GEN PHILIC

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Innovations in Medical Biotechnology

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We all can sense!

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Introduction

Since the advent of the first oxygen biosensor by Led and Clark in 1962, biosensors have attained extensive fame and recognition in the scientific community, especially in the biomedical field and nanotechnology. The future and potential of biosensors proves to be boundless with applications in fields ranging from and not limited to, pharmaceuticals, food and beverages, environment and many such biotechnological industries. Biosensors break the norm by their ability to methodically detect the target molecule even when it's present in very low quantities. This property is considered crucial in detecting diseases at an early stage and thus start their treatment promptly.

A biosensor is defined as a self-contained analytical device that combines a biological element (biosensing components) with a physicochemical component (bio transducer component) to generate a measurable signal for detection of an analyte of biological importance.

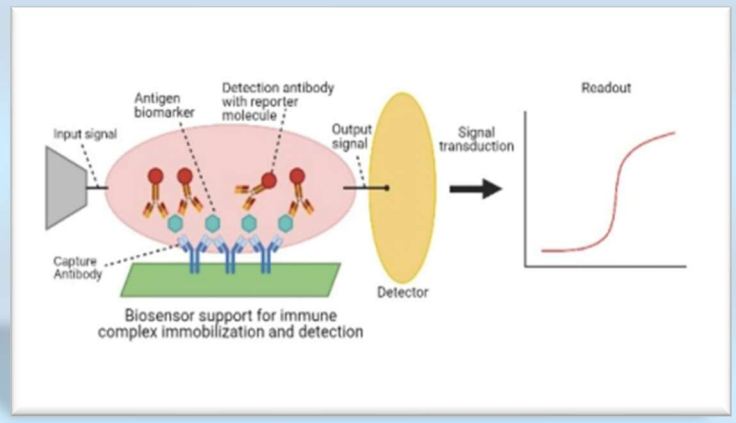
Biosensing elements

Biosensing elements are essentially a set of biological entities that are capable of detecting a compound by either carrying out reactions or binding to it. This detection yields a signal which is subsequently read and transformed by transducers to human-readable format.

Commonly used biosensing elements are of two types

1. Catalytic type: enzymes, microbes, organelles, cells, or tissues

2. Affinity type: antibodies, receptors, and nucleic acids



Enzyme based biosensors utilize the principle of enzyme catalytic reactions accompanied by consumption or generation of detectable compounds like O2, CO2, H2O2, NH3 and H+ or by activation or inhibition of the enzyme activity by the analyte that can be easily detected by the transducers.

❖Microbial biosensors enjoy an advantage—over their enzyme-based counterparts—of being economical and having the means to detect the bioavailability of contaminants. They do so by being utilised as a bio-sensing matrix in the contriving of biosensors. Factors like being omnipresent, having the ability to adapt and metabolise new molecules also give them an upper hand.

❖ Cell organelles play specific roles inside of a cell and hence are capable of detecting analytes exclusive to them with precision. The powerhouse of the cell—mitochondria—measures calcium concentration which is then used to determine water quality.

❖ Cells demonstrate adhesiveness to surface, a property which makes them suitable for immobilization on the matrix surface and attachment of receptors on cell membrane. Tissues are advantageous over cells and organelles because of high content of enzymes,

cofactors, higher activity, and stability, however they lack specificity because of presence of unwanted enzymes which leads to ambiguous catalytic reactions.

❖ Antibodies are an indispensable component of immunosensors. The antibodies immobilised on matrix have transducers covalently linked to them, and interact directly with analytes and causing detection via transducers and subsequently quantification.

❖ DNA is suitable for biosensing because of its specific property of base pairing with a complementary sequence. Nucleic acid biosensors (NABs) commission short synthetic single-stranded oligonucleotide probe that is immobilized on the transducer to detect the DNA/RNA in the sample.

❖ New receptors called aptamers bind to the target with selective affinity and efficiently discriminate between closely related targets.

Biotransducer Elements

Transducers are the elements which identify the stimulus released from the interaction of the analyte with the biosensing component and transform it into a detectable signal. Of all the developed biosensors, the commonly used are electrochemical, optical, and piezoelectrical.

❖ Electrochemical sensors measure the electrochemical changes that occur on the sensing surface of electrodes on interacting with the analyte.

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❖Optical sensors measure output transduced signal based on its optical diffraction which is then measured by a photodetector. The measured optical signals often include absorbance, fluorescence, chemiluminescence, surface plasma resonance, or changes in light reflectivity.

❖ Piezoelectric biosensors are based on the measurement of changes in resonance frequency of a piezoelectric crystal due to mass changes on the crystal structure.

Conclusion

High level precision and accuracy, high specificity, ultra-sensitivity, fast and simple assay techniques, very low reagent consumption, and many biological sensing elements that are reusable and allowable combined with the freedom to design an idiosyncratic device that can be programmed to provide continuous monitoring, change and specify parameters as well as being quick while doing it are the expansive assets proffered to scientists in the form of biosensors.

However, the practical application of biosensors in medical world is still in its infancy. In order to meet the criterion of a precise diagnostic tool, these devices need further advancement in terms of simplicity, sensitivity, multiplex analysis of multiple biomarkers, and integration of different functions by the same chip.

Editing the DNA?

