WETWARE TECHNOLOGY
(TECHNOLOGY OF THE FUTURE)

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Abstract: New generation of fast and flexible computers that can work out for themselves how to solve a problem, rather than having to be told exactly what to do. Ordinary computers need absolutely correct information every time to come to the right answer. A biological computer will come to the correct answer based on partial information, by filling in the gaps itself. The device the team has built can "think for itself" because the neurons are able to form their own connections from one to another. Normal silicon computers only make the connections they are told to by the programmer. This flexibility means the biological computer works out it own way of solving the problem.

I. INTRODUCTION TO WETWARE:

Wetware is a term drawn from the computer-related idea of hardware or software, but applied to biological life forms. Here the prefix "wet" is a reference to the water found in living creatures. Wetware is used to describe the elements equivalent to hardware and software found in a person, namely the central nervous system (CNS) and the human mind. The term wetware finds use both in works of fiction and in scholarly publications.

A **wetware computer** is an organic computer (also known as an artificial organic brain or a neuro computer) built from living neurons. Professor Bill Ditto, at the Georgia Institute of Technology, is the primary researcher driving the creation of these artificially constructed, but still organic brains. One prototype is constructed from leech neurons, and is capable of performing simple arithmetic operations. The concepts are still being researched and prototyped, but in the near future, it is expected that artificially constructed organic brains, even though they are still considerably simpler in design than animal brains, should be capable of simple pattern recognition tasks such as handwriting recognition.

The "hardware" component of wetware concerns the bioelectric and biochemical properties of the CNS, specifically the brain. If the sequence of impulses traveling across the various neurons are thought of symbolically as software, then the physical neurons would be the hardware. The amalgamated interaction of this software and hardware is manifested through continuously changing physical connections, and chemical and electrical influences that spread across the body[Fig:1.1]. The process by which the mind and brain interact to produce the collection of experiences that we define as self-awareness is still seriously in question.

A cell's survival depends on how well it can detect and respond to environmental cues. In this sense, a cell is an organically derived computer — it takes input from its surroundings and uses logic circuits to result in a specific output. The central argument of Wetwareis that an individual cell contains thousands of enzymes, each performing reiterative, molecular processes. Enzymes act similarly to transistors, in which enzymatic allostery or competitive inhibition alters activity, much like a change in voltage over a transistor.

Scientists believe they are close to building the first truly biological computer made from the organic molecules of life and capable of working within the living cells of organisms ranging from microbes to man.

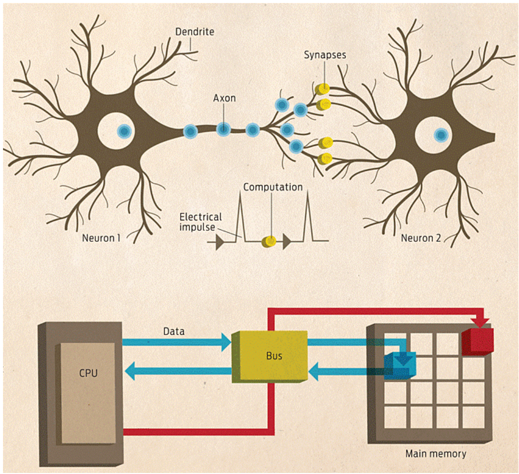

Fig:1.1

II. BIOLOGICAL COMPUTERS:

Biological computers have emerged as an interdisciplinary field that draws together molecular biology, chemistry, computer science and mathematics. **Biology is not just a science of discovery, but also a**

technology for making things. Biological computers have been the dream of electronic engineers for decades because they open the possibility of a new generation of ultra-small, ultra-fast devices that could be incorporated into the machinery of living organisms.

Using only biomolecules (such as DNA and enzymes), scientists at the Technion-Israel Institute of Technology have developed and constructed an advanced biological transducer, a computing machine capable of manipulating genetic codes, and using the output as new input for subsequent computations. The breakthrough might someday create new possibilities in biotechnology, including individual gene therapy and cloning.

Interest in such bio-molecular computing devices is strong, mainly because of their ability (unlike electronic computers) to interact directly with biological systems and even living organisms. No interface is required since all components of molecular computers, including hardware, software, input and output, are molecules that interact in solution along a cascade of programmable chemical events.

