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Editorial ...

''Every day, think as you wake up, today I am fortunate to be alive, I have a precious human life, I am not going to waste it. I am going to use all my energies to develop myself, to expand my heart out to others; to achieve enlightenment for the benefit of all beings. I am going to have kind thoughts towards others. I am not going to get angry or think badly about others. I am going to benefit others as much as I can.''

- Dalai Lama

Covid-19! A way of living for past two years. We all have been affected by the COVID-19 pandemic. However, the impact of the pandemic and its consequences are felt differently by different individual of our society. While some try to adapt to working online, homeschooling their children, ordering food online, others have no choice but to be exposed to the virus while keeping the society functioning. Our different social identities and the social groups we belong to determine our inclusion within society and, by extension, our vulnerability to epidemics & pandemics. As we welcome the year 2022, we have to be more adaptive in taking the challenges that comes in our way. The never giving up attitude and fighting till the end has put us in verge of bringing the new edition of The Chemical Axis 2022.

The past years has taught us to swallow the hard part. So despite of all uncertainity, we are back even more stronger, passionate, engrossed in chasing our dreams and making the society a better place to live in.

The motto of "The Chemical Axis" had always been to ignite, inspire and nurture the creative instincts of budding mind to mold them for better tomorrow. In this regard, various articles relating to the present scenario and other fields are listed. In this edition a wide array of topics have been covered, apart from usual ones. A highly informative piece on how to write research proposal has also been included.

The series of bhatnagar awardees, history of chemistry, and chemistry in movies has been continued in this edition too.

Date: 05-02-2022
Place: Guwahati

The abstract sketched on the cover page has been designed by ***Lotus Deka*** *on the quotation*

''Science and everyday life cannot and should not be separated.''

- Rosalind Franklin

Given the prevailing situation, it is essential that COVID-19 protocols and directives given by international health organizations are maintained.

It is very important to keep maintaining physical and social distancing, ventilating indoor spaces, covering while sneezing and coughing, washing hands as much as thought to be necessary, keeping unwashed hands away from the face, maintaining healthy and hygienic diet, exercising and the use of face masks should be prioritized in public settings to minimize the risk of transmissions.

Taking the given measures will help us to create a healthy, safe and COVID-19 free society.

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CRISPR -Cas: The Cutting Edge of DNA Editing

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Abstract :

The ability to control and modify DNA - the code of life, has long been cherished by the scientists. They want to use genome editing to investigate different diseases that affect humans. With this easier access to DNA sequences, scientists are on the verge of a third revolution that will deeply impact our lives, to the extent that computers have changed society: we are entering the era of "gene editing", following the era of "gene reading". Gene editing is the rational and precise modification of DNA sequences program in living cells and organisms. Nuclease-based gene editing is already widely used in research as a cost-effective, fast, and easy way to conduct genetic experiments. Other recent approaches to targeted genome modification - zinc-finger nucleases [ZFNs] and transcription-activator like effector nucleases [TALENs]- enable researchers to generate permanent mutations by introducing double-stranded breaks to activate repair pathways. These approaches are costly and time-consuming to engineer, limiting their widespread use, particularly for large scale, high-throughput studies. A new gene editing technology known as CRISPR-Cas9 offers the potential for substantial improvement over previous technologies in that it is simple to use and inexpensive and has a relatively high degree of precision and efficiency. These characteristics have led many in the scientific and business communities to assert that CRISPR-Cas9 will lead to groundbreaking advances in many fields, including agriculture, energy, ecosystem conservation, and in the investigation, prevention, and treatment of diseases. The advent of facile genome engineering using the bacterial RNA-guided CRISPR-Cas9 system in animals and plants is transforming biology. This article is an aim to understand CRISPR (CLUSTERED REGULARLY INTERSPACED PALINDROMIC REPEAT) biology from its initial discovery through the elucidation of the CRISPR-Cas9 enzyme mechanism, which has set the stage for remarkable developments

using this technology to modify, regulate, or mark genomic loci in a wide variety of cells and organisms from all three domains of life. CRISPR-Cas9 has triggered a revolution in which laboratories around the world are using the technology for innovative applications in biology. The power of this technology to systematically analyze gene functions in mammalian cells, study genomic rearrangements and the progression of cancers or other diseases, and potentially correct genetic mutations responsible for inherited disorders. CRISPR-Cas9 is having a major impact on functional genomics conducted in experimental systems. Its application in genome-wide studies will enable large-scale screening for drug targets and other phenotypes and will facilitate the generation of engineered animal models that will benefit pharmacological studies and the understanding of human diseases. CRISPR-Cas9 applications in plants and fungi also promise to change the pace and course of agricultural research. Future research directions to improve the technology will include engineering or identifying smaller Cas9 variants with distinct specificity that may be more amenable to delivery in human cells. Understanding the homology- directed repair mechanisms that follow Cas9-mediated DNA cleavage will enhance.

Keywords : DNA, gene editing, CRISPR, Cas9, Zinc Finger Nucleases, TALEN

1. Background

Humans have an estimated 100 trillion (1012) cells. If the DNA contained in each cell's nucleus was completely unfolded, it would measure nearly 2 meters in length. In other words, if the all the DNA from every cell in a person's body were patched up together they would form a strand of 200 billion kilometers, or more than 1,000 times the distance between Earth and the Sun. We can imagine that the genome is a book. There are twenty three chapters, called CHROMOSOMES. Each chapter containsseveral thousand stories, called GENES. Each story is made up of paragraphs, called EXONS, which are interrupted by advertisements called INTORNS. Each paragraph is made up of words, called CODONS. Each word is written in letters called BASES.[1]

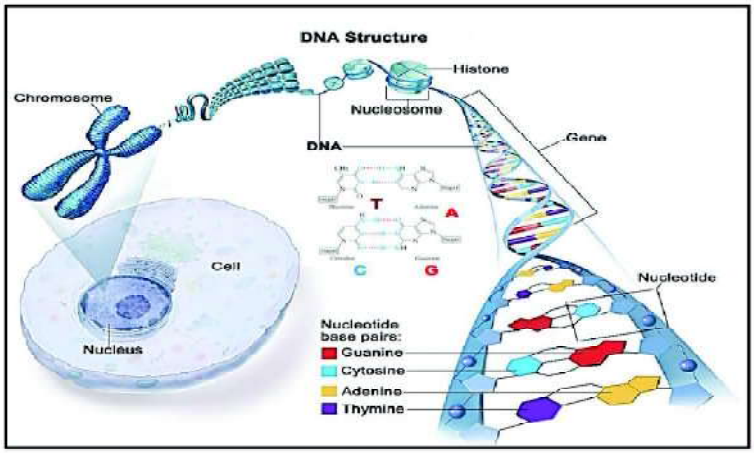

Figure 1. Organization of Cell: Chromosome to DNA structure.

The four letters A, T, G, and C represent the molecules that make up our DNA, which is subject to potentially deadly or disabling mutations from the moment of conception. A single letter can change our fate. The four letters are four bases-Adenine (A), Thymine (T), Guanine (G) and Cytosine (C). A always pairs with T, while G always pairs C. Such pairs are called base pairs. In RNA, thymine is replaced by uracil. In 1953, Watson and Crick discovered the double helical structure of DNA. The Human Genome Project (HGP) was initiated in 1990 and completed in 2003 and which aimed to sequence the whole human genome. Human beings have 23 pairs of chromosomes in every cell, which makes 46 chromosomes in total. These chromosomes contain 3164.7 million (~3 $x10^9$) nucleotide bases (A, T, G, and C). Genes are part of DNA, which codes for protein. The average gene consists of 3000 bases, but sizes vary greatly. The total number of genes is estimated at 20,000 -25,000. Throughout the DNA there are gene-rich areas and gene-poor areas. The 99.9% of DNA sequence of all people are exactly same. The functions of 50 % of gene discovered to date are unknown. There are coding (introns) and noncoding regions (exons), which are sometimes called "junk DNA". Only approximately 2% of our genome encodes proteins. It was also determined that a large part of the non-protein coding regions of human genome are functional. This so-called junk DNA is composed either of deactivated genes that were once useful for our non-human ancestors (like a tail), or parasitic DNA from virus that have entered our genome and replicated themselves hundreds or thousands of times over the generations, but generally serve no purpose in the host organism. One famous retrovirus that copies itself into the human genome is HIV. Genome size is not related to the complexity of life. For example, the genome of *Polychaos dubium,* a microscopic unicellular being, has been reported to contain more than 200 times the amount of DNA found in the human genome.[2] The information generated by the human genome project has been started to act as the source book for biomedical fields - genetic diseases, ageing, cancer, developmental biology and neurobiology, where scientists are just beginning to understand the underlying molecular mechanisms. The human genome project is expected to immensely benefit medical science. The number of identified disease genes had risen to more than 6,000. HGP focused on the DNA sequence of an individual. The next step was to analyze DNA sequences from different populations. This catalog of human genetic variation - Hap Map will help us to understand and eventually treat the genetic diseases that afflict mankind, as well as the many multifunctional diseases in which genetic predisposition plays an important role. New technologies emanating from the genome project will also find application in other fields such as agriculture and the environmental sciences. But despite discovering genetic changes associated with many cancers, Alzheimer's disease, and thousands of other diseases with deleterious genetic mutations, we have only just discovered how to directly edit DNA. Coupling this fundamental discovery with further clinical exploration has the potential to transform human health, vastly increasing our scientific knowledge and leading to new therapies for previously incurable illnesses.

Human chromosomes contain all different sorts of genes, some bad, some good. The "bad" genes, or ones that cause deformities and disease, can be altered using genetic editing. The techniques are often used in manipulating genes and making life healthier and scientists have endeavored to develop new technologies to modify or manipulate the genome. Precise gene editing and regulation of genomic information is essential to understanding the function of a given gene.

2. Gene Editing

For decades, scientists have altered genes using radiation or chemicals. These methods produce unpredictable results. The invention of recombinant DNA technology in the 1970s allowed scientists to insert new DNA into genes in a directed way, but inserting a specific gene or sequence within the genome remained technically challenging and imprecise. Gene editing is a newer technique that is used to make specific and intentional changes to DNA.[3] Gene editing can be used to insert, remove, or modify DNA in a genome. All gene editing technologies involve an enzyme known as a nuclease for cutting the DNA, in addition to a targeting mechanism that guides the enzyme to a specific location on the DNA strand (i.e., a gene within the genome). Gene editing has traditionally involved the insertion, removal, or modification of a single gene, but with CRISPR-Cas9 technique multiple genes can be targeted simultaneously. Such multi-gene editing is generally referred to as genome editing.

Genome editing, or genome editing with engineered nucleases (GEEN) is a type of genetic engineering in which DNA is inserted, deleted or replaced in the genome of a living organism using engineered nucleases, or "molecular scissors. In 2007, Capecchi, Evans and Smithies were awarded a Nobel Prize in Physiology & Medicine for their discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells.[4] However, to truly understand a gene's role in human biology and disease, human cells and tissue must be studied. This approach will enable researchers to observe the effects of a mutation, SNP [Single Nucleotide Polymorphism] or deletion in combination with the added layers of regulation present within the cell, including post-translational modification, epigenetic changes associated with chromatin structure and transcriptional mechanisms.[5]

Humans were genetic engineers long before anyone knew what a gene was. They could give living things new traits-sweeter kernels of corn, flatter bulldog faces- through selective breeding. But it took time, and it didn't always pan out. Scientists bombarded seeds and insect eggs with x-rays, causing mutations to scatter through genomes like shrapnel. If one of hundreds of irradiated plants or insects grew up with the traits scientists desired, they bred it and tossed the rest. That's where red grapefruits came from, and most barley for modern beer. Genome modification has become less of a crapshoot. Recombinant DNA is the general name for taking a piece of one DNA, and combining it with another strand of DNA. Recombinant DNA is also sometimes referred to as "chimera." By combining two or more different strands of DNA, with restriction endonucleases (cut at

specific sequences) and ligases (join) scientists are able to create a new strand of DNA. The most common recombinant process involves combining the DNA of two different organisms. Different vaccines, bacterial insulin etc prepared by this technique.

3. The Basics of Gene Editing

The gene editing toolbox encompasses several types of molecular scissors. Zinc finger nucleases (ZFN) were one of the first editing tools to show specific targeting of the genome as exemplified nearly 25 years ago in Drosophila.[6] More recently, transcription activator-like effector nucleases (TALENs) derived from plant pathogens were discovered and applied to gene-editing approaches.[7] These were shown to be simpler to design and less expensive than ZFNs but still required significant expertise and resources. CRISPR/Cas 9 is derived originally from an endogenous bacterial defense mechanism. In its most simplified form, it functions with two modified components: a short chimeric single guide RNA (sgRNA) and a Cas 9 nuclease. The sgRNA acts as homing guide for Cas 9, thus making it easy to target different genomic loci by simply replacing the sgRNA sequence in the presence of the same nuclease. It is this flexibility and ease of use which has allowed CRISPR/Cas 9 to be adopted widely, where it has been used to target DNA sequences from a number of different organisms. CRISPR/Cas 9 has been described by one of the pioneers of gene editing, Harvard University chemist George Church, as 'a real gift from biology'. We will now discuss below the gene editing technologies briefly.

3.1. Homologues Recombination - HR

Historically, targeted gene inactivation, replacement or addition via homologous recombination has been achieved and it was a powerful method capable of providing conclusive information for evaluating gene function.[8] However, the use of this technique has been hampered by several factors, including the low efficiency at which engineered constructs are correctly inserted into the chromosomal target site, the need for time-consuming and labor-insensitive selection/screening strategies, and the potential for adverse mutagenic effects.

3.2. RNA interference - RNAi :

Targeted gene knockdown by RNA interference (RNAi) has provided researchers with a rapid, inexpensive and high-throughput alternative to homologous recombination.[9] However, knockdown by RNAi is incomplete, varies between experiments and laboratories, has unpredictable off-target effects, and provides only temporary inhibition of gene function.