CRISPRoff- Don't cut your genes, just turn them off!

Article and Illustration by
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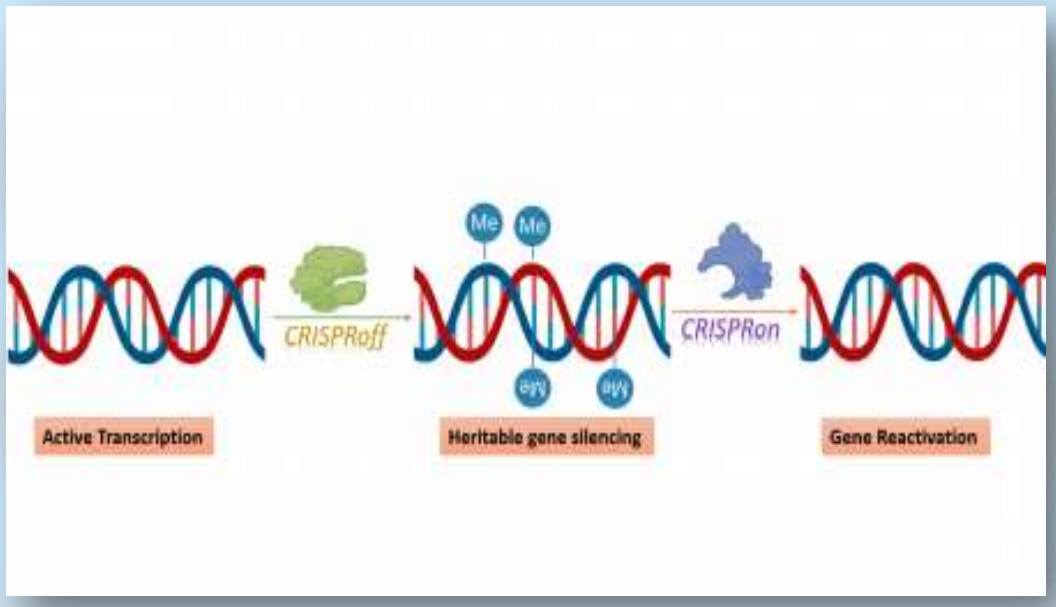
CRISPRoff

The CRISPR technology caused ripples and echoes in the scientific community in view of the fact that it made possible the alteration of DNA- a very sci-fi like scenario. Just the same, any revolution has its cons. CRISPR system alters the genetic sequence—the keyword being 'alter'— and is hence, a permanent effect. Added to it is the fact that CRISPR relies on the cells own repair mechanism to do the end job of patching up the DNA strand break, which can be pretty hard to control, thus leading to unpredictability.

Be That as it may, rub the frown off your face! There's a avant-garde technique called CRISPRoff. Like the classical CRISPR this too is world-changing, but unlike CRISPR, CRISPRoff DOES NOT alter the gene sequences. Rather it uses epigenetic tools to turn off the expression of a gene, thus leaving your DNA in peace. Epigenes—or epigenetic marks—are like 'caps' on our regular DNA, these include methyl groups, acetyl groups, etc. Epigenes like regular genes are heritable but epigenetic changes are reversible unlike genetic changes, and this fact is exploited by CRISPRoff. It uses an RNA guide (just like CRISPR) to guide a protein—an enzyme— to a specific location on DNA and add a methyl group to it. Methyl groups make it impossible for the RNA polymerase to access DNA, hence preventing transcription. Since no RNA strand is made, corresponding protein too isn't made and gene is said to have been silenced. But this silencing isn't permanent and genes can be turned on by using enzymes to remove the methyl tags - this process is called CRISPRon.



Two of the things that surprised scientists were:

1. CRISPRoff could target even the non-protein coding regions of DNA that don't make protein but affect gene expression!

2. Scientists had believed that methylation can only occur at specific sites called CpG islands (stretches of DNA having high density of CG base pairs).

But surprisingly, methylation can also occur at sites that lack CpG islands!

Will it actually work?

In an effort to understand the extent of its reach on therapeutics, scientists reduced the expression of Tau gene - the gene involved in causing Alzheimer's disease. Still, targeting specific tissues is the present hurdle, but Jonathan Weissman, the head scientist offers a sliver of hope by saying- "You can deliver it transiently as a DNA or as an RNA, the same technology that's the basis of the Moderna and BioNTech coronavirus vaccine".

Détendez-vous!

***Gene Therapy** - Ray of Hope for Hemoglobinopathies*

Hemoglobinopathies encompass all the genetic disorders of haemoglobin, either due to its abnormal production or structure. It affects the red blood cells. These ailments can be categorised as:

1) Thalassemia syndromes (Alpha thalassemia, beta thalassemia, etc)

2) Structural haemoglobin variants (HbS, HbE, HbC, etc)

Although the routine therapies for these conditions such as blood transfusion have improved the condition of these patients, it's not the permanent cure. Gene therapy is a novel experimental technique proposed to treat genetic disorders by transferring desired genes into the host cells, compensating for the lack or abnormality of said genes in the cell. It offers an alternative approach aimed at curing patients afflicted by hemoglobinopathies by globin gene transfer. It is showing promise in the case of both, beta-thalassemia and sickle cell anaemia. The gene

transfer tools for the treatment of both these diseases based on lentiviral vectors have proven safe in the research and clinical trials being carried out for two decades.

