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Letter from the journal

Dear readers,

We are proud to announce our third issue of the Youth Science Journal! We would like to thank all our readers for their support and feedback to improve our upcoming publishes. We also hope you enjoy reading this issue as our issue's theme is Biotechnology/Biomedical Engineering! There are a lot of remarkable articles in this issue, covering from bionic eyes to DNA sequencing. You may notice that our format is different this issue. We have changed it to fit our needs and be easier for writers.

Furthermore, we are excited to announce that 16 extraordinary students from different high schools are now part of our writers' crew! We have been on hiatus for the past months, conducting training sessions for them by the senior writers. Now, they are ready to publish their articles in our upcoming issues. So, stay tuned!

However, if you were not able to join our team, we are very proud to announce that the Youth Science Journal is open for publication! You can now publish your article on our website about any topic in science through: www.ys-journal.com/publish. Publishing a review article about a specific topic will not only let you learn about it more, but also share awareness for that topic! All you have to do is to make sure that your article is following our guidelines that are available on our website. We have already started accepting articles and we would like to thank Ziad Khaled for being the first to publish onto our journal!

Best Regards,
Youth Science Journal Community

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Bionic Eyes: the definitive solution for visually impaired individuals?

Ahmed Nassar, STEM High School for boys 6th of October

Abstract

Once a topic of folklore and science fiction, the notion of retaining vision to the blind is now much closer to becoming a reality than it ever was before. As the rise of microelectronics and microfabrication has given way to drastic improvements in the field of prosthetic devices. the developing technology has given rise to a plethora of approaches and designs to achieve said purpose. yet these visual prosthetics operate on the same premise: relying on intact neural circuitry whenever possible in order to take advantage of any intact sensory processing available [1]. Thus, lowering the need to deal with the complexity of the neural code for perception. However, as a direct consequence of that, it is highly unlikely that this technology will ever see the light for patients diagnosed with congenital blindness as they often lack a fully developed neural perception system. Although a functioning mechanism may very well be feasible, the rehabilitation of the blind and reintegrating them into society will continue to be a challenge against establishing this technology as a viable solution for the blind.

I. Introduction

Unlike what many would assume, Prosthetic eyes have, in fact, long been in development, with succeeding irritations improving using more microelectrodes that mimic the function of photoreceptors in the human cornea. The Argus II, for example, is the second generation of a prosthetic retinal implant with the goal of vision restoration for patients diagnosed with Retinitis pigmentosa. The implant study was first initiated back in 2002 in which implantation in six patients in the trial proved to be successful. The implant has proven that the device has the potential to allow legally blind patients to detect light, and possibly distinguish between objects. The device is basically meant to take place of photoreceptors.

However, the use of only 16 electrodes in first-generation devices was the most limiting factor in terms of vision fidelity. And henceforth the Argus II comprised 60 electrodes providing higher resolution images. The new device is approximately one-quarter the size of the original device, reducing surgery and recovery times by a significant margin.

II. Mechanism

In its very essence, the retina is merely a matrix of nerve cells firing signals upon being struck by lights of specific wavelengths and degrees. These neurons then send an electrical signal to the brain's visual cortex in which color, light intensity, edges, and more information are processed to try and work out what the person is seeing. This processing part, in fact, does not simply translate these electrical signals into images interpretable by the human but rather edits out what may be irrelevant and focuses on the more significant pieces of the image such as motion: an incredible process in the very least. Obviously, vision involves much more complexity than is shown, but this complexity is beyond the scope of this paper. Our primary focus here is to make it clear how a prosthetic eye could manipulate this system in

order to produce comprehensible images. The bionic eye can be viewed as a replacement for a retina that can no longer perform this function.

III. Improving Vision Quality

Several approaches have been devised to improve vision quality. The most obvious of which was to increase the number of implanted electrodes, allowing them to target certain neurons accounting for more pixels and thus better resolutions. However, normal sized-micro electrodes would not fit in such a confined space. For that reason, attempts at shrinking the size of the microelectrodes have been made [2]. By electrically stimulating retinal ganglion cells using thousands of microscale nitrogen-doped ultra-nanocrystalline diamond (N-UNCD) feedthroughs that act as electrodes. Aside from the expensiveness of the diamond coating, the use of such technology has not yet proven feasible and requires further research.

Another technique is to artificially increase the resolution by sharing electrical current between electrodes, producing additional "virtual electrodes". These new techniques can possibly improve visual fidelity, reduce blurriness, and give rudimentary control over color: a distinctive feature of natural eyesight.

The ultimate goal would be to fully understand the code sent from the retina to the brain. Theoretically, If the firing patterns of the receptors can be replicated, vision will appear exactly as perceived by a healthy individual's eye.

IV. The Future of Bionic Eyes

Taking the technology to the next level, there is a possibility to go beyond what a normal human eye could do. Once the code between the retina and the brain has been deciphered, there would be an unlimited potential for the technology from the ability to see infra-red, night vision, or x-ray. To magnifying images naturally, running software that processes images, blocking out bright sunlight, and substituting sunglasses. In fact, being able to watch a movie, scrolling through your newsfeed, or even playing a simple video game, seems equally plausible using the same technology that could, theoretically, help the blind see again.