3.3. Zinc Finger Nucleases - ZFN :

In the past decade, a new approach has emerged that enables investigators to directly manipulate virtually any gene in a diverse range of cell types and organisms. This core technology - commonly referred to as "genome editing" - is based on the use of engineered nucleases composed of sequence-specific DNA-binding domains fused to a non-specific DNA cleavage module.[10,11] These chimeric nucleases enable efficient and precise genetic

modifications by inducing targeted DNA double-strand breaks (DSBs) that stimulate the cellular DNA repair mechanisms, including error-prone non-homologous end joining (NHEJ) and homology-directed repair (HDR).[12] Zinc finger is an ideal platform for the design of novel DNA binding domain. The ZFP region provides a ZFN with the ability to bind a specific base sequence. This region contains a tandem array of Cys-His2 fingers, each recognizing approximately 3 base pairs of DNA, previous studies of individual ZFNs used three fingers to construct a 9-bp target, which enabled ZFN dimmers to specify 18bp of DNA per cleavage site. More recent studies added up to six fingers per ZFN for increasing the specialty. The Fok1 DNA cleavage domain is fused to DNA binding domain. It can cleave both DNA strands when two nuclease domains unite to form a functional endonuclease.

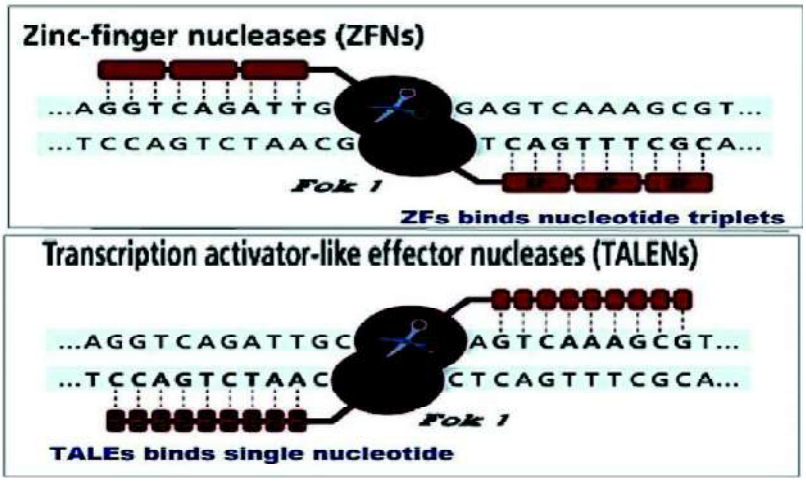

Figure 2. ZFNs:Zinc-finger nucleases are fusions of the nonspecific DNA cleavage domain from the FokI restriction endonuclease with zinc-finger proteins. TALENs: transcription activator-like effector nucleases are fusions of the FokI cleavage domain and DNA-binding domains derived from TALE proteins.

3.4. Transcription Activator-Like Effector Nucleases' -TALEN :

The DNA-binding domain of TALENs is made of transcription activator-like effector (TALE) domains. There are four different TALE domains, one for each DNA base, so they can be engineered to bind to specific DNA sequences much more easily than ZFNs. Like ZFNs, the nuclease part of TALENs is normally a Fok1 nucleus.[13] Two Fok1 molecules must come together to make a cut in the DNA, so two TALENs are made, one for each strand.TALEs are naturally occurring proteins from the plant pathogenic bacteria genus Xanthomonas, and contain DNA-binding domains composed of a series of 33-35-amino-acid repeat domains that each recognizes a single base pair. TALE specificity is determined by two hyper variable amino acids that are known as the repeat-variable di-residues (RVDs). Like zinc fingers, modular TALE repeats are linked together to recognize contiguous DNA

sequences. However, in contrast to zinc-finger proteins, there was no re-engineering of the linkage between repeats necessary to construct long arrays of TALEs with the ability of targeting single sites in a genome.

Molecular biologists learned to delete or replace specific genes using enzymes called zinc-finger nucleases, ZFN; the next-generation technique used enzymes named TALENs. ZFNs and TALENs comprise a powerful class of tools that are redefining the boundaries of biological research. These chimeric nucleases are composed of programmable, sequence-specific DNA-binding modules linked to a non-specific DNA cleavage domain. ZFNs and TALENs enable a broad range of genetic modifications by inducing DNA double-strand breaks that stimulate error-prone nonhomologous end joining or homology-directed repair at specific genomic locations. However, difficulties of protein design, synthesis, and validation remained a barrier to widespread adoption of these engineered nucleases for routine use.

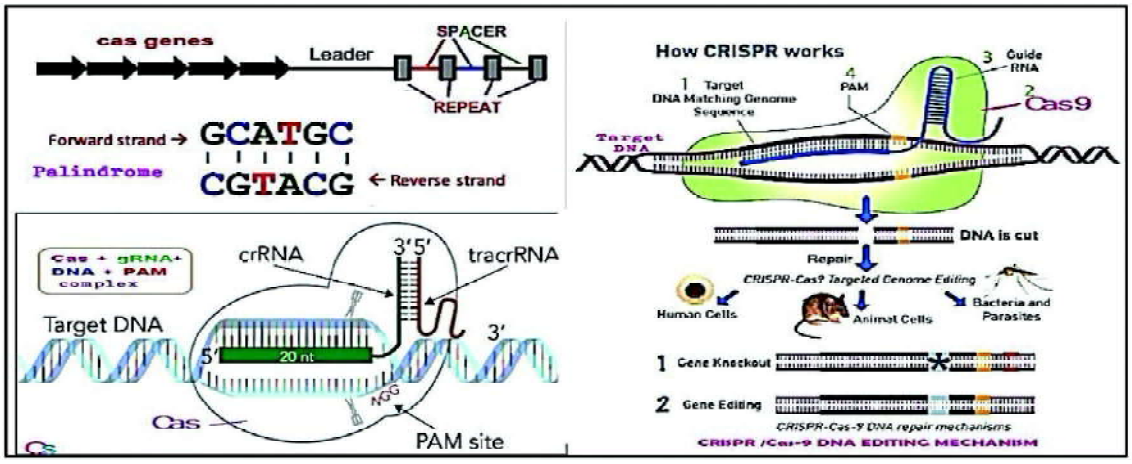

Figure 3. Cas gene structure & How CRISPER works: Cas+ gRNA+ Target DNA + PAM sequence.

4. CRISPR : The new frontier of genome engineering with CRISPR-Cas9

CRISPR-Cas9 is the most common, cheap and efficient system used for genome editing. CRISPR stands for 'CLUSTERED REGULARLY INTERSPACED SHORT PALINDROMIC REPEATS'. CRISPR is the DNA-targeting part of the system which consists of RNA molecule, or 'guide', designed to bind to specific DNA bases through complementary base-pairing?. Cas9 stands for CRISPR-associated protein 9, and is the nuclease part that cuts the DNA. The CRISPR-Cas9 system was originally discovered in bacteria that use this system to destroy invading viruses?

4.1. CRISPR

The field of biology is now experiencing a transformative phase with the advent of facile genome engineering in animals and plants using RNA-programmable CRISPR-Cas9.[14] The CRISPR-Cas9 technology originates from type II CRISPR-Cas systems, which provide

bacteria with adaptive immunity to viruses and plasmids. The CRISPR associated protein Cas9 is an endonuclease that uses a guide sequence within an RNA duplex, tracrRNA: crRNA, to form base pairs with DNA target sequences, enabling Cas9 to introduce a site-specific double-strand break in the DNA. The dual tracrRNA: crRNA was engineered as a single guide RNA (sgRNA) that retains two critical features: a sequence at the 5' side that determines the DNA target site by Watson-Crick base-pairing and a duplex RNA structure at the 3' side that binds to Cas9. This finding created a simple two-component system in which changes in the guide sequence of the sgRNA program Cas9 to target any DNA sequence of interest. The simplicity of CRISPR-Cas9 programming, together with a unique DNA cleaving mechanism, the capacity for multiplexed target recognition, and the existence of many natural type II CRISPR-Cas system variants, has enabled remarkable developments using this cost-effective and easy-to-use technology to precisely and efficiently target, edit, modify, regulate, and mark genomic loci of a wide array of cells and organisms.

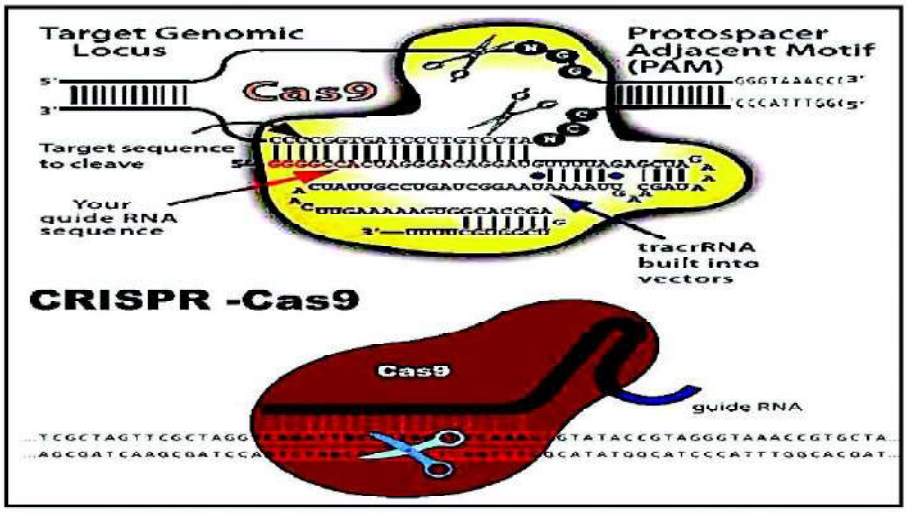

Figure 4. DNA Editing by CRISPER-Cas9

4.2. CRISPR /CAS 9: A GIFT FROM MOTHER NATURE

The CRISPR system is an adaptive immune mechanism present in many bacteria and the majority of characterized Archaea. CRISPR-containing organisms acquire DNA fragments from invading bacteriophages and plasmids before transcribing them into CRISPR RNAs (crRNAs) to guide cleavage of invading RNA or DNA.[15] This CRISPR immune system works through the cooperation of many diverse Cas-proteins. Based on differences in their components and mechanisms of action, CRISPR systems have been divided into two major classes. RNA guided target cleavage in class 1 systems (types I, III, and IV) requires a large complex of several effector proteins, but in the class 2 systems [type II, putative types V and VI], only one RNA-guided endonuclease [e.g., Cas9 in type II

and Cpf1 (CRISPR from Prevotella and Francisella-1) in type V] is required to mediate cleavage of invading genetic material.

In general, a CRISPR system works in three stages to carry out a full immune response to invading foreign DNA. In the first stage, or acquisition stage, DNA fragments of invading plasmids or phages (termed protospacers) are incorporated into the hostCRISPR locus as spacers between crRNA repeats. In the second stage, Cas proteins are expressed,

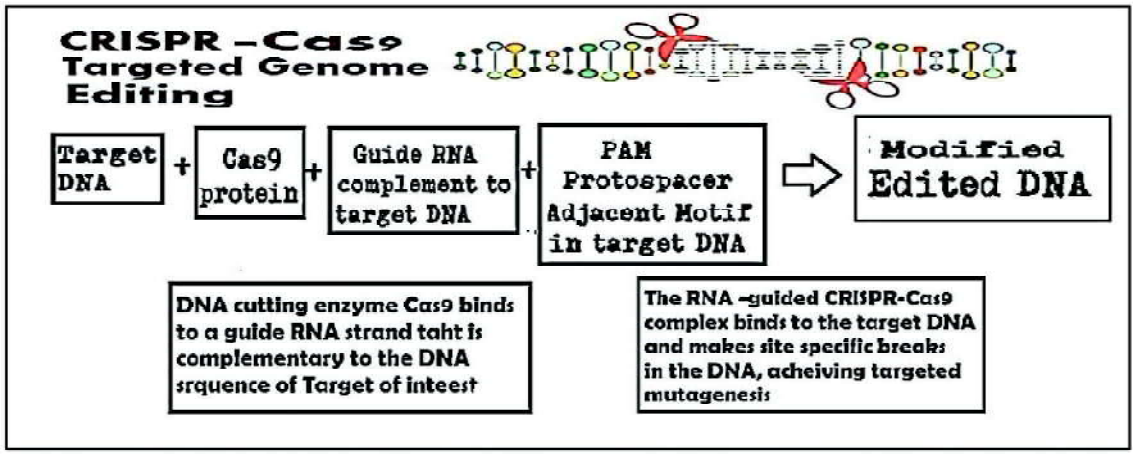

Figure 5. CRISPER -Cas9 Targeted Genome editing components.

the CRISPR array containing acquired spacers is transcribed into pre-crRNA, and the pre-crRNA is cleaved and processed into mature crRNAs by Cas proteins and host factors. The fully processed crRNA is a guide that contains a spacer sequence responsible for targeting it to the invading genome, as well as all or part of the crRNA repeat sequence, which allows for recognition of the crRNA by Cas proteins and other RNA components. In type II CRISPR systems, the presence of a noncoding trans-activating CRISPR RNA (tracrRNA) that hybridizes with the crRNA repeat sequence is critical for crRNA processing, Cas9 binding, and Cas9-mediated target cleavage. In the third

stage, Cas proteins recognize the appropriate target with the guidance of the crRNA and mediate the cleavage of the invading genome, thus protecting the host cells from infection. The action of many CRISPR systems depends on the presence of a sequence-specific PAM that is adjacent to the crRNA target site in the invading genome. The absence of this PAM sequence at the CRISPR locus in the host genome protects it from self-cleavage in type I and type II CRISPR systems.

4.3. History of CRISPR

The CRISPR story began in 1987. While studying the iap enzyme involved in isozyme conversion of alkaline phosphatase in E. coli, Nakata and colleagues reported a curious set of 29 nt repeats downstream of the iap gene.[16] Unlike most repetitive elements, which

typically take the form of tandem repeats like TALE repeat.Transcription activator-like (TAL) effectors specifically bind to double stranded (ds) DNA through a central domain of tandem repeats. Each TAL effector (TALE) repeat comprises 33-35 amino acids and recognizes one specific DNA base through a highly variable residue at a fixed position in the repeat. Structural studies have revealed the molecular basis of DNA recognition by TALE repeats. Unlike most repetitive elements, which typically take the form of tandem repeats like TALE repeat monomers, these 29 nucleotide repeats were interspaced by five intervening 32 nucleotide nonrepetitive sequences.