Sickle cell anaemia:

Sickle cell anaemia is a genetic disease wherein red blood cells are shaped as sickles or crescent moons which can retard the blood flow instead of normal bi-concave red blood cells (RBCs) that can move through the blood vessels easily.

While Gene therapy targets genes, they don't necessarily have to be the disease-causing ones, it can also be aimed at those facilitating/complementing the disease or those suppressing it. This is demonstrated by the two approaches of Gene therapy for Sickle cell anaemia:

1) *HBB* (Haemoglobin Subunit Beta) gene located on chromosome 11, codes for the beta subunit of haemoglobin protein. In the patients suffering from sickle cell anaemia, this gene is mutated which leads to the structural abnormality of the RBCs. One way to treat this disease is to replace this mutated copy of the gene with a healthy one in the patient's haematopoietic stem cells so that they produce normal RBCs.
2) Foetal haemoglobin is the main oxygen carrying protein in human foetus and is produced seven months before the birth. It doesn't sickle like the adult haemoglobin. Scientists have been trying to boost the production of foetal haemoglobin in adults by removing one of the genes that suppresses its production, it can greatly benefit the patients suffering from sickle cell anaemia.

β-Thalassemia:

β-thalassemia is caused when the synthesis of beta globin chain is absent or is reduced, which can be attributed to a variety of mutations occurring in the beta globin gene, this results in decrease of HbA (normal adult haemoglobin) synthesis in the red blood cells.

Bluebird Bio Inc.— a clinical stage Biotechnology company — has successfully completed the clinical trials for β-thalassemia using gene therapy.
Here the stem cells from the bone marrow of the patients are taken out of the body and are purified (through clinical trials it has been observed that if the number of stem cells collected from patient is higher followed by proper purification, correction and reinsertion into the patient's body,
then the chances of a successful gene therapy are higher).

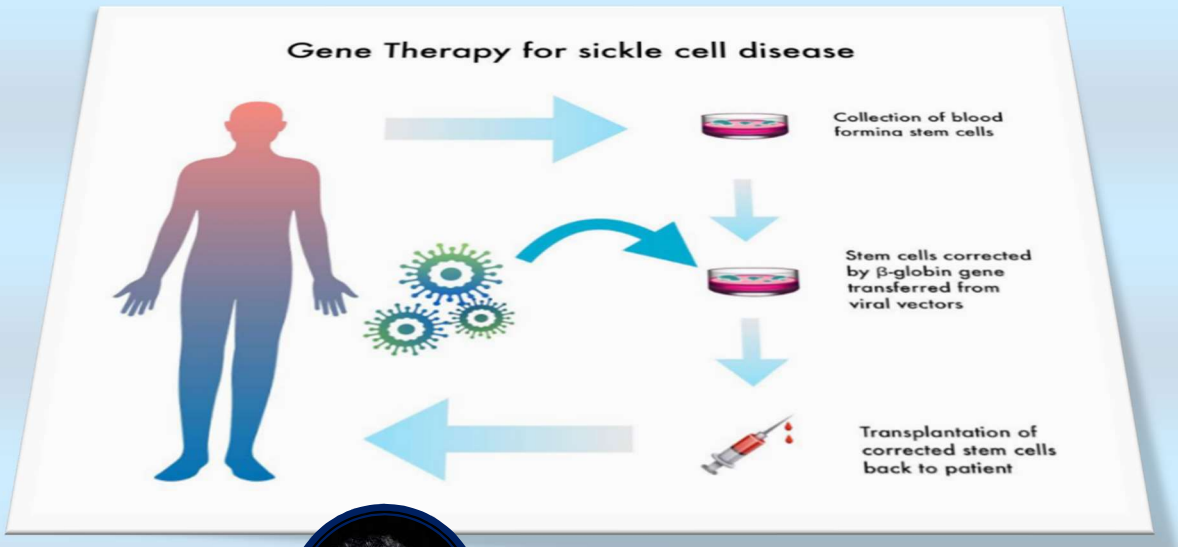


Illustration by
Hrishikesh Hardikar
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Next, a functional copy of the beta globin gene which has also been made ex-vivo (in-vitro) is inserted in the defective stem cells obtained from the body. This step utilises a Lentivirus, which in this case will act as a vector (used to transfer gene of interest in host cells). The Lentivirus has to be first and foremost genetically modified in the laboratory so as to render it harmless to humans and to prevent any possible complications along with imparting it the ability to transfer the functional beta globin gene to the stem cells.

The laboratory preparations are done. Now comes the time to reinsert the corrected stem cells into the patient's body. At this point, the patient undergoes through Myeloablative Chemotherapy - where the resident cells of bone marrow are killed and it is prepared to receive the genetically modified/corrected stem cells. After this chemotherapy, the modified stem cells are then inserted in the bone marrow of the patient.

It is devastating to live with such genetic disorders whose cure is unknown. Nevertheless, after many decades of research, a new era of Gene Therapy has come for the treatments of genetic disorders, carrying with itself a curative potential. Although many clinical trials are still ongoing, we can surely say that Gene therapy is the ray of hope for millions of people suffering from previously thought incurable genetic diseases.