V. Conclusion

Undoubtedly, the goal of restoring some degree of vision to the blind using bionic eyes certainly seems feasible, but providing them with fully detailed vision like that of healthy individuals while seemingly plausible with the progress the technology is seeing and with its technological challenges continuing to be solved, it is questionable whether these individuals will be able to fully interpret the images processed in the brain, and understand features like their depth, edges, and advanced details like color. Casting further doubt on the subject matter, it is yet to be understood how the brain of a once visually impaired individual would react to perceiving light once again and whether that would influence the recovery speed.

Rehabilitation is certainly going to be needed for a successful recovery. Furthermore, this technology shows no potential for treating cognitive blindness, and it is unlikely to be cured in the next decade. While the bionic eye does not yet seem to be a definitive solution for the blind. There is certain ground to be optimistic about the technology. What is now clear is that the feasibility of this technology is dependent on the mandatory collaboration between physicians, doctors, and scientists from different fields.

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Genetically Modified Organisms

Ziad Khaled, STEM High School for boys 6th of October

Abstract

Genetically Modified Organisms have been around two decades, and they are considered safe for human, but on the other side, other studies show that GMO have some risks and deleterious effects on animals, GM food just like any new drug requires many tests to prove that these new organisms are safe for human and can exist in the markets. Ongoing independent studies to evaluate safety are needed. Scientific, economic, environmental, social, ethical, and political perspectives will need to be considered.

I. Introduction

Genetically Modified Organisms (GMO) are organisms whose genetic information (DNA) has been changed by inserting a gene from another organism to give specific functions that it cannot do before this technique called "modern biotechnology" or "gene technology", which improve the yield through introducing resistance to plant diseases or of increased tolerance of herbicides, GMO can also allow for reductions in food prices through improved yields and reliability [1]. There are a lot of Genetic Modification Organisms that have been developed in recent time, all of them are inserted by genes from another organism for example the BT corn, a Bacteria called Bacillus thuringeinsis (BT) produce a protein toxic to the larvae of certain insects, such as the European corn borer. These Insects are found widely in Europe, North Africa, Canada, and most of the United States. These insects reduce the yield by 5%. The Bt corn is the corn that had the BT gene from Bacillus thuringeinsis inserted into its cells. This gene provides information that causes the plant cells themselves to produce the Bt protein. As a result, the offspring of the modified plants are protected from the corn borer.

II. How does the process of genetic engineering happen?

i. DNA isolation:

The needed gene is determined then they isolate the DNA from the organism that contains this gene by breaking the cell structure and this often happens physically by smashing the organism y, then protease (protein enzyme) is added to degrade DNA-associated proteins and other cellular proteins. After that the DNA separate by adding alcohol by this process all the cell material precipitate while the DNA become at the top and it will appear like white cotton.

ii. Use the plasmid as a vector:

A restriction enzyme is DNA-cutting enzymes. Each enzyme recognizes one or a few target sequences and cuts DNA at or near those sequences, this enzyme used to cut a specific sequence from the gene that has the needed treat, then the same restriction enzyme is used to cut the plasmid which is used as a vector to enter the gene to the organism, then the plasmid inter the organism by using a gene gun. After this process the cell will contain the foreign gene and when the cell division accrues the new daughter cells will contain this gene.

III. What are the benefits of GMOs?

GM foods are developed because of some perceived benefits to the producers and the consumers The World Health Organization (WHO) and the United States Department of Agriculture (USDA) have outlined a comprehensive list of the
benefits of GM foods. This list is discussed below.

i. Insect resistance:

Agricultural biotechnology has been used to make the plants insect resistant, this is achieved by introducing the gene of a toxin called Bacillus thuringeinsis come from BT Bactria, this toxin is considered for humans and it currently uses as an insecticide, the plants that uptake this gene become resistance against borer insects. This technology

makes the crop requires lower quantities of external insecticides. Such genetic modification can make crop production cheaper and more manageable, as well as make pest control safer. Additionally, there is decreased contamination of the groundwater and the environment from pesticides.

ii. Disease Resistance:

Some diseases can be resisted by using genetic modification organisms, as these crops resist some diseases better than the normal crops [7]. For example, when many diseases significantly threatened the Hawaiian papaya industry, the papayas were made disease-resistant through genetic engineering. This technology is expected to increase in the future, and it will be applied in many crops like potatoes, squash, tomatoes.

iii. Nutritional:

Some GMO can produce nutritionally enriched plants, as these organisms are uptake gene that will produce specific vitamin like golden rice, this rice is uptake biosynthesize beta-carotene gene, which is not normally produced in rice. The beta carotene gene is converted into Vitamin A when it is metabolized by the human body. Vitamin A is essential for healthier skin, immune systems, and vision.