1987	Ishino et al	First report of CRISPR clustered repeats
2000	Mojica et al	Recognition that CRISPR families are present throughout prokaryotes
2002	Jensen et al	Coined CRISPR name, defined signature of Cas
2005	Mojica et al & Pourcel at al	Identified foreign origin of spacers, proposed adaptive immunity function
2005	Bolotin et al	Identified PAM
2008	Marraffini et al	CRISPR acts upon DNA targets
2008	Brouns et al	Spacers are converted into mature crRNAs that acts as small guide RNA.
2009	Hale et al	Type II-B Cmr CRISPR complexes cleave RNA
2010	Gameau et al	Cas9 is guided by spacer sequences and cleave target DNA via double Stranded Breaks (DSBs)
2011	Deltcheva et al	TracrRNA forms a duplex structure with cr RNA in association with Cas9
2011	Sapranauskas et al	Type II CRISPR systems are modular and can be heterologuesly in other organisms
2012	Jinek et al & Gasiunas et al	In vitro characterization of DNA targeting by Cas9
2013	Cong et al & Mali et al	First demonstration of Cas9 genome engineering in Eukaryotic cells
2014	Wang et al & Shalem et al	Genome-wise functional screening with Cas9
2014	Jinek et al	Crystal structure of apo-Cas9
2014	Nishimasu et al	Crystal structure of Cas9 in complex with guide RNA and target DNA

4.4. CRISPR: Bacteria Immune System

It does not happen very often in a science history when a single discovery becomes a technological keystone, especially in biology. CRISPRs (clustered regularly interspaced short palindromic repeats) discovery and a path to its application in genetic engineering is a perfect example of such breakthrough, which is comparable to the discovery of the polymerase chain reaction or development of the next-generation sequencing technology. To date, there are few known defensive strategies in archaea and bacteria that can be referred to as the multilayer prokaryotic immune system: the restriction-modification system, the adsorption inhibition, abortive infection, blocking DNA injection, and the CRISPRs discovered during 1980s. CRISPR-Cas9 has taken the world by storm with the promise of making gene editing much easier and faster than ever before.[17] Since it was developed in 2012, this gene editing tool has revolutionized biology research, making it easier to study disease and faster to discover drugs. It has the potential for treating diseases ranging from cancer to type2 diabetes. The technology has been moving full-steam ahead, with a trial in humans already started, even as the repercussions of gene editing remain largely unknown.In 2012, scientists turned CRISPR from a bacterial shield into a gene-editing tool. They replaced the bacterial CRISPR RNA system with a modified guide RNA. This RNA acts as a kind of 'wanted poster' - it tells a bounty hunter enzyme called CAS 9 where to look.So far scientists have used it to reduce the severity of genetic deafness in mice, suggesting it could one day be used to treat the same type of hearing loss in people. They've created mushrooms that don't brown easily and edited bone marrow cells in mice to treat sickle-cell anemia. Down the road, CRISPR might help us develop drought-tolerant crops and create powerful new antibiotics. CRISPR could one day even allow us to wipe out entire populations of malaria-spreading mosquitoes or resurrect once -extinct species like the passenger pigeon.[18]

A CRISPR clinical trial in humans is already underway in China, in which cancer patients' T-cells are edited to remove a protein that halts immune responses. The cells are then reinserted into the patients. The first CRISPR clinical trial in the U.S. has also been approved, which will involve three edits to T cells. The researchers will remove T cells from 18 patients with several types of cancers and perform three CRISPR edits on them. One edit will insert a gene for a protein engineered to detect cancer cells and instruct the T cells to target them, and a second edit removes a natural T-cell protein that could interfere with this process.[19]

The enzyme scans the cell's genome to find a DNA match then slices for the DNA in the cell's enzymes. To repair damage at that point, scientists can change or add DNA within the cell. By feeding CAS9 the right sequence or guide RNA, scientists can cut and paste parts of the DNA sequence, up to 20 bases long, into the genome at any point.

CRISPR, or Clustered Regularly Interspaced Short Palindromic Repeat, is at the most basic level a very precise way of tinkering with genes. Whereas gene editing was once a

very imprecise and expensive process, scientists can now go into your DNA and essentially cut and paste it at specified places. The technology can be traced back to bacteria, which protect themselves by cutting out invading viruses' DNA and inserting it into their own, then replicating the new sequences to prevent future viral invasions.

In 2012, researchers refined the system and revealed that any DNA (not just bacteria) has this ability - and the process works in humans.

The development of efficient and reliable ways to make precise, targeted changes to the genome of living cells is a long-standing goal for biomedical researchers.Gene targeting (also, replacement strategy based on homologous recombination) is a genetic technique that uses homologous recombination to change an endogenous gene. The method can be used to delete a gene, remove exons, add a gene, and introduce point mutations. Gene targeting can be permanent or conditional. Conditions can be a specific time during development / life of the organism or limitation to a specific tissue, for example. Gene targeting requires the creation of a specific vector for each gene of interest. However, it can be used for any gene, regardless of transcriptional activity or gene size. Gene targeting has been widely used to study human genetic diseases by removing ("knocking out"), or adding ("knocking in"), specific mutations of interest to a variety of models. Previously used to engineer rat cell models, advances in gene targeting technologies are enabling the creation of a new wave of isogenic human disease models. These models are the most accurate in-vitro models available to researchers to date, and are facilitating the development of new personalized drugs and diagnostics, particularly in the field of cancer. Recently, a new tool based on a bacterial CRISPR-associated protein-9 nuclease (Cas9) from *Streptococcus pyogenes* has generated considerable excitement.

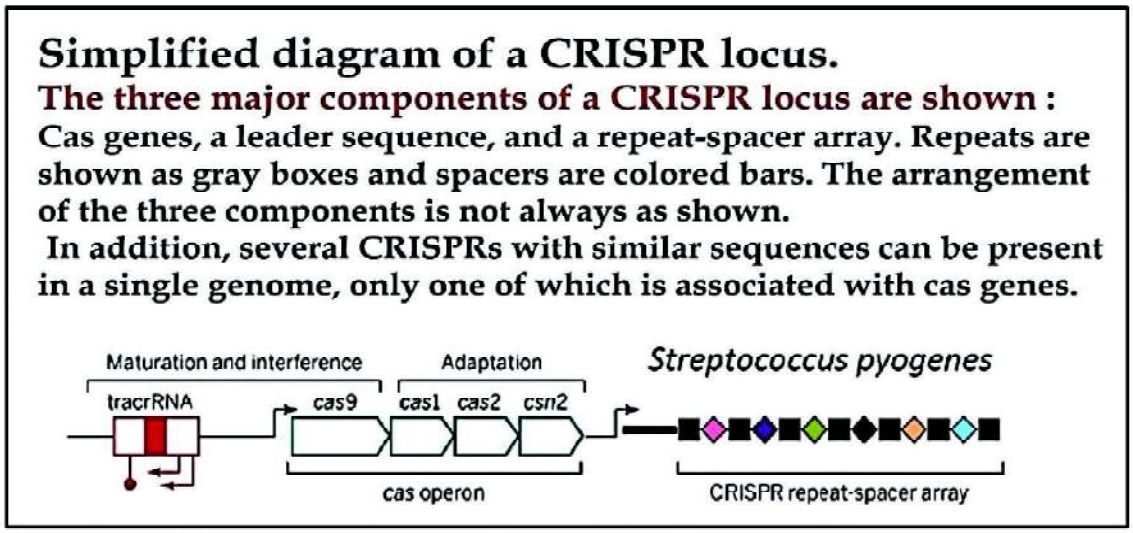

Figure 6. Simplified diagram of a CRISPER locus.

5. The Biology of Cas9

The functions of CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) and CRISPR-associated (Cas) genes are essential in adaptive immunity in select bacteria and archaea, enabling the organisms to respond to and eliminate invading genetic material. These repeats were initially discovered in the 1980s in *E. coli* [11], but their function wasn't confirmed until 2007 by Barrangou and colleagues, who demonstrated that *S. thermophilus* can acquire resistance against a bacteriophage by integrating a genome fragment of an infectious virus into its CRISPR locus.[20]

Three types of CRISPR mechanisms have been identified, of which type II is the most studied. In this case, invading DNA from viruses or plasmids is cut into small fragments and incorporated into a CRISPR locus amidst a series of short repeats (around 20 bps). The loci are transcribed, and transcripts are then processed to generate small RNAs (crRNA - CRISPR RNA), which are used to guide effector endonucleases that target invading DNA based on sequence complementarity.[21] In the acquisition phase, foreign DNA is incorporated into the bacterial genome at the CRISPR loci. CRISPR loci is then transcribed and processed into crRNA during crRNA biogenesis. During interference, Cas9 endonuclease complexed with a crRNA and separate tracrRNA cleaves foreign DNA containing a 20-nucleotide crRNA complementary sequence adjacent to the PAM sequence. One Cas protein, Cas9, has been shown, through knockdown and rescue experiments to be a key player in certain CRISPR mechanisms (specifically type II CRISPR systems). The type II CRISPR mechanism is unique compared to other CRISPR systems, as only one Cas protein (Cas9) is required for gene silencing.[14] In type II systems, Cas9 participates in the processing of crRNAs, and is responsible for the destruction of the target DNA. Cas9's function in both of these steps relies on the presence of two nuclease domains, a RuvC-like nuclease domain located at the amino terminus and a HNH-like nuclease domain that resides in the mid-region of the protein.[15] To achieve site-specific DNA recognition and cleavage, Cas9 must be complexed with both a crRNA and a separate trans-activating crRNA (tracrRNA or trRNA), that is partially complementary to the crRNA. The tracrRNA is required for crRNA maturation from a primary transcript encoding multiple pre-crRNAs. This occurs in the presence of RNase III and Cas9.

During the destruction of target DNA, the HNH and RuvC-like nuclease domains cut both DNA strands, generating double-stranded breaks (DSBs) at sites defined by a 20-nucleotide target sequence within an associated crRNA transcript. The HNH domain cleaves the complementary strand, while the RuvC domain cleaves the noncomplementary strand.

The double-stranded endonuclease activity of Cas9 also requires that a short conserved sequence, (2-5 nts) known as protospacer-associated motif (PAM), follows immediately 3´- of the crRNA complementary sequence. In fact, even fully complementary sequences are ignored by Cas9-RNA in the absence of a PAM sequence.[22]

6. Cas9 and CRISPR as a New Tool in Molecular Biology

The simplicity of the type II CRISPR nuclease, with only three required components (Cas9 along with the crRNA and trRNA) makes this system amenable to adaptation for genome editing. This potential was realized in 2012 by Doudna and Charpentier labs.[23] Based on the type II CRISPR system described previously, the authors developed a simplified two-component system by combining trRNA and crRNA into a single synthetic single guide RNA (sgRNA). sgRNA programmed Cas9 was shown to be as effective as Cas9 programmed with separate trRNA and crRNA in guiding targeted gene alterations.

To date, three different variants of the Cas9 nuclease have been adopted in genome-editing protocols. The first is wild-type Cas9, which can site-specifically cleave double-stranded DNA, resulting in the activation of the double strand break (DSB) repair machinery. DSBs can be repaired by the cellular Non-Homologous End Joining (NHEJ) pathway,[24] resulting in insertions and/or deletions (indels) which disrupt the targeted locus. Alternatively, if a donor template with homology to the targeted locus is supplied, the DSB may be repaired by the homology-directed repair (HDR) pathway allowing for precise replacement mutations to be made.[25,26] Cong and colleagues[27] took the Cas9 system a step further towards increased precision by developing a mutant form, known as Cas9D10A, with only nickase activity. This means it cleaves only one DNA strand, and does not activate NHEJ. Instead, when provided with a homologous repair template, DNA repairs are conducted via the high-fidelity HDR pathway only, resulting in reduced indel mutations. Cas9D10A is even more appealing in terms of target specificity when loci are targeted by paired Cas9 complexes designed to generate adjacent DNA nicks.[28]

The third variant is a nuclease-deficient Cas9 (dCas9).[29] Mutations H840A in the HNH domain and D10A in the RuvC domain inactivate cleavage activity, but do not prevent DNA binding. Therefore, this variant can be used to sequence-specifically target any region of the genome without cleavage. Instead, by fusing with various effector domains, dCas9 can be used either as a gene silencing or activation tool. Furthermore, it can be used as a visualization tool. For instance, Chen and colleagues used dCas9 fused to Enhanced Green Fluorescent Protein (EGFP) to visualize repetitive DNA sequences with a single sgRNA or nonrepetitive loci using multiple sgRNAs.[30]

7. Applications as a Genome-editing and Genome Targeting Tool

The CRISPR/Cas9 system has been widely adopted and already been successfully used to target important genes in many cell lines and organisms, including human,[31] bacteria,[32] zebrafish, C. elegans, plants,[33] Xenopus tropicalis, yeast, Drosophila, monkeys, rabbits, pigs, rats and mice. Several groups have now taken advantage of this method to introduce single point mutations (deletions or insertions) in a particular target gene, via a single Grna.[7,29,32] Using a pair of gRNA-directed Cas9 nucleases instead, it is also possible to induce large deletions or genomic rearrangements, such as inversions or translocations.[34] A recent exciting development is the use of the dCas9 version of the

CRISPR/Cas9 system to target protein domains for transcriptional regulation.[35,36] The CRISPR/Cas9 system requires only the redesign of the crRNA to change target specificity. This contrasts with other genome editing tools, including zinc finger and TALENs, where redesign of the protein-DNA interface is required. Furthermore, CRISPR/Cas9 enables rapid genome-wide interrogation of gene function by generating large number of gRNA libraries [35,37] for genomic screening.