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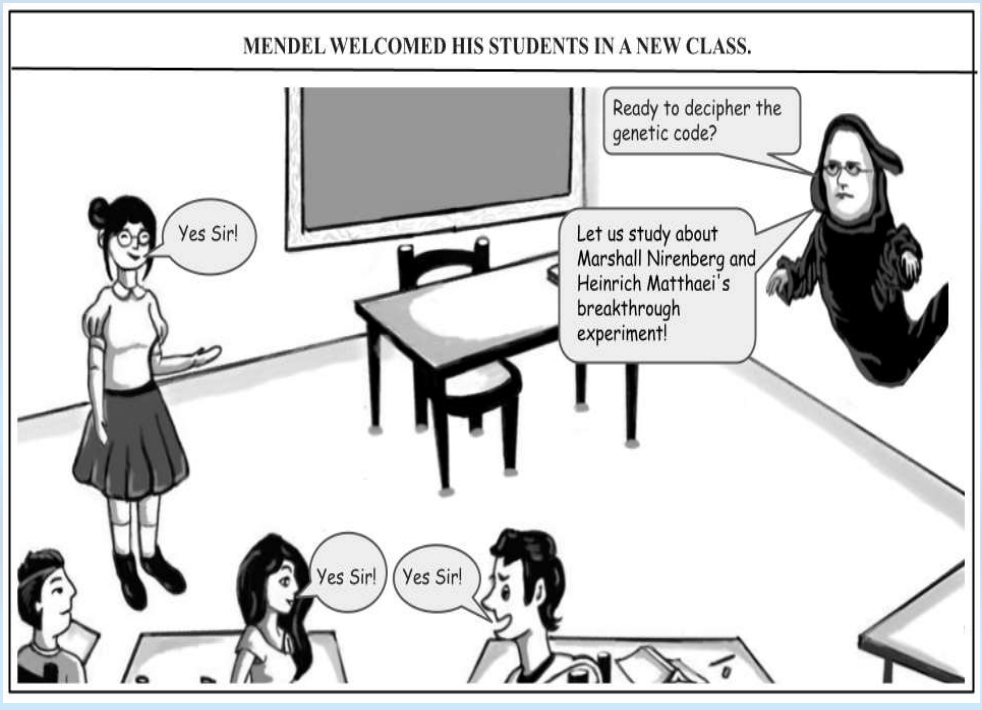
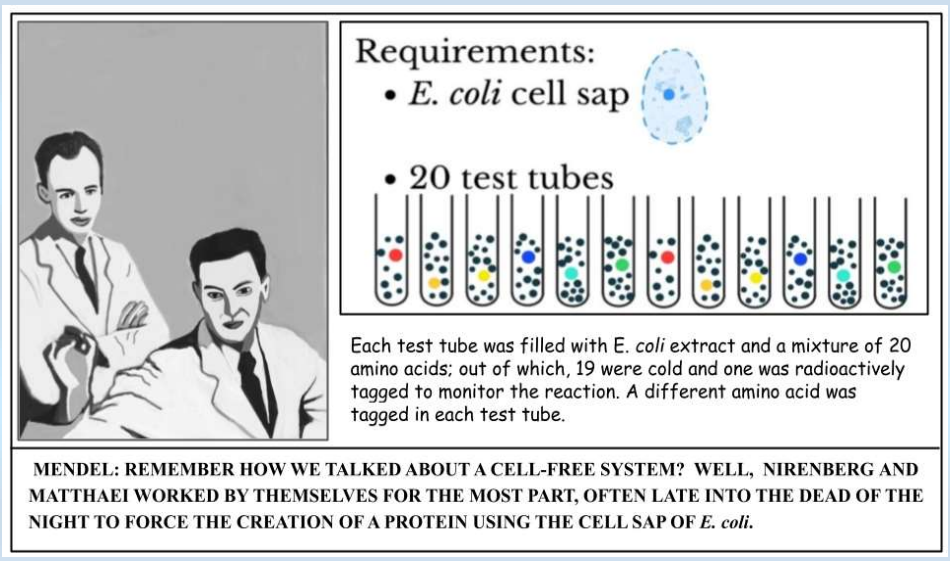
Back to Basics with Friendly Grandpa Ghost Mendel!

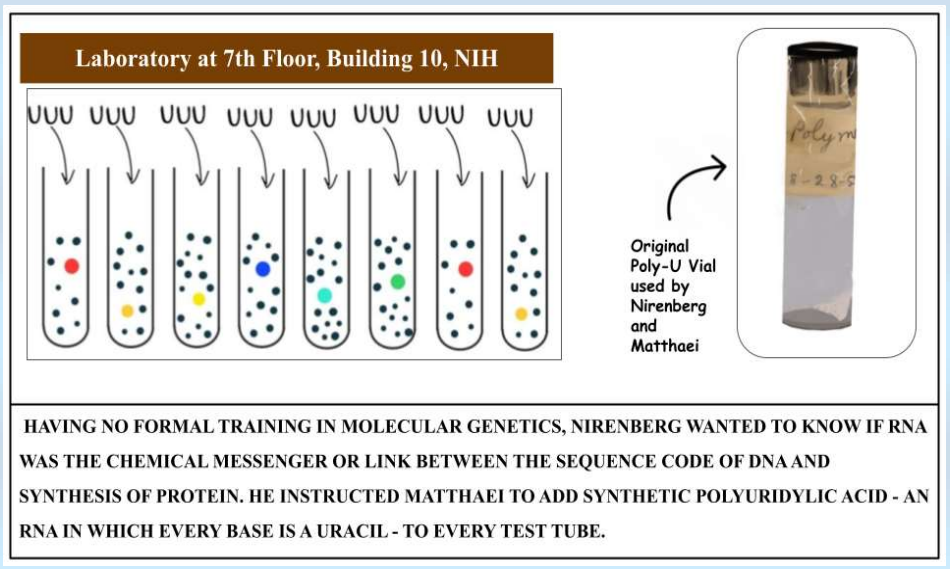
You know the legendary Gregor Mendel. You might not know the legends in the race to find messengers of life! Come, discover the story with Mendel himself, and see where the journey takes you!