All biological systems, and even entire living organisms, are natural molecular computers. Biochemical "nano-computers" already exist in nature; they are manifest in all living things. Every one of us is a bio-molecular computer, that is, a machine in which all components are molecules "talking" to one another in a logical manner. The hardware and software are complex biological molecules that activate one another to carry out some predetermined chemical tasks. The input is a molecule that undergoes specific, programmed changes, following a specific set of rules (software) and the output of this chemical computation process is another well-defined molecule.

But bio-computers are largely uncontrollable by humans**. We cannot, for example, program a tree to calculate the digits of pi.** The idea of using DNA to store and process information took off in 1994 when a California scientist first used DNA in a test tube to solve a simple mathematical problem.

Using bio-computers, we could partner with microbes and plants to record events, natural or otherwise, and convert this information into easily observed signals. That would greatly expand our ability to monitor the environment. Several research groups have proposed designs for DNA computers, but those attempts have relied on an energetic molecule called ATP for fuel. "This re-designed device uses its DNA input as its source of fuel," said Ehud Shapiro, who led the Israeli research team.

III. "TRANSCRIPTORS" IN PLACE OF TRANSISTORS:

When Charles Babbage prototyped the first computing machine in the 19th century, he imagined using mechanical gears and latches to control information. ENIAC, the first modern computer developed in the 1940s, used vacuum tubes and electricity. Today, computers use transistors made from highly engineered semiconducting materials to carry out their logical operations.

In electronics, Silicon transistors control the direction of flow of electrical impulses along a circuit within computer chips. Similarly, in biologics, a transcriptor controls the movement of an enzyme called RNA polymerase along a strand of the DNA molecule. A transcriptor is a biological transistor made from genetic material — DNA and RNA — in place of gears or electrons of a transistor

A group of natural proteins, called integrases, have been repurposed, to realize digital control over the flow of RNA polymerase along DNA, which in turn allowed to engineer amplifying genetic logic. Transcriptor-based logic gates are referred as "Boolean Integrase Logic gates" (the biological equivalent of AND, NAND, OR, XOR, NOR, and XNOR logic gates) or "BIL gates" for short. Transcriptor-based gates alone do not constitute a computer, but they are the third and final component of a biological computer that could operate within individual living cells. With transcriptors, a very small change in the expression of an integrase can create a very large change in the expression of any two other genes[Fig:1.2].

Like a transistor, which enables a small current to turn on a larger one, one of the key functions of transcriptors is signal amplification. A tiny change in the enzyme's activity (the transcriptor's gate) can cause a very large change in the two connected genes (the channel). By combining multiple transcriptors, a full suite of Boolean Integrase Logic (BIL) gates have been created. With these BIL gates, a biological computer could perform almost computation inside a living cell. Ultimately, the aim is to use the biological transistors (transcriptors) to make simple but extremely small biological computers that could be programmed to monitor and perhaps affect the functioning of the living cells in which they operate.

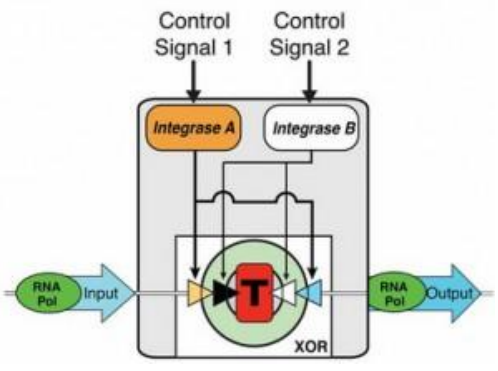

Fig: 1.2

IV. TRANSCRIPTORS IN HUMAN BODY:

Transcriptors are a biological version of electrical engineers' "logic gates' -- the building blocks of digital circuits that send and receive signals. A team of engineers has invented genetic transistors, completing a simple computer within a living cell, a major step forward in the emerging field of synthetic biology. The creation of the transcriptor allows engineers to compute inside living cells to record, for instance, when cells have been exposed to certain external stimuli or environmental factors, or even to turn on and off cell reproduction as needed.