IV. What are the risks of GMOs?

The world health organism has identified three main risks for the genetic modification organisms which are discussed below.

i. Allergenicity:

Some GM foods have the potential to cause allergic reactions, as the gene that is transferred to the food have the potential to cause allergic reactions, also another risk is introduced a new gene to the food that did not previously exist in the food chain [6]. Many, but not all, genes that are used in GM foods are novel and do not have a history of safe food use. An example of the allergenicity, GM soybeans that uptake a gene from the brazilin nuts, this gene is considered causative to allergic reactions in some people.to prevent this risk, the transfer of genes from commonly allergenic foods is discouraged unless it can be proven that the protein produced by the introduced gene will not be allergenic, also some tests happen to be sure that the introduced gene is not allergenic.

ii. Gene transfer:

Another risk for GMOs is the transfer of genetic material from the GM food to the human cells, the DNA that comes from GM food is not completely digested by the digestion system and small fragments of the DNA have been found in different parts of the gastrointestinal tract [3]. This could result in gene transfer by absorption of the DNA fragments by the somatic cells. Scientists hypothesize that uptake of GM DNA into the cells will have no biological consequences due to degraded of this DNA by the cells, However, it is not clear if people with gastrointestinal diseases will be able to completely degrade this GM DNA. An example for gene transfer, in Canada they found the BT toxin in 93% of the pregnant women tested.

iii. Outcrossing:

Outcrossing means that the genes of GM foods move to the natural plants or the related species, this could make other plants uptake unwanted genes that could cause health problems to the human and damage the plant itself [7]. To avoid this problem, farmers use buffer zones, pollen barriers, crop rotation, and monitoring during harvest, storage, transport, and processing to manage outcrossing.

V. Conclusion

GM food has numerous potential risks and benefits, many studies have shown positive and negative results for GM food. GM food has positive impacts on health, economic, environmental, and social. Corn is extensively used in processed foods and animal feeds, and GM corn now makes up almost the entire U.S. crop. GM soybeans are not far behind [4]. A team of Italian scientists has summarized 1,783 studies about the safety and environmental impacts of GM foods and did not find a single credible example demonstrating that GM foods pose any harm to humans or animals [5]. On the other side, GM food has many potential risks, to avoid these risks this technology must be studied and tested before this food becomes available in the market.

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DNA Sequencing evolution

Nabil Youssef, STEM October High School

Abstract

The genetic code is a universal language present in all known living organisms. The sequence of the four bases (adenine guanine thymine and cytosine) determines the genotype and phenotype of a living being. DNA sequencing can be used to determine the nucleotide sequence of specific genes, larger genetic regions, whole chromosomes, or the entire genome of an organism. Knowing this helps scientists answer fundamental biological questions about evolution and how life works. Known genomes in humans can be scanned for diseases and plants modified to create GM crops that are resistant to pests or have a higher yield. This technology is crucial to all genetic engineering. This article will cover the evolution of DNA Sequencing and explain the complete procedure of two of the most common methods of sequencing DNA, Sanger sequencing as well as next-generation sequencing.

I. Introduction

The last five to 10 years have seen some extraordinary feats in biology, among them determination of the entire DNA sequences of several extinct species, including woolly mammoths, Neanderthals, and a 700,000-year-old horse. Pivotal to those discoveries was the sequencing of the human genome, essentially completed in 2003 [1]. This endeavor marked a turning point in biology because it sparked remarkable technological advances in DNA sequencing. The primary human genome sequence took several years at a price of 1 billion dollars; the time and price of sequencing a genome are in free fall since then [1].

The discovery of the structure of the DNA molecule (Figure 1), with its two complementary strands, opened the door for the event of DNA sequencing and lots of other techniques utilized in scientific research today. Key to several of those techniques is macromolecule hybridization, the pairing of 1 strand of DNA to the complementary sequence on a strand from another DNA molecule.

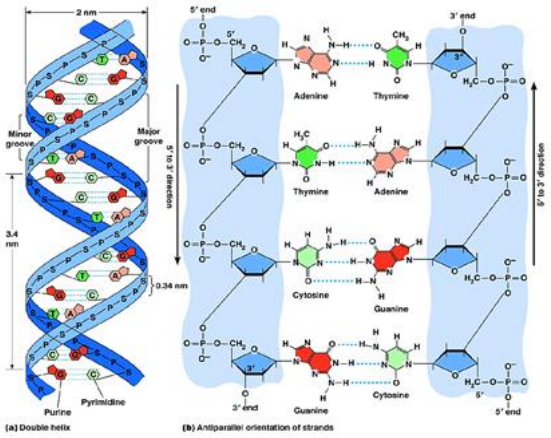


FIGURE 1 STRUCTURE OF THE DNA MOLECULE

II. The invention of DNA Sequencing

Early attempts to sequence DNA were unwieldy. In 1968, Wu and Kaiser reported the utilization of primer extension methods to work out 12 bases of the cohesive ends of bacteriophage lambda [2]. In 1973, Gilbert and Maxam reported 24 bases of the lactose-repressor binding site, by copying it into RNA and sequencing those fragments. This took two years; one base per month [3].