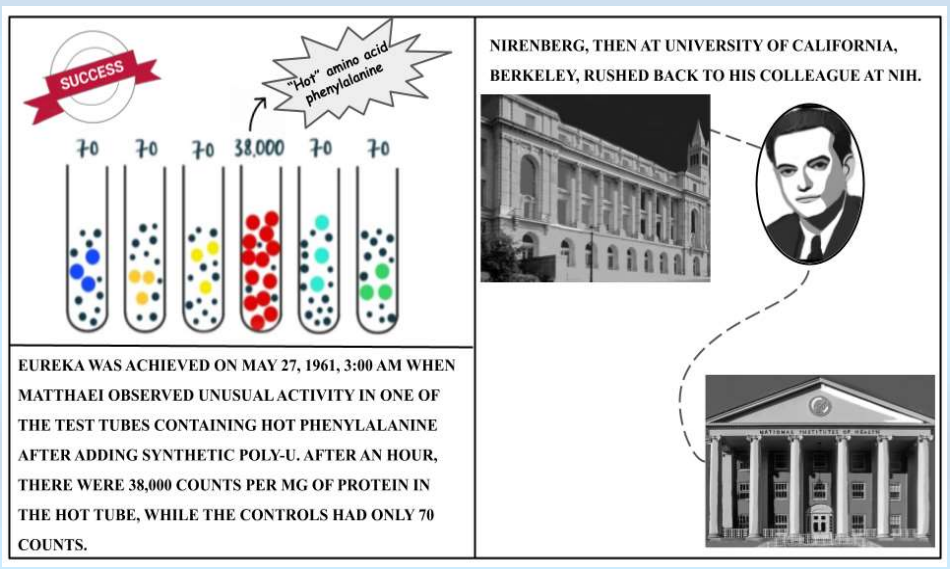
(Note: Read Left to Right)

