rutherford.

iHuman at the University of Sheffield brings together researchers from the social sciences and humanities with psychological and biological sciences to give new understanding on what it means to be human in a time of rapid growth where technology affects all our daily lives.



The event, called “Who decides the future? Science, politics or the people?”, was chaired by Rutherford and introduced by professor Dave Petley, vice-president for Research and Innovation at the University of Sheffield.

Robots from Sheffield Robotics greeted the public as they arrived at Sheffield Town Hall.

Following the format of BBC's Question Time programme, experts from different sectors and disciplines answered questions from the public such as “Who has the power to decide where our societies are heading?”

Professor Paul Martin, from the University of Sheffield and iHuman co-director, said, “We live in a world where technology touches every aspect of our lives. Apps change the way we communicate, automation modifies the way we work and augmented reality can alter our perception of the world entirely.”

Professor Dan Goodley, iHuman co-director at the University of Sheffield said, “Do we have free will or are we made by society? What is the difference between humans, animals and machines? How are technological developments changing how we understand what it means to be human? How might the human condition be expanded to include all kinds of gender, sexuality, disability and race identities?

“These are just some of the difficult questions bringing together researchers in iHuman. We seek to address rather than avoid controversy, and break down barriers between academic fields to advance understanding of what a changing world means for us all.”

The iHuman institute is based within the Faculty of Social Sciences at the University of Sheffield. A network of fully-funded PhD students is working on projects as part of iHuman and has the chance to work with world-leading experts.

For more information, visit *http://ihuman.group.shef.ac.uk/*