In around 1976, the development of two methods that would decode many bases in a day transformed the sector [4]. Both methods, the chain terminator procedure developed by Sanger and Coulson, and the chemical cleavage procedure developed by Maxam and Gilbert, used distances along a DNA molecule from a radioactive label to positions occupied by each base to find out nucleotide order. Sanger's method involved four extensions of a labeled primer by DNA polymerase, each with trace amounts of 1 chain-terminating nucleotide, to supply fragments of various lengths [4]. Gilbert's method took a terminally labeled DNA-restriction fragment, and, in four reactions, used chemicals to make base-specific partial cleavages [4]. For both methods, the sizes of fragments present in each base-specific reaction were measured by electrophoresis on polyacrylamide slab gels, which enabled the separation of the DNA fragments by size with single-base resolution. The gels, with one lane per base, were put onto X-ray film, producing a ladder image from which the sequence might be read off immediately, rising the four lanes by size to infer the order of bases.

III. Dideoxy Chain Termination Method for Sequencing DNA

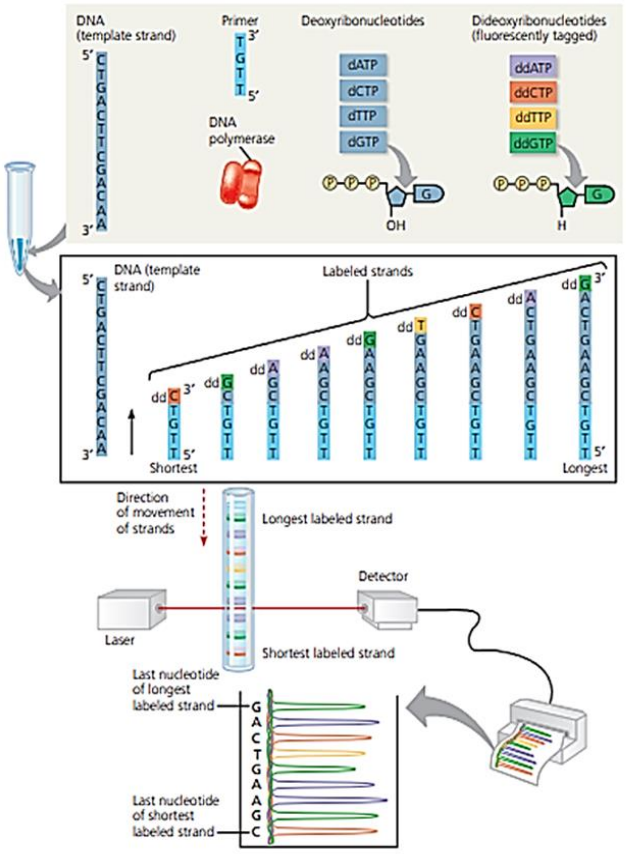
Sanger sequencing, also referred to as chain-termination sequencing, refers to a way of DNA sequencing developed by Sanger in 1977 (Figure 2). This method is predicated on the synthesis of a nested set of DNA strands complementary to one strand of a DNA fragment. Each new strand starts with an equivalent primer and ends with a dideoxy ribonucleotide (ddNTP), a modified deoxyribonucleotide (dNTP). The incorporation of a ddNTP terminates a growing DNA strand because it lacks a 3' OH group, the location for attachment of subsequent nucleotide. within the set of latest strands, each nucleotide position along the first sequence is represented by strands ending at that time with the complementary ddNTP.

Procedure

1) The fragment of DNA to be sequenced is denatured into single strands and incubated in a test tube with the necessary ingredients for DNA synthesis

2) Synthesis of each new strand starts at the 3′ end of the primer and continues until a ddNTP happens to be inserted instead of the equivalent dNTP. The incorporated ddNTP prevents further elongation of the strand. Eventually, a set of labeled strands of every possible length is generated, with the color of the tag representing the last nucleotide in the sequence.

3) The labeled strands in the mixture are separated by passage through a gel that allows shorter strands to move through more quickly than longer ones. For DNA sequencing, the gel is in a capillary tube, and its small diameter allows a fluorescence detector to sense the color of each fluorescent tag as the strands



come through. Strands differing in length by as little as one nucleotide can be distinguished from each other.

Because each type of ddNTP is tagged with a unique fluorescent label, the identity of the ending

nucleotides of the new strands, and ultimately the entire original sequence, can be determined. The color of the fluorescent tag on each strand indicates the identity of the nucleotide at its 3'-end. The results can be printed out as a spectrogram.

IV. Next-Generation Sequencing

The main difference between NGS (Figure 3) and Sanger sequencing is the construction of the sequencing library. Sanger sequencing libraries need multiple steps that combine molecular biology with microbiological culture to represent the DNA sample of interest as a series of subclones in a bacterial plasmid or phage vector. These subclones then need growth in culture and DNA isolation before sequencing. This multistep process can be completed in approximately one week, at which point the purified DNAs are ready for sequencing [3]. On the other hand, the simplicity and speed of NGS library construction are remarkable. Starting from a variety of input DNA sources ranging from high molecular weight genomic DNA to a pool of PCR products, to short stretches of histone-bound DNA released after chromatin immunoprecipitation (ChIP) or reverse transcriptase–converted RNA [1].

Procedure

1) Genomic DNA is fragmented, and fragments of 400 to 1,000 base pairs are selected.

2) Each fragment is isolated with a bead in a droplet of aqueous solution.