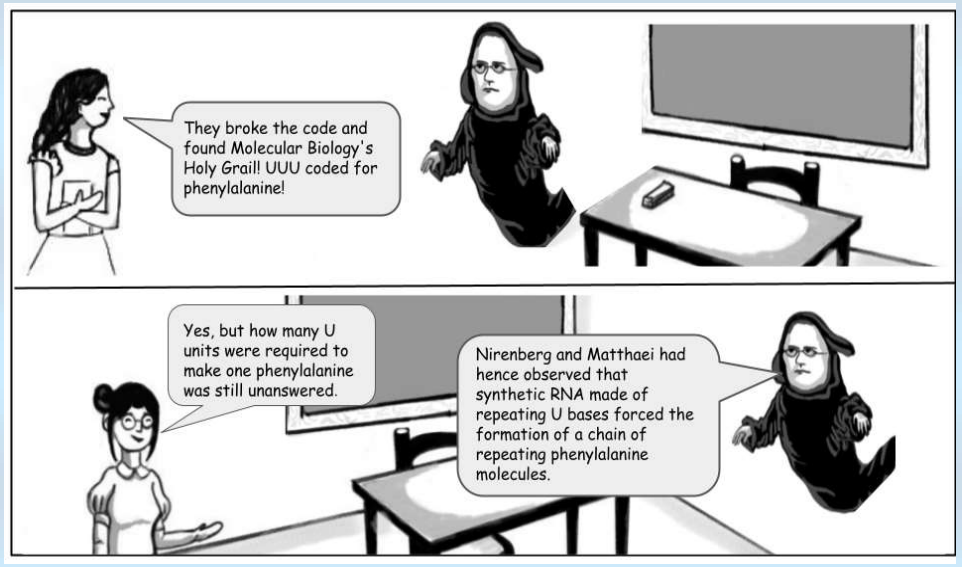


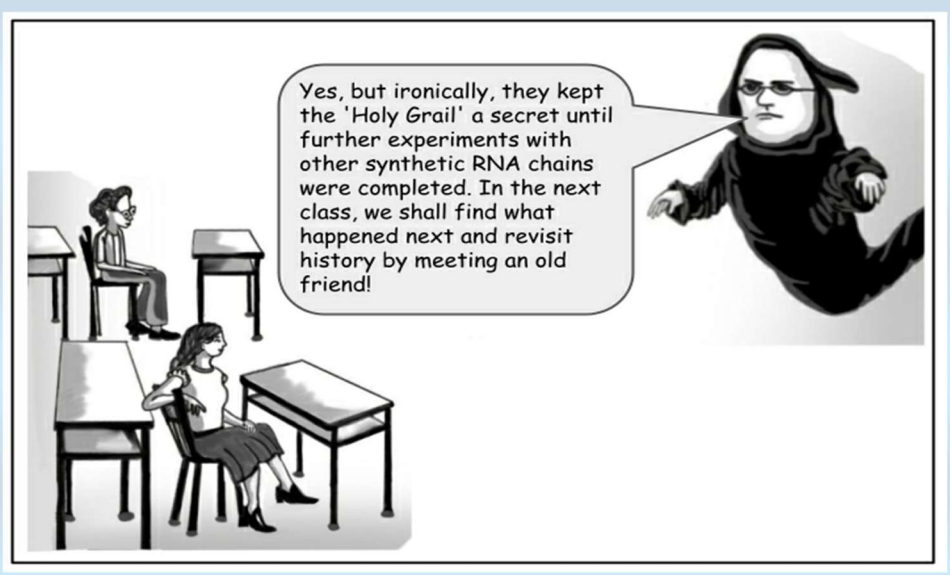


The test tubes in the image have been drawn for visual representation only and are not to scale. The colored circles represent the tagged amino acid ,while the ones in black represent a mixture of 20 different amino acids as mentioned above









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Bio-Printing

The Printer who printed its way In the MEDICINAL FIELD

Article and Illustration by:
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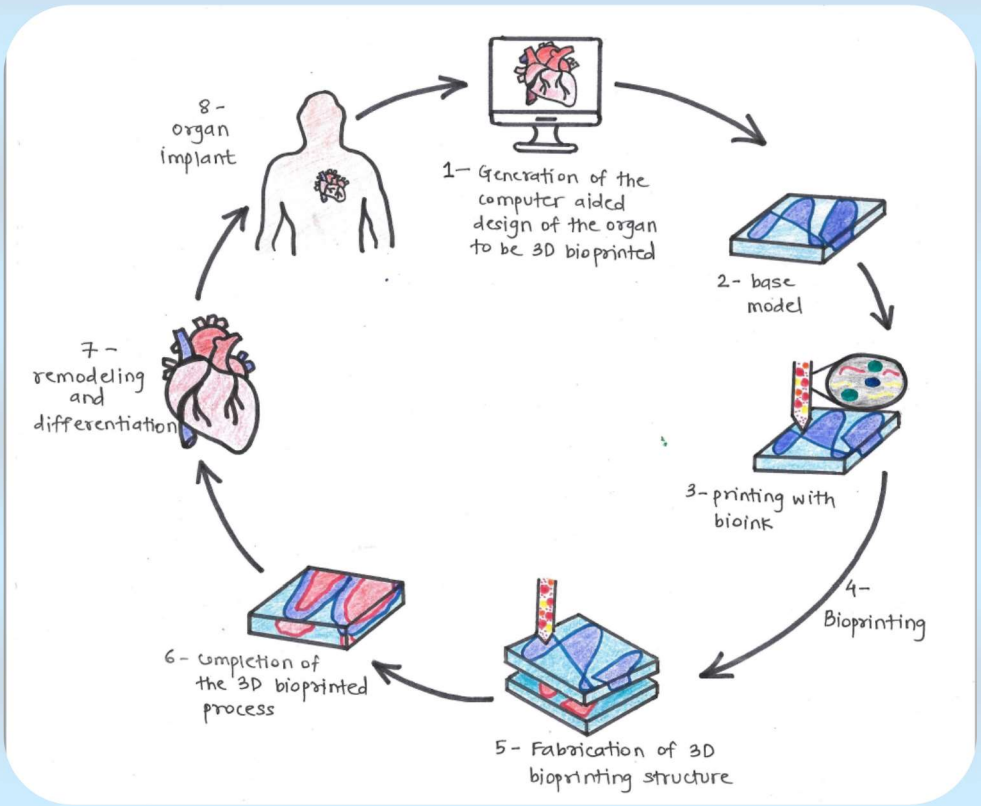
Medical technology has been progressing each year and it never fails to amaze us with its unique innovations. From CRISPR to robotic surgeries to artificial organs the list just goes on. Out of these, 3D Bioprinting is the new point of discussion in the field of medicine and technology.

Erik Johansson once quoted that “the only thing that limits us is our imagination”. This same quote must’ve led Thomas Boland to design the first bioprinter in 2003 which helped connect biology and technology and revolutionized the course of regenerative medicine.

3D Bioprinting is the remodeling of required tissues, ligaments, or organs to repair any damage with the help of a blueprint and printing ink of specific biomolecules (bio-ink). It plays a huge role in human transplants and the field of research by helping scientists study any tissue or organ under influence of drugs in detail. There are mostly three types of bioprinters namely inkjet-based bioprinters, laser-assisted bioprinters and extrusion-based bioprinters out of which inkjet-based bioprinters are easier, faster and cheaper than the other printers but low in quality.