CRISPR used in COVID-19 diagnostic - US FDA has granted Sherlock Biosciences an emergency use authorization (EUA) for its COVID-19 diagnostic assay for Covid-19, beating out other companies and academic groups trying to use the powerful gene-editing technology to figure out who is infected with the novel coronavirus. Sherlock's test the first use of CRISPR technology for anything, allows the company to scale up production of its assay for use by laboratories that do complex diagnostics. Like those standard tests, Sherlock's assay detects the presence of the viral RNA. It starts with a respiratory specimen from, for example, the mouth, nose, or lungs. To make the viral genome easier to identify, scientists convert it into DNA, which can be copied over and over. The method they use-isothermal amplification-is done at a constant temperature, unlike the method used by most conventional diagnostics, polymerase chain reaction. Then, the sample goes through Sherlock's CRISPR gauntlet. CRISPR-Cas chops up invasive viral RNA; scientists have turned it into a technique that makes precise cuts in genetic code through various Cas enzymes. Sherlock's system uses Cas13, which is a little more flexible in what genetic regions it can target than other Cas enzymes. The CRISPR part of the assay involves converting the amplified DNA back into RNA, which is the type of genetic information the Cas13 enzyme recognizes. The enzyme is led to any viral RNA in the sample based on "guides," short bits of RNA scientists add to the reaction that match the actual code of the virus. Once it's there, the enzyme cuts the viral RNA. The assay targets two distinct parts of the SARS-CoV-2 genome: the recipe for the nucleocapsid (N-protein), which helps the virus assemble itself, and *ORF 1ab,* a stretch of the genome that leads to the precursor of an enzyme that helps the virus copy itself. These targets were chosen over better known ones like the SARS-CoV-2 spike protein and the protease because viruses are a bit sloppy when they copy their genetic information. Sometimes they make mistakes, and while those mistakes may not affect the virus' ability to copy itself and infect, it might affect the precision of a diagnostic based on CRISPR. Once it's activated, the Cas13 enzyme cuts other nucleic acids as well as the viral RNA. Within the assay are strands of genetic material that have a fluorescent molecule at one end, and a molecule that quenches, or blocks, the fluorescence, on the other. As activated Cas13 chomps its way around the genetic material in the sample, it cuts those strands, freeing the fluorescents bits from the quenching bits. That most fluorescent plate readers can read the test.

The SHERLOCK COVID-19 detection protocol works in three steps and can be completed in 1 hour, starting from nucleic acid extraction as used for qRT-PCR [Quantitative reverse transcription PCR] tests. Step (1) - 25 min incubation - isothermal amplification of

the extracted nucleic acid sample using a commercially available recombinase polymerase amplification (RPA) kit; Step (2) - 30 min incubation - detection of pre-amplified viral RNA sequence using Cas13;& Step (3) - 2 min incubation - visual read out of the detection result by eye using a commercially-available paper dipstick.[38]

8. Future of CRISPR/Cas9

The rapid progress in developing Cas9 into a set of tools for cell and molecular biology research has been remarkable, likely due to the simplicity, high efficiency and versatility of the system. Of the designer nuclease systems currently available for precision genome engineering, the CRISPR/Cas system is by far the most user friendly. It is now also clear that Cas9's potential reaches beyond DNA cleavage, and its usefulness for genome locus-specific recruitment of proteins will likely only be limited by our imagination.

Launching a new chapter in the fast-moving cancer immunotherapy field, scientists have blended two cutting-edge approaches: CRISPR, which edits DNA, and T-cell therapy, in which sentries of the immune system are exploited to destroy tumors. Two women and one man, all in their 60s-one with sarcoma and two with the blood cancer multiple myeloma-received CRISPR-altered versions of their own cells.[39] The uses of CRISPR-Cas9 to manipulate cells and organisms continued to mount, it seemed inevitable that researchers somewhere would test the technique in human eggs, sperm or embryos, with a view to creating heritable alterations in people.

9. Ethical Issues

The fact that CRISPR-Cas9 is among the important discoveries of the 21st century is widely accepted in the scientific community and related industries. However, the rapid rise of CRISPR-Cas9 has led to new bioethical, social, and legal issues in medicine, agriculture, livestock, and the environment. The most notable concern is that of the generation of 'designer babies'. However, there remain viable technical reasons why this technology is not ready for embryo modification, and most Centre on eliminating or selecting-out deleterious off targets effects. Another factor that negates the use of edited embryos lies in the fact that few known genetic conditions exist for which pre implantation genetic diagnosis (PGD) cannot be used to screen-out embryos with pathogenic mutations. Moreover, three parent babies (in the case of mitochondrial disease) cannot be used to exclude inheritance of disease associated mutations. Nevertheless, as recently commented by Paul Knoepfler, patients carrying incurable mutations are likely to have a higher degree of risk tolerance than scientists.[40] Researchers in China announced that they had used the nascent gene editing tool CRISPR-Cas9 to modify the genomes of human embryos, triggering a major ethics debate.[41]

10. CRISPR Prospects

CRISPR/Cas9 gene editing technology is being touted as one of the biggest biotechnology breakthroughs of the century with Jennifer Doudna of the University of

California, Berkeley, and Emmanuelle Charpentier of the Helmholtz Centre for Infection Research in Braunschweig, Germany, receiving Nobel Prize in Chemistry, 2020.

Regardless, CRISPR/Cas9 has been revolutionary facilitating a wealth of research unmatched in over three decades since the inception of genome editing. It has opened up gene editing to the broad scientific community and allowed what used to take years to do to be achieved in a matter of weeks. Recent research has also propelled CRISPR/Cas9 system beyond just gene editing tool allowing study of DNA epigenetics and understanding what non-protein coding segments of our genome encodes. Its potential for research, human medicine and agriculture will likely only be limited by our imagination.

CRISPR/Cas9 may well be considered one of the most important biological tools identified in recent years. There is no end to the number of ways this system can be tweaked for a vast array of molecular exploits. This is especially the case in stem cells, where the application of CRISPR/Cas9 technologies will likely be profound. Although hurdles remain, especially the warranted concern of off-target effects, continued improvements in Cas9 and guide RNA engineering will allay the fears of even the most ardent critics of CRISPR-based therapy. Already, there is unprecedented investment by large and small biotechnology and pharmaceutical industry players alike, which shows the palpable excitement generated by the vast array of possibilities brought by this technology. Eventually, the early hype will subside, but there is little doubt that CRISPR/Cas9, and its application in stem cell engineering, will have an extraordinary impact in the progress towards curing many previously intractable diseases.

11. Conclusion

Biologists are using CRISPR-Cas9 to better understand genomes - not just by editing DNA, but by devising variations on the technique to precisely manipulate the activity of genes. And, armed for the first time with a method that can easily introduce genetic changes to many animals, researchers have edited a veritable menagerie of beasts - from ferrets to elephants to koi carp - in an attempt to combat disease, improve agriculture and even make designer pets. The repurposing of bacterial CRISPR-Cas immune systems as genome engineering tools has heralded an era in which RNA-programmed genome editing is a democratized and broadly accessible technology. In the clinic, therapeutic success is likely to be attained in localized tissues (liver, blood, eye), with longer-term goals of targeting systemic diseases dependent on future delivery options. Screen-based drug discovery approaches, together with the ability to use RNA-programmed genome editing technology to produce disease-recapitulating cell line models and animals, will continue to identify potential therapeutic targets. The application of genome-wide, Cas9-based screens to complex diseases, such as leukemia, provides intriguing opportunities for the selection of therapeutic targets and the design of anti-cancer drugs. Over the long term, the potential for CRISPR-enabled production of synthetic tissues or animals and immune-compatible donor organisms for xenotransplantation is vast. In the short term, with the proof of concept

already provided for the correction of genetic diseases, such as Duchenne muscular dystrophy and beta-thalassemia, there is potential for gene and antiviral CRISPR-based therapies. Investigations of toxicity and safety will need to accompany advances in our understanding of CRISPR-system efficacy to ensure an appropriate risk-benefit profile for therapeutic interventions. Notwithstanding the promise of RNA-programmed genome editing in somatic cell therapy, a key outstanding issue is whether applications in zygotes and human germ line cells should be considered in the light of the associated ethical issues. The pace of the science is faster than our grasp of the regulatory ramifications, an issue that is being addressed by the scientific community, together with key stakeholders. For better or for worse, CRISPR-Cas9 is transforming biology. We are now at the dawn of the gene-editing age.

12. Acknowledgements

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Proton conducting solid polyelectrolytes: An emerging material for solid state electrical applications

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Introduction :

The term 'polyelectrolyte' comprises 'polymer' and 'electrolyte.' Polyelectrolytes are those polymers with the repeating units having an electrolyte group, which dissociate in polar solvents, making the polymers charged. They are also sometimes known as polysalts. The charge on the repeating units of the polyelectrolytes is neutralized by oppositely charged smaller counter ions that tend to preserve electroneutrality. The existence of charges on the polymeric background leads to inter and inter-molecular interaction, which are of much longer range than that of uncharged polymers. The type of ionic groups present and the repeating units determine the properties of the polyelectrolytes. They may be classified as anionic, cationic, and ampholytic based on the charge carried by the ionized polymer. With the development of perfluorinated sulfonic membranes, the interest in solid polyelectrolytes has started. A solid phase contains a vast number of atoms, all identical in the case of an element or of several different kinds in the case of an alloy or chemical compound. These atoms are linked with one another using their electrons on which the cohesion of the solid depends. But, depending on a great deal on the total ionization energies of the atoms present, these bonds can be of several different types, one of the prominent bonding being ionic, primarily observed in polyelectrolytes. The ionic conduction in solid-state polyelectrolytes occurs mainly due to defects in the lattice, which may be Schottky or Frenkel defects[1]. After the initial trial and failed attempts, the breakthrough was achieved with the advent of polyelectrolyte multilayers, the layered analog to polyelectrolyte complexes formed by the so-called layer-by-layer deposition of polyions with the alternating sign of charge [2]. The process is predominantly driven by multiple electrostatic interactions and is therefore very versatile concerning the different charged building blocks that can be employed in multilayer formation. The use of a salt solution with the polymeric fragments to obtain solid, non-crystalline polymer salts is one of the common ways to form a proton-conducting solid polyelectrolyte. Salts of alkali and alkaline earth metals are the most

common to obtain ionic solid polyelectrolyte with high mobility of ions. In addition, recent reports also suggest the use of dilute acids to form the proton-conducting polyelectrolytes.

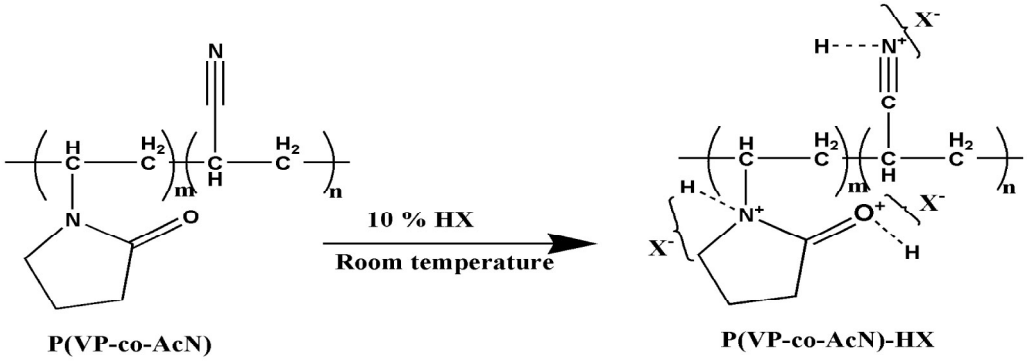
Proton conducting solid polyelectrolyte

The major success in the field of solid polyelectrolyte complexes is the development of proton-conducting polyelectrolytes. The most exciting feature of this class of polyelectrolytes is that they do not require the use of any salts or other toxic chemicals. Because of their easy synthesis, and high and tunable conductivity, they find a lot of applications in solid-state batteries and fuel cells.

Some common ways to obtain proton-conducting polyelectrolytes are:

1. Incorporation of dilute acids [3].
2. Incorporation of ionizable proton conducting materials, such as ammonium salts [4].
3. In certain instances, ionizable biomolecules have also been reported [5].

An example of proton-conducting polyelectrolyte reported by our group is shown below (Scheme 1), which shows the formation of HNO_3 and HCl (denoted as HX) incorporated polyelectrolyte of poly (N-vinylpyrrolidone-co-acrylonitrile) [6].



Scheme 1. Formation of polyelectrolyte of poly (N-vinylpyrrolidone-co-acrylonitrile).

Characterization of solid-state polyelectrolyte

The prominent spectroscopic and analytical techniques are used to analyze the solid polyelectrolytes, such as FT-IR spectroscopy, NMR, GPC, TGA, DSC, etc. Apart from the common spectroscopic techniques, ionic AC conductivity can be measured by an impedance analyzer. The method helps us to calculate the bulk resistivity from the Nyquist plot and hence gives us the range of conductivities at different temperatures and frequencies.

In addition, the Wagner polarisation technique is used to determine the ionic characteristics of a polyelectrolyte, which gives us the value of the total transport number. In other words, we can calculate the percentage of ionic characteristics in polyelectrolytes based on the polarization of the ionic current on reaching a steady state.

Applications :

1. Polyelectrolytes are mainly useful for energy storing dry cells applications. Different polyelectrolytes in solution, solid, or gel forms are useful for dry-cell applications. For example, gel polyelectrolyte is used for rechargeable Li-ion batteries [7], which provide higher specific energy than other lithium battery types, like mobile devices and radio-controlled aircraft.
2. Drug delivery: The drug delivery applications of the polyelectrolytes are primarily due to their charged nature and thus their ability to form complexes with oppositely charged ions. Polyelectrolytes form networks by interaction with oppositely charged fragments in the body, which help in efficient drug release. In general, these polyelectrolyte networks are well tolerated, biocompatible, and are more sensitive to changes in environmental conditions. A typical example is a chitosan, a positively charged polyelectrolyte, which is used for drug delivery.
3. Bio-imaging: As a result of their highly electron-delocalized backbones, polyelectrolytes have a larger absorption extinction coefficient and more efficient intramolecular / intermolecular energy transfer than small fluorophores and fluorescent proteins [8]. They have minimal cytotoxicity and are more biocompatible.
4. Sensing: Conjugated polyelectrolytes have become one of the most utilized materials in chemo and bio-sensory systems. Useful properties, such as amplified quenching effects and aggregation behavior, are responsible for polyelectrolyte-based sensors. Well-established sensing mechanisms, such as conformational changes and energy transfer, have also been explained by many groups. Target species include small ions, small biomolecules, proteins, enzymatic activities, and DNA.
5. Device fabrication: Polyelectrolytes have found a wide range of applications in the fabrication of devices, such as diodes, transistors. Conjugated polyelectrolytes, having semiconducting and metallic behaviors, respectively, have been reported to produce materials with enhanced optical and electrical properties. The interaction of anionic/ cationic conjugated polyelectrolytes produces blends with tunable electrical and optical properties.
6. Water purification: In the drinking water treatment process, cationic polyelectrolyte can be used as the primary coagulant instead of Salts due to their high charge density and low molecular weight, for example, PDADMAC (Poly Diallydimethyl ammonium chloride). Polymer primarily used with Alum can effectively treat the water with high turbidity. Polyelectrolytes with low molecular weight can be used as a primary coagulant which forms long-chain polymer and treats the water very effectively with very high turbidity. It can also help to remove organics from the water [9].
7. Food packaging materials: The polyelectrolytes obtained from natural sources are reliable sources for food packaging materials. Reports have suggested that these materials are safer than those often used.