3) The fragment is copied over and over by a technique called PCR (to be described later). All the 5′ ends of one strand are specifically" captured" by the bead. Eventually, 106 identical copies of the same single strand, which will be used as a template strand, are attached to the bead.

4) The bead is placed into a small well along with DNA polymerases and primers that can hybridize to the 3′ end of the single (template) strand.

5) The well is one of 2 million on a multiwell plate, each containing a different DNA fragment to be sequenced. A solution of one of the four nucleotides is added to all wells and then washed off. This is done sequentially for all four nucleotides: dATP, dTTP, dGTP, and then dCTP. The entire process is then repeated.

6) In each well, if the next base on the template strand (T in this example) is complementary to the added nucleotide (A, here), the nucleotide is joined to the growing strand, releasing PPi, which causes a flash of light that is recorded.

7) The nucleotide is washed off and a different nucleotide (dTTP, here) is added. If the nucleotide is not complementary to the next template base (G, here), it is not joined to the strand and there is no flash.

8) The process of adding and washing off the four nucleotides is repeated until every fragment has a complete complementary strand. The pattern of flashes reveals the sequence of the original fragment in each well.

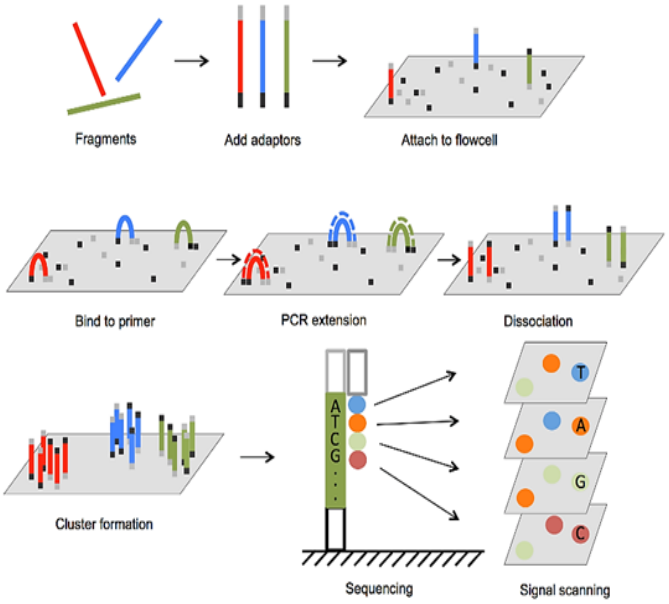


FIGURE 3 NEXT-GENERATION SEQUENCING

V. Conclusion

Improved DNA sequencing techniques have transformed the way in which we can explore fundamental biological questions about evolution and how life works. Little more than a decade after the human genome sequence was announced, researchers had completed sequencing roughly 4,000

bacterial, 190 archaeal, and 180 eukaryotic genomes, with more than 17,000 additional species underway [1]. Complete genome sequences have been determined for cells from several cancers, for ancient humans, and for the many bacteria that live in the human intestine.

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Brain-Machine Interface: Review of Current State and Clinical Applications

Gasser Alwasify, STEM High School for boys 6th of October

Abstract

Brain-machine interface (BMI) is a novel device that allows the translation of brain activity like action potentials in the neurons into commands and data that can be processed by machines and used. In the hope of helping neuromuscular patients with their severe disabilities, research has rapidly increased on BMIs in the past decade and a half. BMIs have been demonstrated to control robotic limbs, wheelchairs, computer cursors, and even allowed patients that are unable to talk to synthesize speech through them. In this review article, BMIs will be reviewed from its definition to the different types, invasive or noninvasive

I. Introduction

Brain-Machine Interfaces (BMIs) are novel devices that allow the translation of brain activity in terms of electric activity on the cortical surface of the brain, allowing the user to communicate with machines without moving peripheral nerves and muscles [1]. These devices provide a novel method of communication and control for humans in general with the outside world like the ability to control external devices such as personal computers to play video games, robotic arms and wheelchairs [2] [3] [4]. BMIs also show strong promise for critical neuromuscular disorders such as amyotrophic lateral sclerosis (ALS), Parkinson's disease, multiple sclerosis, etc. as it allows the usage of different neural pathways.

BMIs are typically characterized into dependent and independent BMIs. Dependent BMIs don't use the brain's normal output pathways to carry the message, but rather depends on the activity of the brain to detect a certain action. For example, in a visual experiment, instead of trying to track eye movement to activate a certain machine, dependent BMIs can detect the visual evoked potential (VEP) caused by said eye movement [5]. On the other hand, an independent BMI does not depend in anyway on the normal brain pathways, but rather depend on the intent of a user to do an action instead of actually doing it [5]. Like in the same example, an independent BMI would detect the intention to move your eyes and not the actual activity of the peripheral nerves and muscles to move the eye [6]. Because of this difference, independent BMIs have proven to have a lot more potential in clinical applications.

Any BMIs, regardless of its purpose and application, goes through four main processes as shown in figure 1: signal acquisition, feature extraction, translation algorithm, and device output [42]. These four main processes allow the main translation of the brain signals to device output. This review will go through these four main processes by focusing on Brain-Machine Interface's characterization, the different brain signals, explanation of the four processes, and decoders.