To simply explain its process first, a blueprint is required which can be obtained from a CT scan, MRI scan, X-ray, etc. to create an exact model. Next, the inkjet-based printer is provided with a specific set of instructions to process the required image in the form of a scaffold for support. Finally, bio-ink is used to print the desired model which contains 3D hydrogel solutions like stem cells, collagen, hyaluronic acid, gelatin, etc. The bioprinter is placed in a suitable environment and mild temperature so that the cells can survive in the external environment.



From here the printing process begins. The bio-ink is injected out due to extreme heat pressure (200-300 degrees Celsius) in the form of beads. The beads are then linked together and a 3D model is generated layer by layer with the help of the scaffold. The model is then incubated for several weeks in a bioreactor for tissue maturation. Once fully matured, the new model is ready to be used in transplants or research. Recently this year, skilled surgeons from NYU Langone health centre performed a complex surgery and saved a 22-year-old patient by operating the world's first hand and face transplant via 3D printing. Pretty amazing right!

Bioprinting is a true example of biology and technology working together. 3D printing has the potential to solve many transplant complications, it can make study and experiments easy in the R&D department, can contribute to the development of cancer therapy, etc. However, there are some issues regarding adaptability, toxicity, or price, but we all know there are no innovations that are successful without a few challenges.

The Merry Game-te Corner

Created by Divya Bhardwaj
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Code Decode

Fill in the blanks and unjumble the highlighted letters to decode the word of this issue.

I. Father of Virtual Reality: _ _ _ _ _ _ _ _ _ _ _

II. Bio-Ink is injected in the form of: _ _ _ _ _

III. First oxygen biosensor was made by: _ _ _ _ _

IV. Caps on regular DNA: _ _ _ _ _ _

Word of the Issue: _ _ _ _ _ _ _

Heredity Hunt

Find the words listed in the word search below:

Let the Hunt Begin!

A	F	K	E	I	P	C	T	G	Z	C	U	J	H	D
D	G	L	O	B	I	N	D	S	R	E	K	R	A	M
G	O	E	J	P	T	R	J	H	S	B	T	Y	N	H
H	P	G	R	L	R	T	S	S	B	S	E	S	K	A
K	E	J	S	E	E	N	Y	J	I	T	U	J	A	E
Q	D	W	F	S	H	A	R	R	O	H	G	H	L	H
Y	H	Y	H	G	G	P	S	A	I	S	J	V	Y	N
P	U	H	U	B	S	O	S	I	N	G	C	X	H	Y
A	Q	W	O	I	N	S	J	E	K	C	S	H	T	F
R	H	R	R	X	A	T	R	D	L	X	G	S	E	D
E	K	C	D	L	E	D	O	M	A	E	H	T	M	A
H	D	C	N	O	R	K	W	J	K	U	T	Q	F	G
T	R	A	N	S	D	U	C	E	R	J	K	L	S	T

Find Us :

TELESPHERE
MARKERS
CRISPR
RNA
METHYL
BIO-INK
TRANSDUCER
THERAPY
GLOBIN
MODEL

Gags by Gregor

Q. What did the snooty metacentric say to the telocentric?

A. Two arms are better than one.

Reality is Virtual?

Article and Illustration by
Akanksha Mahajan
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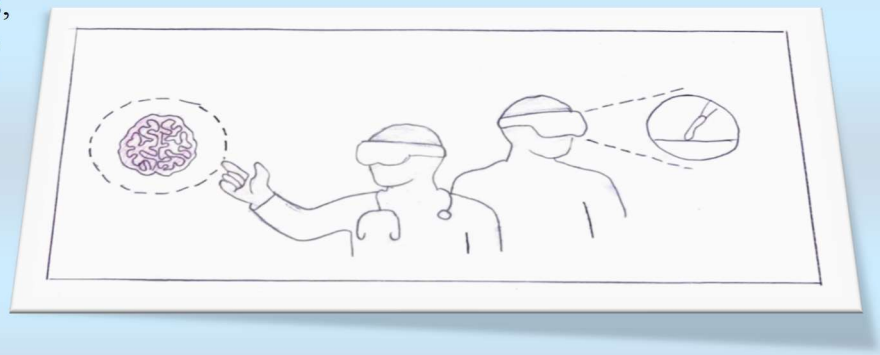
Virtual reality (VR) is a technique that replaces reality with a completely new 3D digital environment and is becoming more perfect with the aid of increasing computer technologies which can stimulate the real world dynamically. Virtual reality technology, controlled by artificial intelligence has been applied in sports training, competitive sports, medicine etc.VR consists of various components such as:
1)Positional tracking
2)Visualization
3)Environment

The visualization of image data in virtual reality can take place through two main paths:
(1) The visualization of derived models, such as those that are 3D-printed.
2) The visualization of unsegmented (raw) image data.

History of VR:



Morton Heilig is said to be the “Father of Virtual Reality” and in the mid-1960’s, Sutherland first described VR as a vision through which a user could perceive the virtual world which looked and sounded real. It provides a viewer-centered experience which is immersive and interactive, involving multiple sensory experiences. In 1960, Morton received his first related patent for the “Telesphere Mask” which enabled stereoscopic (3D) display. In 1962, Sensorama, the first commercially available 3D immersive simulator was invented. “VIDEOPLACE” was said to be an
“Artificial Reality” in which an image of the operator, captured by cameras, was projected onto a screen and incorporated into a video of a scene. The ‘Data Glove’ added to incorporating hand gestures and position for interacting with the VR environment.
At the end of the 80’s, Fake Space Labs created a Binocular-Omni-Orientational Monitor (BOOM), incorporating stereoscopic-display and a

mechanical arm which is tracked and represented in the virtual images. In the 90's the first clinical systems for surgery, telemedicine, and therapy began to appear. Medical VR applications research has emphasized surgical training/ planning and even various therapeutic applications

Applications:
VR technology has a wide range of application such as military, nursing, medical,entertainment and training. In the medical field, users are visually impressed with their experience. This technology can make up for many inadequate resources and equipment and improve the various teaching methods. VR compromises of many features that are ideal for surgical, training, pain management and behavioraltherapy.