8. Tissue engineering: Polyelectrolytes have been found to be useful in tissue engineering. The layer-by-layer assembly of sequentially adsorbed, alternating polyelectrolytes has been found to be very applicable in this field. The ability to manipulate the chemical, physical, surface, and topographical properties of these multilayer architectures by merely changing the pH, ionic strength, thickness, and post-assembly modifications render them highly suitable to probe the effects of external stimuli on cellular responsiveness [10].

Apart from the above applications, polyelectrolytes have also been found useful in wound healing, air purification, adhesive modifiers, etc. Scientists around the globe are exploring the possible applications of polyelectrolytes with advanced properties.

Conclusion and prospects

The researchers for various applications have explored the area of polyelectrolytes and their complexes. Many of these complexes are novel, biodegradable, and biocompatible, can be used for a variety of applications in the pharmaceutical and biomedical fields. The concept of polyelectrolyte complexes is being used in targeted drug delivery systems, membranes for dialysis, biosensor development, and vaccine development. A comprehensive description of the properties, classifications, characterization, and applications of the polyelectrolytes has been included. The structural models, the effect of salt, pH, etc., have also been summarised. The trend has been started for applying the concepts of polyelectrolytes in gene expression and tissue engineering. In the future, polyelectrolytes will have multiple applications in various fields according to their ionic interactions. The pharmaceutical industry will consider polyelectrolytes as successful pharmaceutical excipients as replacements for conventional polymers.

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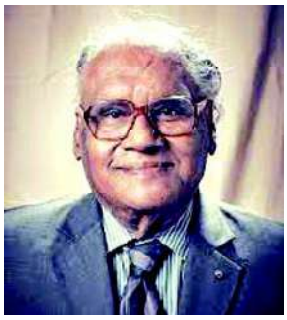
Series

Shanti Swaroop Bhatnagar Awardees in Chemical Science: Chintamani Nagesa Ramachandra Rao; The Tenth Recipient



The Shanti Swaroop Bhatnagar Award for Science and Technology is a science award in India given annually by the Council of Scientific and Industrial Research (CSIR). The award was instituted in 1958 with the objective to recognize conspicuously important and outstanding contribution to human knowledge and progress - fundamental and applied. The award is named after the founder director of the CSIR, Shanti Swaroop Bhatnagar. It was first awarded in 1958. Any citizen of India engaged in research in any field of science and technology up to the age of 45 years is eligible for the award.

In 1968, Dr. Chintamani Nagesa Ramachandra Rao was awarded the prestigious Shanti Swarup Bhatnagar Award for his contributions in the field of chemical sciences. Dr Rao's research work is related to the application of spectroscopic methods for the study of chemical compounds, the main emphasis being of UV and IR spectra.

Early Life :

CNR Rao was born on 30th June, 1934 in Bangalore city, Andhra Pradesh, to a kannada family. In 1947 he passed secondary school leaving certificate, achieving first class and later pursued Bachelor's degree from Mysore University in 1951. In 1953, He got his masters in chemistry from Banaras Hindu University. In the same year he received scholarship for PhD in IIT Kharagpur. He was offered financial aide by four foreign university like Purdue, Columbia, Penn State and MIT. And selected Purdue for his oldest research paper which was published in 1954 in Agra Journal of Research. Aged 24, he achieved his PhD in the year 1958.

Academic Career :

CNR Rao joined IISC Bangalore as lecturer in 1959, initiating his PhD research witch six PhD students. During 1962, he was appointed as the Head of the Department of Chemistry, at IIT Kanpur. He was elected as a fellow of Indian Academy of Sciences in 1964, which was conveyed to him by CV Raman. He also served as the director of IISC from 1984 to 1994 and visiting professor at university of California, Santa Barbara, University of Oxford and University of Cambridge.

He also works as the Director of International Centre for Materials Science. During 2005, he was made the Chair of Scientific Advisory Council to the Prime Minister of India.

Research Work :

He is considered to be a key figure of the World's solid state materials chemists.

His research area included Solid state chemistry, Atomic layer deposition and pulsed laser deposition, two dimensional materials, catalysis.

His work on transition metal oxides enabled easier understanding of the relationship between structural chemistry of metal oxides and material properties and 'novel phenomena'.

Rao was the first Indian scientist to have synthesized two dimensional oxide materials like La_2CuO_4.

He conducted various scientific studies which facilitated studies in superconductivity of high temperature and also magneto resistance.

Apart from his work on hybrid materials, he was also a great contributor to nano materials since the last twenty years.

Awards :

Dr. CNR Rao received several national and international awards, some notable awards include

- Shanti Swarup Bhatnagar Award in (1968)
- Royal society of chemistry medal (1981)
- Hevrosvsky gold medal of the Czechoslovak Academy of sciences (1989)
- Centenary medal of the Royal Society of Chemistry , London (2000)
- Dan David Prize from Tel Aviv University
- Ernesto Illy Trieste Science Prize for Material Research
- Distinguished Academician Award from IIT Patna
- Padma shri (1974), Padma Vibhushan (1985), Bharat Ratna(2013)
- Great Cross of the National Order of Scientific Merit from the President of Brazil (2002)
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Molecular Imprinting Technology in Selective Creatinine Determination

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Molecular imprinting technology is an advanced technique in the field of physical sciences. It is an emerging trend in which highly selective recognition sites are created through polymerization of monomers in the presence of the template molecule [1]. It is used to design molecularly imprinted polymers, which are cross-linked polymers [2]. These polymers have high affinity towards analytes of interest [3]. For the synthesis of molecularly imprinted polymers, a cross-linker and a functionalized monomer are polymerized around the template molecule [2]. The monomer-template interaction can be characterised using physicochemical methods, such as, NMR spectroscopy [1], IR spectroscopy, UV-Visible spectroscopy [4]. This helps in a better understanding of the recognition processes and hence will further help in the preparation of better molecularly imprinted polymers [1]. The ligand-polymer interactions have been characterised using Raman spectroscopy, circular dichroism, fluorescence and chemiluminescence based techniques [4]. Any thin-film molecularly imprinted polymers have been characterised with high resolution atomic force microscopy [4]. Some other methods are also used, such as, X-ray diffraction, X-ray absorption and X-ray photoelectron spectroscopy [4]. Computational and theoretical strategies have been in use for quite some time to explain the mechanism involved in the synthesis of the molecularly imprinted polymers. These theories also elucidate the mechanisms of polymer-template recognition processes [4].

The principle which drives the idea of molecularly imprinted technology is molecular recognition, i.e., the "lock and key" principle observed in bio-recognition systems [1,5,6].

Molecularly imprinted polymer is a synthetic recognition polymer system, which is specific to a given template molecule in terms of shape, size and functionality [3]. Moreover, the three-dimensional memory of the imprinted polymers towards the template molecule is not reduced for a period of time [1,5], ensuring the reproducibility of the polymer.

Molecular imprinting technology has been developed using two approaches: covalent binding and non-covalent binding, of the template molecule to the monomer. In the first approach, the template molecule is made to covalently bind to the monomer in a reversible

manner, to define the template - monomer interaction. In the second approach, functionalized monomers are made to arrange around the template molecule via non-covalent interactions, viz., ionic bonding, hydrogen bonding, π - π interaction, van der Waal's interaction, etc. After the polymerization is complete, the template molecule is removed from the polymer, leaving behind a recognition site selective to only the template molecule. The recognition site has an 'induced molecular memory', which can selectively recognise the template molecule [1,3].

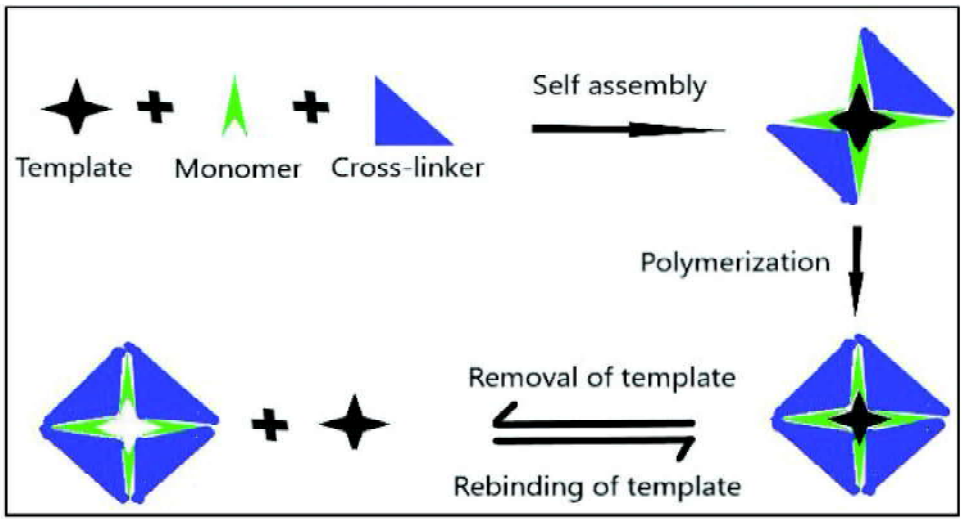

Figure: Schematic representation of the process of molecular imprinting

Molecularly imprinted polymers have the following applications:

(i) Separation of compounds: They have been in use as materials which separate mixtures. They have accomplished stereoselective as well as regioselective separations. They can also be used to separate the clinically useful enantiomers from their harmful part [1,2].

(ii) Bio-mimics: Molecularly imprinted polymers have been synthesized to act as enzyme mimics, i.e., having enzyme like properties, as anti-body mimics, etc [1]. The polymer may act as a catalyst in these processes [2,4].

(iii) Substitutes for biological molecules: They can be used as substrate-selective sensors, where they can replace the biological part of a biosensor. In this manner, a more selective sensing system can be obtained [1].

(iv) Solid-phase extraction: The molecularly imprinted polymers can be used as chromatographic solid stationary phase due to their selectively adsorbing properties [4].

(v) Sensors: Molecularly imprinted polymers have been used in the development of electrochemical, optical and acoustic sensors [2,4]. In electrochemical sensors,

surface modification achieved by immobilization of recognition constituents results in a high binding affinity towards the target analyte [2].

(vi) Biological applications: Molecularly imprinted polymers are in use as a drug delivery agent and they have been synthesized to have biological functions [4].

Creatinine is a waste product of muscle creatine catabolism in vertebrates [3,7-9]. It is the dehydrogenated form of creatine and is present in the blood serum [2]. Abnormalities in renal, thyroid or muscular functions [2,10] can be assessed by studying the levels of creatinine in the blood. The normal creatinine level in the blood serum of adult males is 0.62 to 1.10 mg/dL and is 0.45 to 0.75 mg/dL in adult females [7]. A content higher than this margin is an indication of poor renal health.

Creatinine level is currently determined in clinics using techniques based on colorimetry and enzymatic activity upon creatinine [7,10]. These techniques require the expense of time, money and equipment [10]. Jaffé's reaction is the method to determine creatinine concentration based on colorimetry. It is an easy method but is not free from interference from blood metabolites, urea and dopamine, thereby reducing the selectivity of the method [2,7].

Due to the disadvantages following the conventional clinical methods to determine creatinine levels, biological recognition agents can be used [8]. These are selective, but again are labile, expensive and have low binding sites [8]. As a result, selective, cost-effective and stable molecularly imprinted polymers have been developed for a better analysis. These polymers can mimic the bio-recognition agents [8].

There are numerous literatures reporting the determination of creatinine using molecularly imprinting technology. Ang et al. reported a creatinine receptor, using Al (III) as the functional cross-linker, TEOS as the monomer and molecularly imprinted sol-gel technology [3]. Darmokoesoemo et al. reported potentiometric carbon paste electrode creatinine sensor using aniline as the monomer for the molecularly imprinted polymer [7], while Khasanah et al. reported a voltammetric carbon paste electrode for creatinine using melamine and chloranil [11]. A novel biosensor device for the quantification of creatinine in human urine samples has been reported by Diouf et al. based on molecularly imprinted polymer functionalised electrode system. The results have been obtained with the use of voltammetric and impedance spectroscopic techniques [8]. Haghdoust et al. reported a novel thin layer imprinted polymer and monodisperse imprinted polymer-nanoparticle for creatinine detection. The sensor responses have been studied on quartz crystal microbalance electrode [9]. A creatinine imprinted polyacrylamide hydrogel, incorporated with fluorescent nanodiamond has been reported for the detection of creatinine by Almotiri et al. [10]. Khadro et al. fabricated an electrochemical sensor for creatinine using PVA-co-PE via solvent evaporation process [12]. Lakshmi et al. reported a molecularly imprinted polymer modified hanging mercury drop electrode for the determination of creatinine using melamine and chloranil [13].

Therefore, molecularly imprinted polymers hold advantage over conventional sensing materials because of their high selectivity towards the template or analyte molecule in terms of size, shape, chemical and physical properties. Also, these techniques require less time and are cost-effective [6]. They do not alter their properties with time, change in temperature and pressure, and can be considered as inert compared to other biological recognition systems [14].

Additional information: This write up is based on literature survey.

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Understanding the Fundamentals of Microwave Processing: A Brief Study of Basic Engineering Mathematical Models

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Abstract

The study of foods has been an interesting subject since the history of mankind, be it intentionally or unintentionally. The way humans evolved has a lot to do with what and how humans consumed the food over the course of time. It all began when the early humans discovered fire and used it as a means to cook the raw food which eventually resulted in tastier foods. Overtime, humans became smarter and their fascination with science led them to discover the unknown and unseen principles of nature that surrounds us all. He began using these principles to his own advantage and one of the purposes was to preserve the foods for a long time. This led to the creation of methods such as salting, curing, smoking, roasting, frying, cooling, drying, and many more. Fast forward to present, we now have advance food processing and preservation techniques such as infrared heating, refrigeration, ohmic heating, and microwave heating, among others. Among these unconventional methods of heating, microwave processing is quite popular in the food industry. Hence, it is certainly interesting to study about its principle and learn about the fundamental engineering models that led to the development of the popular heating appliances- the microwave oven (both domestic and industrial).