II. Noninvasive and Invasive BMIs

BMIs are also divided into two types: non-invasive and invasive. Non-invasive BMIs depend

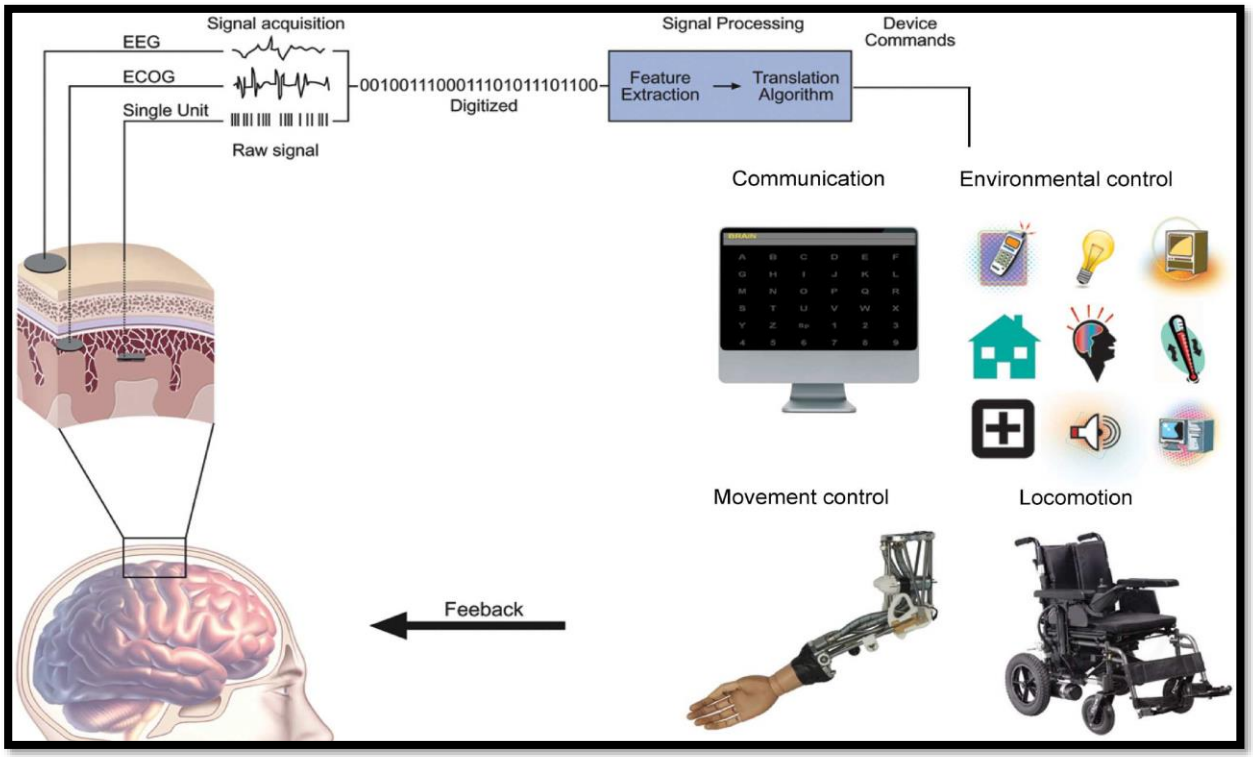

Figure 1 [42]: The components of the BMI operation, which includes signal acquisition, feature extraction, feature translation and device output. This figure further shows the potential clinical applications of these BMIs.

on electroencephalography (EEG) to detect electrical activity in the brain [10]. As neurons communicate through electric pulses in postsynaptic potentials, and thousands of neurons are firing per second, this activity is detectable through the use of small metal electrodes that are pasted on patients' scalp [7] [8] [9]. As the detected changes in voltage due to the many neurons' firing is very small, the electric pulse is usually amplified and then printed as a sequence of voltage changes over a certain brain area [9]. The area over which the electrodes are placed depends on the purpose of the EEG as for example, if examining the reaction to visual stimuli, electrodes are placed over the occipital cortex [7] [9].

Invasive BMIs require surgical implantation of electrodes in the brain, which means they require opening the scalp and skull and penetrating the brain tissue [10]. They are not preferred over non-invasive BMIs due to the possible risks like infection, especially if the implant is not entirely contained within the brain. Invasive BMIs are classified into five main types: local field potentials, single-unit activity, multi-unit activity, electrocorticography (ECoG) and calcium channel permeability [10].

Local field potential (LFP) is the transient electrical signals, which are formed from the combination of large neuronal populations, in the order of tens of thousands [11]. While singe-unit invasive BMI detects the activity of single neuron's action potentials, the multi-unit invasive BMIs detect the activity of multiple neurons at the same time. For instance, a single-unit BMI would only decode specific neuronal activity in an area like motor commands in M1 or cognitive signals in PP [12]. These methods usually employ extracellular methods to record and discriminate postsynaptic potentials generated by the hundreds of cortical neurons [12].