It could lead to new biodegradable devices based on living cells that are capable of detecting changes in the environment, or intelligent microscopic vehicles for delivering drugs within the body, or a biological monitor for counting number of times a human cell divides so that the device could destroy the cell if it became cancerous

The gates could derive true-false answers to virtually any biological question that might be posed within a cell. For instance: Is toxic mercury present? It could detect it. They can also count. This would be a useful tool when treating diseases like cancer, where cells divide uncontrollably. Suppose a liver cell carries a counter that records how many times it divides. Once the counter hits 500, for instance, the cell could be programmed to die. The so called "living computers" inside the human body could screen for cancer, detect toxic chemicals or even turn cell reproduction on and off.

V. DNA COMPUTING:

DNA computing is a form of parallel computing in that it takes advantage of the many different molecules of DNA to try many different possibilities at once. For certain specialized problems, DNA computers are faster and smaller than any other computer built so far. Furthermore, particular mathematical computations have been demonstrated to work on a DNA computer. As an example, DNA molecules have been utilized to tackle the assignment problem. Aran Nayebi has provided a general implementation of Strassen's matrix multiplication algorithm on a DNA computer, although there are problems with scaling. In addition, Caltech researchers have created a circuit made from 130 unique DNA strands, which is able to **calculate the square root of numbers up to 15.**

DNA computing does not provide any new capabilities from the standpoint of computability theory, the study of which problems are computationally solvable using different models of computation. For example, if the space required for the solution of a problem grows exponentially with the size of the problem (EXPSPACE problems) on von Neumann machines, it still grows exponentially with the size of the problem on DNA machines. For very large EXPSPACE problems, the amount of DNA required is too large to be practical.

DNA computer coupled with an input and output module will also be capable of diagnosing cancerous activity within a cell, and releasing an anti-cancer drug upon diagnosis.

Catalytic DNA (deoxyribozyme or DNAzyme) catalyze a reaction when interacting with the appropriate input, such as a matching oligonucleotide. These DNAzymes are used to build logic gates analogous to digital logic in silicon; however, DNAzymes are limited to 1-, 2-, and 3-input gates with no current implementation for evaluating statements in series.

The DNAzyme logic gate changes its structure when it binds to a matching oligonucleotide and the fluorogenic substrate it is bonded to is cleaved free. While other materials can be used, most models use a fluorescence-based substrate because it is very easy to detect, even at the single molecule limit. The amount of fluorescence can then be measured to tell whether or not a reaction took place. The DNAzyme that changes is then used, and cannot initiate any more reactions. Because of this, these reactions take place in a device such as a continuous stirred-tank reactor, where old product is removed and new molecules added.

A design called a stem loop, consisting of a single strand of DNA which has a loop at an end, are a dynamic structure that opens and closes when a piece of DNA bonds to the loop part. This effect has been exploited to create several logic gates.

HOW DOES A BIO-COMPUTER LOOK EXACTLY?:

A bio-computer is actually built by combining chemical components into a solution in a tube. Various small DNA molecules are mixed in solution with selected DNA enzymes and ATP. The latter is used as the energy source of the device.

It's a clear solution. We don’t actually see anything. The molecules start interacting upon one another, and we step back and watch what happens. And by tinkering with the type of DNA and enzymes in the mix, scientists can fine-tune the process to a desired result.

To the naked eye, the **DNA computer looks like clear water solution in a test tube**. There is no mechanical device. A trillion bio-molecular devices could fit into a single drop of water. Instead of showing up on a computer screen, results are analyzed using a technique that allows scientists to see the length of the DNA output molecule.

VI. DNA DIGITAL STORAGE:

Numerous research groups have successfully stored data in DNA — and Stanford has already developed an ingenious method of using the M13 virus to transmit strands of DNA between

A wealth of information can be stored and encrypted in DNA molecules. Although each computing step is slower than the flow of electrons in an electronic computer, the fact that trillions of such chemical steps are done in parallel makes the entire computing process fast. Considering the fact that current microarray technology allows for printing millions of pixels on a single chip, the numbers of possible images that can be encrypted on such chips is astronomically large.

Because of DNA's ability to store information, major computer companies have been extremely interested in the development of DNA-based computing systems. In terms of speed and size, however, DNA computers surpass conventional computers. While scientists say silicon chips cannot be scaled down much further, the DNA molecule found in the nucleus of all cells can hold more information in a cubic centimeter than a trillion music CDs. A spoonful of Shapiro's "computer soup" contains 15,000 trillion computers. And its energy-efficiency is more than a million times that of a PC. In the latest effort to contend with exploding quantities of digital data, researchers encoded an entire book into the genetic molecules of DNA, the basic building block of life, and then accurately read back the text.