Keywords:

Microwave Processing, Innovative Food Processing, Unconventional Heating

Introduction :

With the microwave cooking oven patented on October 8, 1945, started the era of microwaved foods, slowly at first but exponentially after the 1980s. The accidental discovery made by Engineer Maine - Percy Spencer that a chocolate bar in his pocket was melting

when working on a powered radar set, had eventually led to one of the billion dollar markets for the design of microwave ovens, new microwave-heated food by the food industry, new food packaging solutions, new food ingredients and also opened new possibilities for Research and Development. By definition, "microwaves are electromagnetic waves in the frequency range from 300 to 300 000 MHz, corresponding to wavelengths from 1 m to 1 mm. For food applications we are, however, limited to the ISM (Industrial and Scientific Medical) band of 2450 MHz. In the USA, 915 MHz is also a recognized ISM frequency, which is not generally available in Europe outside of the UK" (Ohlsson & Bengtsson, 2001).

The scope of this brief study is to understand the basic principle of microwave processing, the basic mathematical equations involved, along with some models used in few recent studies and some basic applications of microwave processing in the food industry. This study does not describe about the limitations of microwave processing.

Principle of Microwave heating

The absorption of microwave energy by rotation of dipolar water molecules and translation of the ionic components of the food are both responsible to heat foods using microwave radiation. Heat is produced as a result of the conversion of this energy. Thus, in the microwave cooking of foods, both the water content and the dissolved ion concentration (typically salt) are important considerations (Ohlsson & Bengtsson, 2001).

1. Absorption of microwave energy by rotation of the dipolar water molecules:

When a dipolar water molecule is exposed to a rapidly changing microwave field, the dipole attempts to align itself with the field direction **(Fig 1)**. There is a time lag because the water molecule needs some response time to overcome the inertia and intermolecular interactions in the water. As a result of the electric field, the water molecule can rotate into alignment. The energy is then lost to the water's random thermal motion, resulting in a temperature rise.

2. Translation of the ionic components of the food:

The electric resistance heating effect is achieved when hydrated ions, such as sodium and chloride from table salt, try to flow in the direction of the electrical field **(Fig 2)**. Because the ions are surrounded by water molecules, they will transfer energy to the water molecules at random as they move. These are less firmly linked to ions and more mobile at higher temperatures. The ions will be able to move about more freely and receive and dissipate more energy as a result. The conductive heating caused by dissolved ions increases as the temperature rises.

Dielectric properties

1. Dielectric constant and Dielectric loss factor

Knowing a material's dielectric characteristics can help figure out how well it converts microwave radiation to heat. The dielectric characteristics are material constants that must be measured experimentally (despite the fact that they vary with temperature and

frequency). For basic food components, data is readily available, particularly around 2450 MHz. The real part of dielectric property, known as the dielectric constant, represents the ability to store electric energy, while the imaginary part, known as dielectric loss, represents the ability to transform electric energy into heat. The permittivity, which is made up of the dielectric constant and dielectric loss, is a complex dimensionless number that expresses the macroscopic interaction between a material and a dielectric field.

$$\varepsilon * = \varepsilon' - j\varepsilon' \qquad \text{eq. (1)}$$

where,

$\varepsilon*$ is the permittivity.

ε' is the dielectric constant.

ε'' is the dielectric loss

$$j = \sqrt{-1}$$

There is also another term called the loss tangent, which is the ratio of dielectric loss to dielectric constant and is written as,

$$tan\ \delta = \frac{\varepsilon''}{\varepsilon'} = \frac{\kappa''}{\kappa'} \qquad \text{eq. (2)}$$

where,

κ'' is relative dielectric loss given by $\kappa'' = \frac{\varepsilon''}{\varepsilon_o}$

κ' is relative dielectric constant given by $\kappa' = \frac{\varepsilon'}{\varepsilon_o}$

$\varepsilon_o = 8.854 \times 10^{-12}\ \mathrm{F/m}$ is the permittivity of free space.

The operating temperature and microwave frequency have the greatest impact on the dielectric properties. Materials are classified into :

Absorbers or high dielectric loss materials, which are strong microwave absorbers.

Transparent or low dielectric loss materials, which allow microwave energy to pass through the material with little attenuation.

Opaque or conductors, which reflect microwaves, based on their microwave absorption.

As a result, understanding dielectric properties is required to classify the materials into the three groups listed above (Chandrasekaran et al., 2013).

2 Power penetration depth

The power penetration depth (D_p) is defined as "the distance at which the power density drops to a value of 1/e from its value at the surface". In other words, it is the depth at which only 1/e (approximately 37%) of the microwave's surface energy remains, with e being the base of natural logarithms (Ohlsson & Bengtsson, 2001). It is expressed as

$$Dp = \frac{c}{\sqrt{2}\pi f[\kappa'\left\{\sqrt{1+\left(\frac{\kappa''}{\kappa'}\right)^2}-1\right\}]^{\frac{1}{2}}} \quad \text{eq. (3)}$$

where,

$c = (\mu_o \varepsilon_o)^{-\frac{1}{2}}$, which is the velocity of light.

$\mu_o = 4\pi \times 10 - 7$ H/m, which is the permeability of free space.

There is also the power equation. This equation gives the rate of heat generation per unit volume at a location inside the food during microwave heating. This is expressed as:

$$Q = 2\pi f \varepsilon_0 \varepsilon'' E^2 \quad \text{eq. (4)}$$

where,

f is the frequency

E is electrical field strength in V/m inside the food

Equations in Microwave absorption

Microwave absorption is generally described by Lambert's law and Maxwell's field equations as electromagnetic equations. Lambert's law is based on the exponential decay of microwave absorption within the product. As Lambert's law is limited to semi-infinite samples, this law leads to a poor approximation for various practical situations. On the other hand, Maxwell's equations provide an exact solution for the propagation of microwave radiation within the samples. The Maxwell's equations which govern the propagation of microwave radiation in a dielectric medium are given by

$$\nabla . D = \nabla . (\varepsilon * E) = \rho \quad \text{eq. (5)}$$

$$\nabla . B = \nabla . (\mu H) = 0 \quad \text{eq. (6)}$$

$$\nabla \times E = -\frac{\delta B}{\delta t} \quad \text{eq. (7)}$$

$$\nabla \times H = J + \frac{\delta D}{\delta t} \quad \text{eq. (8)}$$

where,

H is magnetic field intensity (vector quantity)

E is electric field intensity (vector quantity)

J is the current density (vector quantity)

$\frac{\delta D}{\delta t}$ is displacement current density

D is electric flux density (vector quantity)

B is magnetic flux density (vector quantity)

μ is magnetic permeability (scalar quantity)

$\varepsilon*$ is the permittivity (scalar quantity)

ρ is density of food material (scalar quantity), t is time required for heating

During microwave heating, the dielectric properties of the food sample vary significantly with change in the temperature. Hence the combination of electromagnetic equations and the energy equations is necessary to predict the temperature distributions. The governing energy balance equation for microwave heating of food samples in which the heat transport occurs due to conduction and convection is given as

$$C_p\frac{\delta T}{\delta t} + \rho C_p u(\nabla . T) = \nabla .(k\nabla T) + q(x.T) - h_{fg}i \qquad \text{eq. (9)}$$

where,

C_p is specific heat

u is fluid velocity

k is thermal conductivity

T is temperature

x is spatial distance

q is rate of heat generation

h_{fg} is the latent heat of vaporization

i is the volumetric evaporation term

In this equation, the term $C_p\frac{\delta T}{\delta t}$ represents rate of accumulation of heat energy, and the term $C_p u(\nabla . T)$ represents convective energy flow. Convective heat transport plays a major role in microwave heating of liquid samples as well as porous food materials containing liquid and vapor. In microwave heating, the temperature distribution depends upon various factors such as internal diffusion, surface heat transfer and the rate of heat generation. Since, the dielectric properties of food sample vary with food composition, temperature, size and shape, the value of q also varies accordingly (Chandrasekaran et al., 2013).

The boundary condition leading to the convective and radiative heat transfer from the boundaries of the sample to the surrounding is given by,

$$n.k\nabla T = h(T - T_\infty) + \sigma_h \varepsilon_h (T^4 - T_\infty^4) \qquad \text{eq. (10)}$$

where,

n is the outward pointing unit normal on the surface of the sample,

T_{∞} is the ambient temperature,

h is the heat transfer coefficient,

ε_h is the emissivity of the sample and

σ_h is the Stefan Boltzmann constant

In recent years, many studies are performed to investigate the effect of various models to achieve specific results or make changes to their properties such as pasteurization, microbial inactivation, quality improvement, and textural changes, among others. **Table 1** list out a few of these models from research carried out at GEPEA (UMR 6144 CNRS), ONIRIS, Nantes, France.

Applications of microwave in the food industry

1. Microwave cooking

Microwave cooking works on the principle of volumetric heating, which heats food quickly. The microwave's electric field component causes dipoles in foods to rotate, and the heat is generated by molecular friction. Unlike conventional heating, electromagnetic waves flow from the surface of the food and spread inside, causing heat to be generated from the interior to the outside of the food item. Microwave transmits energy in the form of index attenuation because the energy is absorbed and then converted into thermal energy. It's also worth noting that microwave heating causes heterogeneous heating, resulting in hot and cold regions. As a result, in the case of microwave heating, achieving homogeneous heating is rather difficult. This can be avoided by controlling the heating process with a feedback control loop. As a result, it's critical to understand how the temperature of the foods is distributed during the microwave heating process. Studies have been carried out to study the effect of microwave heating on various properties of foods. A comparison was made between boiling and steaming, as well as microwave heating, in one such study. Microwave cooking was shown to be the best method for preserving the color of both fresh and frozen brassica vegetables in this study (Pellegrini et al., 2010). Another study found that when bovine gluteus medium muscle was roasted in a microwave-convection oven, the shear force value and shrinkage rate were much larger than when the muscle was roasted using regular convection heating (Póltorak et al., 2015).

2. Microwave drying

Microwaves heat food by penetrating it and heating it evenly throughout their volume. The interaction of water dipoles and ions dissolved in moist material produces volumetric heating under a changing electromagnetic field. Steam escapes from the middle of the product toward the surface as the temperature of the entire material rises rapidly. Convective air absorbs moisture by evaporation in microwave-assisted processes, and evaporative cooling can occur on the surface. As a result, the food product develops a porous structure that reduces material shrinkage. Microwave-dried food is also crispier in texture. Microwave drying is frequently combined with traditional procedures to improve product quality and retain nutritional and organoleptic characteristics as much as possible. In contrast to traditional drying processes, the humidity and temperature gradients are the same in

microwave drying. As a result, water molecules absorb the energy quickly and the drying time is reduced. Quicker drying is aided by rapid evaporation from the substance. Durian fruit was microwave dried in a vacuum system with a vacuum pump built inside the microwave oven. The experiment was conducted at microwave powers of 150, 200, and 250 watts in a vacuum of 10 and 30 kPa. Larger pore sizes, higher lightness, crispness values, but lower shrinkage and hardness of durian chips dried by microwave vacuum technology resulted in a better quality product compared to combined microwave-hot air and hot air drying, according to a study on the comparison of microwave drying methods of fresh durian *(Duriozibetbinus Murr.)* (Paengkanya et al., 2015).

3. Microwave pasteurization and sterilization

Microwave pasteurization and sterilization are used to preserve foods after they have been packaged. A study was carried out to design a microwave pasteurization and sterilization system for food preservation. The system ran at 915MHz because it was the right wavelength for single-mode cavities to accept single-meal portion food packages, and it had a deeper penetration depth than 2450MHz systems, therefore thicker packaging was not an issue. The method relies on the heated objects being immersed in water to prevent local overheating and overheating at the margins. The system's effectiveness was demonstrated with sterilized chicken breast and dumplings that retained great sensory quality after three years of storage at 38°C (Tang, 2015).

Conclusion : Microwave technology has provided a boost for the food processing industry in particular to the heating or cooking of foods. Recent research trends shows that this technology has tremendous potential for further applications rather than just heating of foods. However, there has also been limitations to this technology which was not part of discussion in this brief study. One primary limitation is its intrinsic characteristic of heterogeneous heating. Hence, future research is to be performed in order to optimize and develop new mathematical models. Simulation of these models is easily possible with softwares such as COMSOL Multiphysics®.

Figures

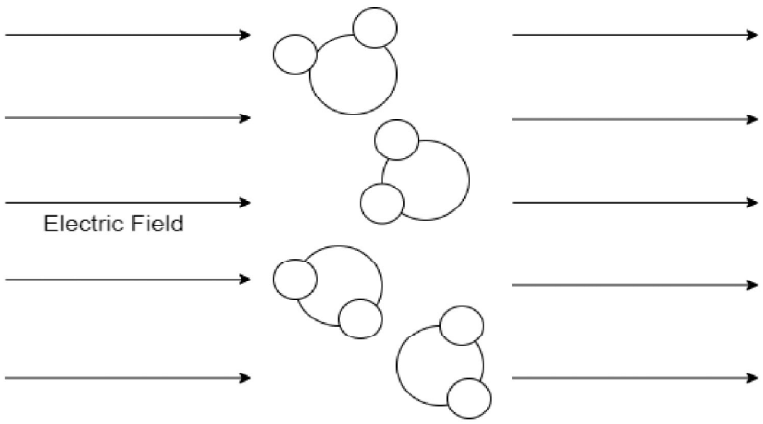

Fig 1: Water molecules aligning in presence of electric field. Modified from (Walker, 1987).

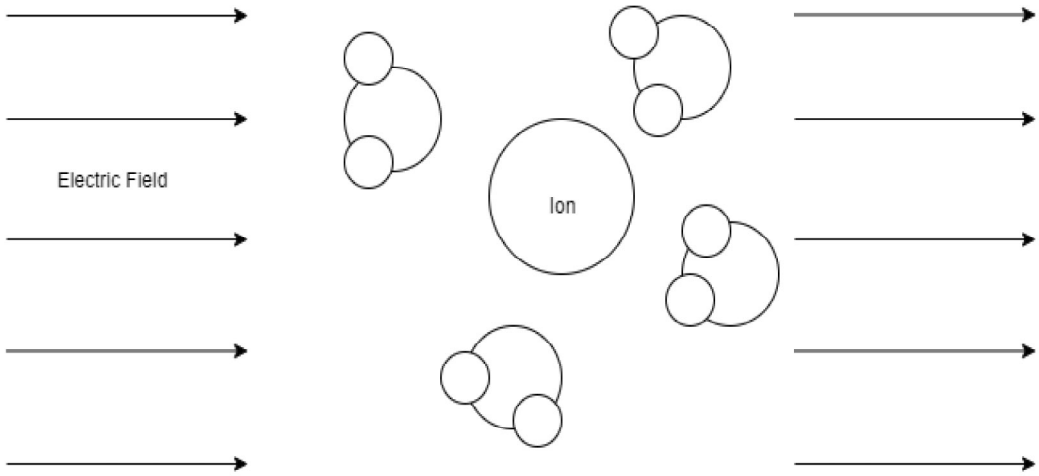

Fig 2: Dissolved ion and H2O molecules in an electric field. Modified from (Walker, 1987).