Furthermore, the fourth type electrocorticography is sometimes considered a semi-invasive method because it requires surgical procedure to remove a part of the skull, but it doesn't penetrate any brain tissue. ECoGs are basically EEGs attached to the surface of the brain itself, where a grid of electrodes detects the activity of the brain [13] [14] [15]. ECoGs could be epidural or subdural, where the difference is that the latter's dura mater is left open. This allows for better accuracy and detection as shown in [16]. They are advantageous over normal EEG-BMIs because they have better

spatial and temporal resolution [17]. Still, its performance and accuracy can't still rival with invasive BMIs [16] [17]. Lastly, the calcium channel invasive BMIs (CaBMI) were developed in [18], where ten mice were genetically modified to express a calcium indicator gCaMP6f in L2/3 of both primary motor M1 and somatosensory (S1) cortices. Two-photon calcium imaging were used to record activity in the small field of view [18].

III. Brain Signals Detectable by Noninvasive BMIs

Non-invasive BMIs detect seven types of signals: slow cortical potentials (SCP), sensorimotor rhythms, P300 event-related potential, steady-state visual evoked potentials, error-related negative evoked potentials, blood oxygenation level and cerebral oxygenation changes.

i. Slow Cortical Potentials (SCP)

Slow cortical potentials are the occurrence of cortical polarization, which can be easily recorded using direct amplifiers from any location on the scalp [5]. They usually occur over 0.5-10.0 seconds. Voltage changes across the scalp can be either positive or negative; while BMIs detect negative SCPs during movement causing cortical activation, they detect positive SCPs which are caused by reduced cortical activation [19] [20]. In Birbaumer studies, it was shown that it is possible to control SCPs and even control the movement of a cursor on a computer screen [21]. In [22], a thought translation device (TTD), a non-invasive BMI, has been developed, where it was able to deliver basic communication with late-stage ALS patients in [23].

ii. Mu and beta rhythms

Mu and beta rhythms from somatosensory cortex sinusoidal frequencies in ranges 8-13 Hz that are detected by BMIs at the somatosensory and motor cortical regions [10]. These rhythms decrease in amplitude as movement of the body increases. Sensorimotor rhythms of Fp1, Fp2, F3, Fz, F4, T7, T8, C3, Cz, C4, Cp3, Cp4, P3, Pz, P4 and Oz were recorded using 16 EEG channels in [24] to control cursor movement in a computer screen, which achieved more than 50% accuracy (p-value lower than 0.001).

iii. P300 event-related potential

When the somatosensory cortex gets activated through significant auditory, visual, or any stimuli, it typically evokes the non-invasive BMI over the parietal cortex at about 300 milliseconds [25]. Thus, it was named P300 event-related potential as it only evokes at 300 ms when any event occurs causing a particularly significant stimuli to the patient [5]. The signal of the potential increases in amplitude when the patient maintains greater attention to that specific stimuli [10]. Using P300 event-related potentials in [26], a paradigm has been introduced that have been used as a BMI spelling application in [27], [28], and [29].

iv. Steady-state visual evoked potential (SSVEP)

Steady-state visual evoked potentials are signals evoked from the occipital cortex during the occurrence of periodic presentation of visual stimuli of 6 hertz [10]. A survey showed that SSVEP can be utilized by presenting a rendered visual stimulus (RVS) to the user through alternating graphical patterns on computer screens [31]. Even more, [30] developed a novel independent SSVEP-BMI based on covert attention that helped locked-in syndrome patients. However, SSVEP BMIs are limited as they depend on attentional capacity and vision, which is mostly compromised in patients with more severe neurological diseases [5].

v. Error-related negative evoked potentials (ERNP)

ERNPs occur 200-250 miliseconds after "the detection of an erroneous response in a continuous stimulus-response sequence [10]." For instance, when a patient is subjected to continuous visual stimuli and then has to pick out a certain stimuli of the bunch, a P300 event-related potential is evoked if the target stimuli is found. However, if any stimuli occur other than the target, then the error-related negative evoked potential occurs [32].

vi. Blood Oxygenation Level

This type of BMI doesn't depend on EEGs but instead of functional MRIs. Blood oxygen level-dependent fMRI detects the metabolic activity in the brain, which represent the changes in neural activity [10] [33] [34] [35]. BOLD was used in the past in patients with neuropsychiatric disorders in which a novel brain self-regulation technique that crosslinked psychological and neurobiological approaches through utilizing the neurofeedback of the fMRI [37]. The results were rather promising as the patients' Hamilton Rating Scale for Depression improved significantly in [37].

Real-time control of robotic arm was demonstrated to be possible using real-time functional MRI that detected the blood oxygenation level dependent signals from the regional cortical activations in the primary motor area M1 [36]. This allowed the movement of the robotic arm only through the subjects' thought processes.

vii. Cerebral oxygenation changes

Near Infrared spectroscopy (NIRS) is an spectroscopic technique that measures light absorbance to calculate oxy-HB and deoxy-HB, which provides insight of brain activity [37]. NIRS is characterized with high temporal resolution and spatial resolution. NIRS has enabled non-invasive measurement of the cerebral oxygenation changes through BMI in patients [40]. As EEG-BMI have not succeeded with complete locked-in state patients [41], metabolic brain-machine interfaces based on near-infrared spectroscopy has provided a novel method to allow the slightest communication for these patients.