"A device the size of your thumb could store as much information as the whole Internet," said Harvard University molecular geneticist George Church, the project's senior researcher. In their work, the group translated the English text of a coming book on genomic engineering into actual DNA. DNA contains genetic instructions written in a simple but powerful code made up of four chemicals called bases: adenine (A), guanine (G), cytosine (C) and thymine (T).

The Harvard researchers started with the digital version of the book, which is composed of the ones and zeros that computers read. Next, on paper, they translated the zeros into either the A or C of the DNA base pairs, and changed the ones into either the G or T.

Then, using now-standard laboratory techniques, they created short strands of actual DNA that held the coded sequence—almost 55,000 strands in all. Each strand contained a portion of the text and an address that indicated where it occurred in the flow of the book. The Harvard effort stands out for its large scale, the scientists said. All told, the book contains 53,426 words, 11 illustrations and a JavaScript computer program. The 5.27 megabits of data are more than 600 times bigger than the largest data set previously encoded in DNA. It is the equivalent of the storage capacity of a 3.5-inch floppy computer disk[Fig:1.3].

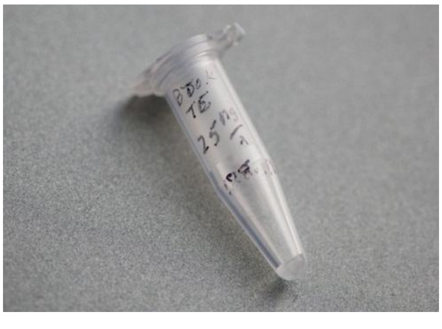

Fig: 1.3

In January 2013, researchers were able to store a JPEG photograph, a set of Shakespearean sonnets, and an audio file of Martin Luther King, Jr.'s speech I Have a Dream on DNA digital data storage.

VII. THE LEECHULATOR:

Neurons are the body's wires that transmit signals in the brain and throughout the nervous system. Putting neurons into semiconductor circuits could create the basis for a new breed of computer-brain like systems that finally live up to their name. A group of scientists from Emory University and Georgia Tech made a calculator (called the "leechulator") with neurons taken from leeches. In normal silicon computers, connections are made between the computer's chips only when the programmer directs the connections to occur. However, in a biological computer the neurons are able to connect on their own and are often said to be "thinking" by making connections with their neighbors, possibly increasing computational power. Normal silicon computers only make the connections they are told to by the programmer. This flexibility means the biological computer works out it own way of solving the problem. With the neurons, we only have to direct them towards the answer and they get it themselves. This approach to computing is particularly suited to pattern recognition tasks like reading handwriting, which would take enormous amounts of power to do well on a conventional computer.

The neurons are harnessed in a Petri dish by inserting micro-electrodes into them. Each neuron has its own electrical activity and responds in its own way to an electrical stimulus. These features can be used to make each neuron represent a number. Calculations are then performed by linking up the individual neurons. Leech neurons are used because they have been extensively studied and are well understood[Fig:1.4]. Though much simpler, the neuron computer works in a similar way to the human brain. Professor Ditto says a robot brain is his long-term aim, noting that conventional supercomputers are far too big for a robot to carry around.

Fig: 1.4

VIII. CONCLUSION:

Biological computers (literally) have a few bugs that need to be worked out before they start appearing regularly in mail order catalogues. For one thing, while they can do rudimentary sort of calculation, input/output is exceedingly slow. That slimy blob would take a long time to do something as simple as balance your checkbook, and it would need regular feedings as well. Silicon computers can switch between calculations. But you would have to construct a biological computer a new for each problem. Transistors are limited by "gating time," which is how long it takes the gate to open and close when you apply voltage. The gates of transistors composing chip snow on the market are 130 nanometers (really small), which make them fast and power efficient. But a biological computer is limited by diffusion, a relatively slow process. Plus, cells need a medium in which they have to grow.

Despite of the above facts, biological computers are tiny devices that could one day fit into cells and supervise biological processes, or even synthesize drugs. DNA strands exist in almost every body cell - they are biological software that tell each cell and molecule what to do. **Considering the mechanism of a cell, a lot of what goes on inside is computation.** We don't need to teach the cell new tricks, we just need to put the existing tricks in the right order.

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