Table

Table 1: Few models used in microwave studies from research carried out at GEPEA (UMR 6144 CNRS), ONIRIS, Nantes, France.

References	Models	Objectives
De Albuquerque et al., 2021	$\rho C_p \frac{\delta T}{\delta t} = div\,(k \nabla T) + Q$	To study microwave food pasteurization by developing finite element model by coupling electromagnetism with standing-wave propagation, heat transfer and microbial inactivation equations.
Sadot et al., 2020	$\frac{\delta H}{\delta t}\rho - \nabla . k \nabla T = Q$ $Q = \frac{1}{2}\omega \varepsilon_o \varepsilon'' \lvert E_{local} \rvert^2$	To develop an innovative process for enhancing the quality of frozen food using microwaves.
Kubo et al., 2019	$\rho C_p \frac{\delta T}{\delta t} + \rho C_p u(\nabla . T) = \nabla . (k \nabla T) + \frac{1}{2}\omega \varepsilon_o \varepsilon'' \lvert E_{local} \rvert^2$ (for heat transfer modeling) $\rho \frac{\delta U}{\delta t} + \rho (U . \nabla) = \nabla . \left[-pI + \eta \left(\nabla U + (\nabla U)^T \right) - \frac{2}{3}\eta (\nabla . U) I \right] - \rho g$ (for fluid flow modeling)	To develop model for understanding the temperature and peroxidase inactivation profiles for microwave processing of fruit juices.

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Review of the Currently Available Monoclonal Antibodies for COVID-19

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Introduction :

Monoclonal antibodies have recently been developed as therapeutic options for the treatment and potential prophylaxis for COVID -19. These specific proteins are made to simulate one of the many defenses of the human immune system. Multiple different monoclonal antibodies have been developed that bind to the spike protein of the SARS-CoV-2 virus, which helps prevent viral attachment and entry into human cells.

In contrast with convalescent plasma, which consists of many antibodies collected from patients who have recovered from infection, monoclonal antibodies are directed toward specific targets. Monoclonal antibodies were developed to help reduce viral load to decrease the risk of developing serious symptoms in patients infected with the SARS-CoV-2 virus.

Current Status :

Currently, 3 monoclonal antibody products have authorized usage for COVID-19.

Bamlanivimab was the first monoclonal antibody given an emergency use authorization (EUA) by the FDA in November 2020 to treat mild-to-moderate COVID-19 in outpatients at high risk of developing severe COVID-19, as further described in **Table 1.** This is a

neutralizing human IgG1k monoclonal antibody that targets the spike protein of SARS-CoV-2, preventing the attachment of the protein with the human cell-surface ACE2 protein.[1] The phase 2 BLAZE-1 trial in patients with mild-to-moderate COVID-19 showed an effect of bamlanivimab on viral loads, but more importantly, the treatment group also had less patients progress to COVID-19-related emergency department visits and hospitalization.[2] This effect was particularly pronounced in a high-risk subgroup of patients (body mass index $\geq$ 35 or aged $\geq$ 65 years). However, an increase in circulating COVID-19 viral variants resistant to bamlanivimab alone led to its EUA revocation. In response, Eli Lilly and Company partnered and developed a new monoclonal antibody to be administered with bamlanivimab, etesevimab. Etesevimab is also a neutralizing monoclonal antibody targeting the spike protein of SARS-CoV-2. The combination of bamlanivimab and etesevimab is infused together to combat resistance and different variants of SARS-CoV-2. Both monoclonal antibodies were isolated from convalescent plasma in patients with COVID-19. The FDA granted an EUA for the same indication as monotherapy bamlanivimab in February based on the phase 3 BLAZE-1 trial, which demonstrated a 70% risk reduction of hospitalization or death in patients who received the combination treatment.[3] In June, the CDC identified an 11% increase in frequency of the COVID-19 Gamma and Beta variants in the United States, which are not effectively treated by either bamlanivimab or etesevimab. This led the US Department of Health & Human Services to halt distribution of these antibodies that month. However, because bamlanivimab and etesevimab are active against the currently dominant Delta variant, distribution was resumed in September.[4]

The second authorized therapeutic consists of the 2 monoclonal antibodies casirivimab and imdevimab. As with bamlanivimab and etesevimab, casirivimab and imdevimab are directed against the spike protein of SARS-CoV-2. Distributed together as a cocktail under the brand name REGEN-COV, casirivimab and imdevimab are administered via intravenous infusion or as subcutaneous injections.[5] The FDA issued an EUA for the use of casirivimab and imdevimab in the treatment of COVID-19 infection in November 2020. The EUA was more recently revised on July 30 to extend its use for postexposure prophylaxis of COVID-19 as well. Both uses are intended for mild-to-moderate disease in the outpatient setting **(Table 1)**. For use as postexposure prophylaxis, patients with a significant exposure to someone with SARS-CoV-2 infection are eligible if they are either not fully vaccinated or are fully vaccinated but expected to have had an inadequate immune response to vaccination because of an immunocompromising disease or medication use. In a phase 3 treatment study, more than 4000 nonhospitalized patients with mild-to-moderate COVID-19 and at least 1 risk factor for severe disease were randomized to receive either casirivimab-imdevimab or placebo. The casirivimab-imdevimab treatment groups demonstrated a decrease in COVID-19-related hospitalization or all-cause death, as well as a more rapid resolution of COVID-19 symptoms compared to placebo.[6] With regard to postexposure prophylaxis, a phase 3 randomized, double-blind clinical trial evaluated 1505 subjects who lived in a household with a patient infected with COVID-19 but were asymptomatic

and had a negative SARS-CoV-2 polymerase chain reaction (PCR) test themselves. They were randomized to receive either placebo or casirivimab-imdevimab and followed for serial PCR testing and assessment for development of symptoms. The treatment group demonstrated an 81% risk reduction in the development of PCR-confirmed COVID-19 infection through 29 days.[7]

TABLE 1. Monoclonal Antibody Indications and Administration

Monoclonal antibody	Emergency use authorization indication	Administration
Bamlanivimab/etesevimab	Mild to moderate COVID-19 in adults and pediatric patients 12 years and older weighing at least 40 kg with positive results of direct SARS-CoV-2 viral testing and at high risk for progression to severe COVID-19, including hospitalization or death	Single intravenous infusion of 700 mg bamlanivimab and 1400 mg etesevimab in sodium chloride 0.9% within 10 days of symptom onset
Casirivimab/imdevimab	1. Same as bamlanivimab/etesevimab 2. Postexposure prophylaxis in patients not fully vaccinated or not expected to mount full immune response to vaccination who have had close exposure to someone with COVID-19	Single intravenous infusion or subcutaneous injection of 600 mg casirivimab and 600 mg imdevimab within 10 days of symptom onset
Sotrovimab	Same as bamlanivimab/etesevimab	Single intravenous infusion of 500 mg sotrovimab in sodium chloride 0.9% within 10 days of symptom onset

Sotrovimab is the third monoclonal antibody currently available for the treatment of COVID-19 since its EUA was announced May 26. A product of GlaxoSmithKline, sotrovimab was created from an antibody identified in 2003 in a survivor of severe acute respiratory syndrome (SARS).[8] It is administered as a single intravenous infusion given over 30 minutes.[9] As with the above-mentioned therapies, sotrovimab is indicated for mild-to-moderate infection in those who are at risk for progression to severe disease. Its use is currently limited to the outpatient setting in patients meeting the criteria in **Table 1**. The ongoing, randomized, controlled phase 3 COMET-ICE trial is investigating the use of sotrovimab in nonhospitalized patients with symptomatic COVID-19 infection and risk factors for disease progression. The primary end point being investigated is hospitalization for more than 24 hours or death within 29 days. An interim analysis of 583 patients showed that risk of progression was reduced by 85% in those treated with sotrovimab compared to placebo.[10]

Though similar in their current indications, the available antibody therapies have several differences. Casirivimab-imdevimab is currently the only monoclonal antibody formulation with an EUA for use as postexposure prophylaxis. It is also the only therapeutic currently available as a subcutaneous injection. Route of administration is important to consider because the need for infusion may limit the access to and feasibility of obtaining treatment in a timely fashion, and it can limit capacity at infusion centers compared to a more quickly administered formulation. Sotrovimab for intramuscular injection is currently under investigation in a phase 3 clinical trial (NCT04913675) and could further improve the logistics of administering monoclonal antibody therapy.

Additionally, when choosing a monoclonal antibody therapy for treatment, it is important to take into consideration the predominant circulating strains of the local area. **Table 2**[11]

highlights the activity of each available monoclonal antibody products against different COVID-19 variant strains. Although these monoclonal antibody products are currently indicated only for patients not hospitalized for COVID-19, their use in the inpatient setting has been evaluated with mixed results. A clinical trial yet to be peer reviewed suggests the use of casirivimab-imdevimab in seronegative patients hospitalized with COVID-19 may reduce 28-day mortality, and bamlanivimab failed in an earlier study of hospitalized patients.[12,13]

TABLE 2. Variants and Monoclonal Antibody Activity Against Them[11]

Variants	PANGO lineage	First identified	Bamlanivimab/ etesevimab	Casirivimab/ imdevimab	Sotrovimab
Alpha	B.1.1.7	United Kingdom	No change	No change	No change
Beta	B.1.351	South Africa	Inactive	No change	No change
Delta	B.1.617.2	India	No change[a]	No change	No change
Epsilon	B.1.427/429	California	Decreased	No change	No change
Gamma	P.1	Japan/Brazil	Inactive	No change	No change
Iota	B.1.526	New York	Decreased	No change	No change

PANGO, phylogenetic assignment of named global outbreak.
[a]Bamlanivimab/etesevimab are unlikely to be active against the Delta Plus variant.

Conclusion:

Health care providers in the emergency department, urgent care, primary care, and testing sites are encouraged to support the administration of these monoclonal antibodies in appropriate patients to help reduce the progression of COVID-19 infection. At present, no other therapies exist that can prevent progression to severe disease that requires hospitalization. Clinician vigilance to refer eligible patients for monoclonal antibody therapy is key to improve outcomes and hospital capacity.

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THE NOBEL PRIZE IN CHEMISTRY, 2021

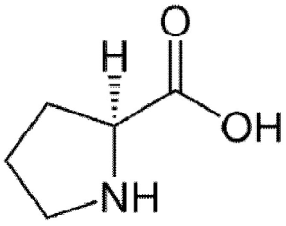
Benjamin List

Benjamin List (born 11 January 1968) is a German chemist who is one of the directors of the Max Planck Institute for Coal Research and professor of organic chemistry at the University of Cologne. He co-developed organocatalysis, a method of accelerating chemical reactions and making them more efficient. He shared the 2021 Nobel Prize in Chemistry with David MacMillan "for the development of asymmetric organocatalysis. Born to a upper-middle-class family of scientists and artists in Frankfurt, list is a great-grandson of the cardiologist Franz Volhard and a 2nd great-grandson of the chemist Jacob Volhard. His aunt, the 1995 Nobel laureate in medicine Christiane Nüsslein-Volhard, is the sister of his mother, architect Heidi List. At age three, his parents divorced.

Career and research :

List obtained his Diplom (M.Sc.) degree in chemistry from the Free University of Berlin in 1993, and his PhD from Goethe University Frankfurt in 1997. His doctoral dissertation was titled *Synthese eines* Vitamin B 12 *Semicorrins* (Synthesis of a vitamin B 12 semicorrin), and was advised by Johann Mulzer. List worked at the Scripps Research Institute Department of Molecular Biology in La Jolla, U.S. as a postdoctoral researcher in Carlos F. Barbas III and Richard Lerner's research groups from 1997 to 1998 with a scholarship from the Alexander von Humboldt Foundation and as an assistant professor from 1999 to 2003.

In 2003 he returned to Germany to become group leader at the Max Planck Institute for Coal Research, and in 2005 he became one of the institute's directors, heading the Homogeneous Catalysis Department. He served as the institute's managing director from 2012 to 2014. He has held a part-time position as an honorary professor of organic chemistry at the University of Cologne since 2004. List is also a principal investigator at the Institute for Chemical Reaction Design and Discovery, Hokkaido University since 2018. He is the editor-in-chief of the scientific journal *Synlett.* As of 2021, he has an h-index of 95 according to Google Scholar and of 86 according to Scopus.



Catalyst for asymmetric reactions, L-proline

List is considered to be one of the founders of organocatalysis, which uses non-metal and non-enzyme catalysts. In particular, while still an assistant professor he discovered the possibility of using the amino acid proline as an efficient chiral catalyst. This takes place in intermolecular aldol reactions, in which carbon atoms from two different molecules are bonded together, induced by proline. The development is based on the Hajos-Parrish-Eder-Sauer-Wiechert reaction. Subsequently, he developed the first proline-catalyzed Mannich, Michael, and α-amination reactions. He found asymmetric catalysis (especially Asymmetric counteranion directed catalysis, ACDC). He developed also new methods of textile organic catalysis, in which soluble organic catalysts and textiles are bound. These methods could, for example, help to treat water where there is no fresh water. Asymmetric organocatalysis is particularly important in bioactive organic compounds, where the chirality of the compounds is important, for example in drug production.

On 6 October 2021, he was awarded the Nobel Prize in Chemistry with David MacMillan "for the development of asymmetric organocatalysis. The development has great influence on pharmaceutical research and the drug production and "made chemistry greener.

List married Dr. Sabine List in La Jolla in 1999 and they have two sons, Theo and Paul. They all survived the 2004 Indian Ocean earthquake and tsunami.

List's parents sought to raise their children with an anti-authoritarian parenting style; he has admitted occasionally using the approach with his own children, stating that "you may only be 12, but if you think it will do you good to eat ten chocolate bars, then go ahead and do it. I have faith in you. But my advice is: I wouldn't do it."