IV. Signal Acquisition

Signal acquisition is basically the measurement of the neurophysiologic state of the brain, where the BMI is tracking the aforementioned signals in the brain [42]. These signals will reflect the person's intent to do a certain action, which is used to drive the brain-machine interfaces [1]. These signals will be acquired in various techniques, which include, but aren't limited to, electrodes on the scalp recording EEG, electrodes beneath the skull and over the cortical surface of the brain recording electrocorticography, and, lastly, LFPs and neuronal action potentials recorded by invasive BMIs – microelectrodes - within the brain tissue [1]. After that, these signals are amplified and then digitized to move into signal processing [42].

V. Feature Extraction

The first step of signal processing is feature extraction, which is the extraction of main changes in signals that are encoding the intent of the user [42]. To have the highest efficiency and effectiveness, the extracted features should be highly coherent with the user's actual intent. The digitized signals from the signal acquisition step are passed through certain procedures like spatial filtering, voltage amplitude measurements, spectral analysis, or single-neuron separation [1]. For example, the firing of a specific cortical neuron or the rhythmic synaptic activation in sensorimotor cortex, producing a mu rhythm. The location, size and function of this cortical area generating the evoked potential is essential to know how it should be recorded and how users will adapt to control its amplitude [1]. To analyze the neuronal signals, time domain or frequency domain analyses is utilized with respect to time or how much a certain signal is present among a given frequency band respectively [43]. Both the time domain, such as evoked potential amplitudes or neuronal firing rates, and frequency domain, such as mu or beta-rhythm amplitudes, are used to analyze the signal features in BMIs [1] [44] [45]. Even more, a study has shown that both these domain and frequency-domain signal features, improving performance and accuracy [46]. Furthermore, BMI could use other pathways like autoregressive parameters, which correlate with the user's intent but don't necessarily represent what is actually happening in the brain [1]. Finally, the signal is sent into the next step: translation algorithm

VI. Decoding of brain signals

After the BMIs extract the features of the signal, either invasive or non-invasive, computational algorithms are employed to translate these neuronal activities for direct communication with the brain [17]. These algorithms, often called decoders, use

statistical and machine-learned techniques to translate these signals. Decoders are especially utilized in BMIs that have multiple input and outputs, which are provided by neural recording channels [17]. This algorithm might use linear methods like statistical analyses or nonlinear methods like neural networks [47]. Through this algorithm, the signal features are changed into commands that could be understood [1].

When a new user first uses the BMI, the algorithm attempts to adapt to the user's static features, adjusting to the user's feature signal like mu-rhythm, P300 event-related potentials and single cortical neuron's firing rate [1]. However, being subjected to different times of day, hormonal levels, recent events, fatigue, illness, and other factors causes short-term variations in the signals detected from BMIs. Therefore, another level of adaption is always employed that reduce those instant variations. To further increase adaption of the algorithm, effective interaction between the BMI and the user's brain is accommodated by engaging the adaptive capacities of the brain. As you train the brain by achieving the expected results of BMI operation, the brain will adapt over time and modify the output signal due to its plasticity, improving the operation of the BMI. Usually, this has been done by rewarding the user by any means after successful use to help increase plasticity's chance to favor strengthening the signal.

VII. Device Output

After signal acquisition, feature extraction and going through decoding algorithms, the signal is then passed through its final phase, which is the translation of that signal into an action. This action could be the selection of words through a computer screen [48], move the cursor on a computer screen as tested in [49], [50] and [51], neuroprosthetic control of wheelchairs [52] [53] and robotic limbs [54] [55] [56].

VIII. Conclusion

Full recovery for patients with motor progressive diseases, as of right now, is not possible, as diseases like amyotrophic lateral sclerosis (ALS), Parkinson's disease, multiple sclerosis still don't have viable treatments that can stop the progression of them [57] [58] [59]. Patients with severe trauma caused by stroke, cerebral palsy, or injury to the spinal cord or brain also have little to no full motor recovery [60] [61]. Thus, researchers have been attempting to develop ways to improve these patients' quality of life as most of these neurological conditions are permeant.

Brain-machine interfaces hold great promise for being that solution for these disabling neurological disorders, from helping completely locked-in patients achieve control of computer cursors, wheelchairs, robotic arms [54] [55] [56], and even speech synthesizers [62]. Although most of these ideas are still early for clinical application, most of them hold promise but are still just lacking due to the limited number of electrodes – no more than 256 electrodes - that can be used in invasive BMIs. However, this is all changing soon as Neuralink, a project started by Elon Musk, is proposing a scalable high-bandwith novel BMI system, that has as many as 3072 electrodes per array. In this ground-breaking project, they have also built a neurosurgical robot capable of inserting 192 electrodes per minute into patients' brains [63]. This new BMI system will also house on-board amplification and digitization system in less than 27 x 18.5 x 2 mm^3 [63]. This approach to BMIs has allowed an unprecedented packaging density and scalability and also in a small footprint that is clinically relevant [63].

IX. References

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