VR medical care training which allows the users to interact with VR, which helps reduce the technical errors caused by negligence. The use of VR to build virtual organs or tissues can assist physicians in their work, enable doctors and nurses to communicate more efficiently and accurately, It can enhance the ability of doctors to diagnose and provide proper treatment about the illness and the progress of surgery
and are low-cost and non-invasive. However, the time spent on VR should not be too long. If VR is used for a long time, it may easily cause health problems. This may result in excessive headaches, dizziness and nausea. For example, in a scenario of a patient with chest pain presenting to the emergency department (ED), the learner can be in the virtual ED, moving and interacting with the virtual environment and patient as they would in real life. They can take the patient history, examine, investigate, diagnose and treat the patient are helpful in context to mitigate effects of COVID-19 and has various advantages in the execution of the virtual reality concept in fighting the COVID-19
pandemic.

VR in particular has been adopted across medical and nursing fields. VR involves the user putting on a VR headset to become completely immersed in an interactive virtual environment. When used with appropriate educational software, this allows the user to learn from experience in the virtual world. VR is already transforming medical education. It is helping to free learning from the classroom, allowing learners to apply their knowledge to practice and learn from mistakes. It focuses on improving competencies.

How did you find it? Any feedback? Suggestions?

We would love to know what you thought of this issue of Genophilic, any suggestions are most welcome.

As we have expanded our horizons, our next issue will be on the topic "Science **and nature: an amalgamation**".

We would appreciate your contributions on said topic.

Contact us on: editor.genophilic@gmail.com

References for Articles:

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1) https://www.intechopen.com/books/biosensors-for-health-environment-and-biosecurity/ biosensors-for-health-applications
2) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4862100/
3) https://www.researchgate.net/publication/221913467_Biosensors_for_health_applications https://www.hindawi.com/journals/bri/2016/3130469/

Editing the DNA?

1) https://news.mit.edu/2021/switch-crispr-gene-editing-0414
2) https://www.ucsf.edu/news/2021/04/420306/new-crispr-technology-offers-unrivaled-control epigenetic-inheritance

Détendez-vous!

1) https://www.thalassemia.org/boduw/wp-content/uploads/2019/10/TIF
2) GENE-THERAPY_FINAL.pdf
3) https://www.sciencedirect.com/science/article/pii/B9780128005637000129
4) https://sicklecellanemianews.com/gene-therapy/

Bio-Printing

1) Bioprinting: What It Is and How It's Used in Medicine (verywellhealth.com)
2) What Is Bioprinting? » Science ABC
3) Benefits of Bioprinting - Brinter™ BioPrinter - 3D Bioprinting
4) Materialise 3D printing and software supports world's first double hand and face transplant - 3D Printing Industry

Reality is Virtual?

1) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6232426/
2) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7214336/
3) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6382635/
4) https://pubmed.ncbi.nlm.nih.gov/23534593/

References for Illustrations:

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https://www.mdpi.com/2079-6374/8/4/104/htm

Editing the DNA?

https://marlin-prod.literatumonline.com/cms/attachment/d9522b74-ce5b-4ee9-94af-3cc1c543c42c/fx1.jpg

Détendez-vous!

https://www.nih.gov/news-events/news-releases/nih-researchers-create-new-viral-vector-improved-gene-therapy-sickle-cell-disease

Bio-Printing
bioprinting-process.jpg (1024×719) (scienceabc.com)

Reality is Virtual?
https://www.mobifilia.com/the-future-of-virtual-reality-in-healthcare/

Back to Basics with Friendly Grandpa Ghost Mendel!

References-

1) https://www.nobelprize.org/prizes/medicine/1962/crick/lecture/
2) https://history.nih.gov/display/history/Nirenberg+History+Poly-U
3) https://profiles.nlm.nih.gov/spotlight/jj/feature/syntheticrna)
4)https://www.acs.org/content/acs/en/education/whatischemistry/landmarks/geneticcode.html

Image references:

1) The Poly-U vial image in the 3rd panel has been adapted from- https://history.nih.gov/download/attachments/8881706/05_vial_pu.jpg?version=1&modificationDate=1548009580036&api=v2
2) The UC Berkeley Image in the 4th panel has been adapted from- https://i1.wp.com/www.dailycal.org/assets/uploads/2020/09/rankings_Ruby-Sapia_staff.jpg?ssl=1&w=900
3) The NIH Image in the 4th panel has been adapted from- https://collections.nlm.nih.gov/pageturnerserver/ajaxp?theurl=http://localhost:8080/fedora/get/nlm:nlmuid-101441205-img/Preview