Honors and awards :

- 1994 NaFöG-Award from the City of Berlin
- 1997 Feodor Lynen Fellowship of the Alexander von Humboldt Foundation
- 2000 Synthesis-Synlett Journal Award
- 2003 Carl-Duisberg-Memorial Award of the German Chemical Society
- 2004 Degussa Prize for Chiral Chemistry
- 2004 Lecturer's Award of the Fonds der Chemischen Industrie
- 2004 Lieseberg Prize of the University of Heidelberg
- 2005 AstraZeneca European Lectureship, the Society of Synthetic Chemistry, Japan
- 2005 Lectureship Award
- 2005 Novartis Young Investigator Award
- 2006 JSPS Fellowship Award of Japan
- 2007 AstraZeneca Award in Organic Chemistry
- 2007 Award of the Fonds der Chemischen Industrie
- 2007 OBC-Lecture Award
- 2008 Visiting Professor at Sungkyunkwan University, Korea
- 2009 Boehringer-Ingelheim Lectureship, Canada
- 2009 Organic Reactions Lectureship, US
- 2009 Thomson Reuters Citation Laureate

- 2011 Boehringer-Ingelheim Lectureship, Harvard University, US
- 2011 ERC Advanced Grant
- 2012 Novartis Chemistry Lectureship Award
- 2012 Otto Bayer Award
- 2013 Horst-Pracejus-Preis
- 2013 Mukaiyama Award
- 2013 Ruhrpreis, Mülheim, Germany
- 2014 Cope Scholar Award, US
- 2014 Thomson Reuters Highly Cited Researcher
- 2015 Carl Shipp Marvel Lectures, University of Illinois at Urbana-Champaign, US
- 2016 Gottfried Wilhelm Leibniz Prize
- 2017 Prof. U. R. Ghatak Endowment Lecture, Indian Association for the Cultivation of Science (IACS), Kolkata, India
- 2017 Ta-shue Chou Lectureship, Institute of Chemistry, Academia Sinica, Taipei, Taiwan
- 2018 Member of the German National Academy of Sciences Leopoldina
- 2019 Herbert C. Brown Lecture, Purdue University, Indiana, US
- 2019 Web of Science Citation Laureate in Chemistry
- 2021 TCR Lecture,100th CSJ Annual Meeting, Japan
- 2021 Nobel Prize in Chemistry
- 2022 Herbert C. Brown Award 2022 for Creative Research in Synthetic Methodes

David MacMillan

David William Cross MacMillan (born 16 March 1968) is a Scottish chemist and the James S. McDonnell Distinguished University Professor of Chemistry at Princeton University, where he was also the Chair of the Department of Chemistry from 2010 to 2015 He shared the 2021 Nobel Prize in Chemistry with Benjamin List for the development of asymmetric organocatalysis

Education and early life :

MacMillan was born in Bellshill, Scotland in 1968 and grew in nearby New Stevenston. He attended the local state-funded schools, New Stevenston Primary and Bellshill Academy and credited his Scottish education for his success. He received his undergraduate degree in chemistry at the University of Glasgow, where he worked with Ernie Colvin.

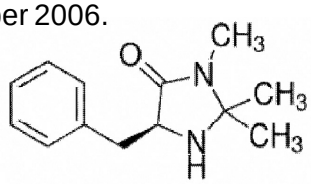
In 1990, he left the UK to begin his doctoral studies under the direction of Professor Larry Overman at the University of California, Irvine. During this time, he focused on the development of new reaction methodology directed toward the stereocontrolled formation of bicyclic tetrahydrofurans. MacMillan's graduate studies culminated in the total synthesis of 7-(–)-deacetoxyalcyonin acetate, a eunicellin diterpenoid isolated from the soft coral *Eunicella stricta.* He earned his Ph.D. in 1996.

He hailed his Scottish upbringing as a reason for his winning the Nobel.

Career and research :

Upon receiving his Ph.D., MacMillan accepted a position with Professor David Evans at Harvard University. His postdoctoral studies centered on enantioselective catalysis, in particular, the design and development of Sn(II)-derived bisoxazoline complexes (Sn(II)box).

MacMillan began his independent research career as a member of the chemistry faculty at the University of California, Berkeley in July 1998. He joined the department of chemistry at Caltech in June 2000, where his group's research interests centered on new approaches to enantioselective catalysis. In 2004, he was appointed as the Earle C. Anthony Professor of Chemistry. He became the James S. McDonnell Distinguished University Professor at Princeton University in September 2006.



First generation MacMillan catalyst

He is considered to be one of the founders of organocatalysis In 2000, MacMillan designed small organic molecules that can provide or accept electrons and therefore efficiently catalyse reactions. He developed catalysts that can drive asymmetric catalysis, in which a reaction produces more of the left-handed version of a molecule than the right-handed one (chirality), or vice versa. MacMillan's research group has made many advances in the field of asymmetric organocatalysis, and they have applied these new methods to the synthesis of a range of complex natural products. He developed chiral imidazolidinone catalysts. MacMillan catalysts are used in various asymmetric syntheses. Examples include Diels-Alder reactions, 1,3-dipolar cycloadditions, Friedel-Crafts alkylations or Michael additions.

MacMillan has also extensively developed photoredox catalysis for use in organic synthesis.

Between 2010 and 2014, MacMillan was the founding Editor-in-Chief of the journal Chemical Science, the flagship general chemistry journal published by the Royal Society of Chemistry.

As of 2021, MacMillan has an h-index of 110 according to Google Scholar and of 100 according to Scopus.

Honours and awards

- 2002 Sloan Research Fellowship
- 2004 Corday-Morgan medal of Royal Institute of Chemistry
- 2012 Elected a Fellow of the Royal Society (FRS)
- 2012 Elected as a member of the American Academy of Arts and Sciences
- 2013 Elected a Corresponding Fellow of the Royal Society of Edinburgh (FRSE)
- 2015 Harrison Howe Award
- 2017 Ryoji Noyori Prize
- 2018 Elected a member of the National Academy of Sciences
- 2021 Nobel Prize in Chemistry

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Series

History of Chemistry

Proteins are extremely complex nitrogen-containing organic compounds found in all animal and plant cells, where they constitute the principal component of the living protoplasm. Protein comprises, with carbohydrate and fat, the three classes of foodstuffs. However, the presence of nitrogen in all proteins sets them apart from carbohydrates and fat (lipids), because as foods, they are the only sources of the nitrogenous complexes necessary to build protoplasm. The term protein had its origin in the earliest attempt to explain the constitution of these substances. t was derived from the Greek adjective ‘proteios’, meaning "primarius," i.e. of the first rank or position, because it was of foremost importance for the living body.

The early branches of protein chemistry—descriptive, analytical, and physical—developed almost independently of each other. Descriptive chemistry had its origin in the observations of those investigators of the middle eighteenth and early nineteenth centuries who sought methods for the extraction of proteins in the native state from different vegetable and animal sources. Jacopo Beccari in 1747 obtained gluten from wheat flour after first kneading with water to remove the starch. In 1805, Heinrich Einhof (1778-1808) discovered that a part of the gluten was soluble in alcohol.

Jacopo Bartolomeo Beccari

Antoine-François de Fourcroy

In 1789, Antoine François de Fourcroy (1755-1809) called attention to the presence in plants of a nitrogenous material that resembled the albumin of egg white and serum. Work by others extended the list. Extracts from numerous plants and vegetables yielded nitrogenous products whose appearance and solubility characteristics resembled those of animal origin. As a result, the terms albumin, fibrin, and casein were soon applied to these nitrogenous plant substance. In addition to nitrogen, all these products contained sulphur and gave positive colour reactions characteristic of animal albumin, casein, and fibrin.

Analysis of these plant and animal products was stimulated by the belief that the "new chemistry" would provide new insights into animal physiology, and by the emergence of agricultural chemistry. Food shortages caused by the wars and political upheavals at the end of the eighteenth century led to a study of the chemical constituents of plants and animals used for human food. In England, Humphrey Davy (1778-1829) urged the government to develop policies to put farming on a scientific basis.

Humphrey Davy

As a result, from the very beginning of the nineteenth century, many chemists turned to the study of substances of plant and animal origin. These materials were extracted with acids, alkalis, and alcohol and the extracts subjected to various methods of precipitation in an attempt to isolate pure substances. It was thought that chemical analysis and a study of their properties would explain many physiological phenomena. It was distressing to the early protein chemists that so many of their techniques, which seemed to be universally applicable, produced adverse effects when applied to protein material. Proteins were known to need careful handling and mild reagents, yet here was a class of compounds whose solubility did not improve with heating, in fact they coagulated irreversibly even at temperatures well below the boiling of water. Exposure to acid or alkali of rather moderate

concentration produced similar damage. Nevertheless, water, acid and alkali were the first solvents to be employed, as methods for the separation and purification of proteins were developed. However, the protein chemist's task was not easy. He was concerned with molecules that were not only among the most complicated and largest which Nature produces, but were also extremely fragile and exceedingly difficult to purify, let alone isolate from other components.

As methods evolved for the separation of proteins by the precipitating action of various reagents, the diverse character of proteins from different sources began to be recognized. As early as 1841, the French physician, Prosper-Sylvain Denis, in a communication to Liebig, described the separation of blood proteins into those which were soluble in water and those only soluble in neutral salt solutions, that is, into categories which we now call albumins and globulins. He later extended these observations when he published his classical report in 1859 as “Memoire sur le sang" in which he described the behaviour of globulins as well as a method for the separation of proteins by means of the solvent action of neutral salts. Thus, more than a century ago, there were already the beginnings of the characterization of proteins as chemical substances and their fractionation. It was not until after 1810, however, that the quantitative analysis of organic compounds began to give reproducible data. There still existed much confusion about atomic weights of elements, and the same compound might be denoted by different empirical formulas. By the mid-1830s, the improvements in analytical procedures resulted in reliable methods for the determination of carbon, hydrogen, and nitrogen in fats, sugars, and other relatively small molecules. The new awareness of the importance of the albuminoid substances made it inevitable that the improved methods would be used for their analysis. The first systematic approach to this problem was made by Gerardus Mulder during the 1830s; soon after, Liebig and Dumas independently joined in.

Gerardus Johannes Mulder

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Writing Competitive Research Proposals for PhD and Post-doctoral Fellowship: Electrochemical Conversion of CO_2 to Fuel as a Potential Topic

Bidyut Bikash Sarma
Karlsruhe Institute of Technology, Germany
Biva Talukdar
Academia Sinica, Taiwan

Over the past few years, we have received numerous queries regarding how to pursue research career abroad, how to find a proper research group, and how to apply for a fellowship or funding. With the pandemic for almost 2 years now, things will get worse in the next few years in terms of job opportunities, new funding for research, etc. Nevertheless, there will be alternative possibilities that will help create a new future. With the crisis that will remain for some time, what do we do to compete with our present situation? In our opinion, the best in this situation will be to prepare yourself for your funding through some prestigious grant agencies for example Alexander von Humboldt foundation (in Germany), Marie Skłodowska-Curie Actions by European union (all Europe including UK and Israel), Fulbright fellowship (for USA) and there are plenty of other possibilities. In this article, we will concentrate on one particular funding agency applicable for both PhD and post-doctoral applications. Our primary concern is writing a research proposal, the topics that have a better chance to get it through, and how to find a proper host to successfully convince the funding agencies for positive evaluation. We would like to discuss particularly on Marie Skłodowska-Curie Actions (applicable to both for PhD and post-doctoral researchers) and their evaluation criteria for a successful research proposal. Electrochemical conversion of CO_2 to fuel or chemicals is one of the demanding topics of research across the globe and we would like to take this topic as our theme. In the following table, we summarized the evaluation criteria and different weightage on a separate proposal section. An applicant must look for all these criteria before writing the proposal. On an average, an excellent proposal requires approximately six months for preparation irrespective of funding agencies.

Table1. Different section of a Marie Skłodowska-Curie Actions proposal, their weightage, and the scores that reviewers are asked to give based on the proposal's originality. The

proposal that scores less than 70% are not allowed to re-submit in the following year and those scores above 85% but fails to get the funding (due to shortage in money) are certified as excellent proposal. Together it should not exceed 10 pages with a Times New Roman font size of 11.

Section	Weightage	Score obtained and what does it mean
Excellence 1.1 1.2 1.3 1.4	50%	0 - The proposal fails to address the criterion or cannot be assessed due to missing or incomplete information 1 – **Poor.** The criterion is inadequately addressed, or there are serious inherent weaknesses 2 – **Fair.** The proposal broadly addresses the criterion, but there are significant weaknesses. 3 – **Good.** The proposal addresses the criterion well, but several shortcomings are present. 4 – **Very good.** The proposal addresses the criterion very well, but a small number of shortcomings are present. 5 – **Excellent.** The proposal successfully addresses all relevant aspects of the criterion. Any shortcomings are minor.
Impact 2.1 2.2 2.3	30%	
Implementation 3.1 3.2	20%	

In the following, each section mentioned above is elaborated and how you can formulate these sections. Remember that 20% weightage on implementation does not mean that this section has less importance, so try to deliver the points precisely.

1. Excellence

1.1 Quality and pertinence of the project's research and innovation objectives (and the extent to which they are ambitious, and go beyond the state of the art)

Introduction: The rapid increase in carbon dioxide (CO_2) in the atmosphere from industrial sources such as cement, steel and coal is a global threat to all of us and serious action is necessary before climate change leads to dramatic changes in weather.[1] The atmospheric CO_2 has reached an unimaginably high value of 418 ppm, in December 2021, compared to 280 ppm in the pre-industrial revolution. Therefore, alternative strategies for reusing CO_2 to high energy-dense products will be an alternative route. To mitigate CO_2 concentration in the atmosphere, the ideal scenario would be to develop an artificial photosynthetic method to combine water splitting, which forms protons and electrons by electrochemical process, and CO_2 reduction to produce carbohydrates via proton-coupled multi-electron transfer steps.[2] CO_2 electro-reduction (CO_2RR) by solid catalysts has gained tremendous attention due to its ambient operating conditions and the most abundant proton source as water. However, the kinetically favored H_2 evolution reaction (HER, E^0= -0.42V vs. SHE)[3] outcompetes the CO_2RR due to competing potential window. The half-reaction reduction potentials for the common CO_2RR products are listed below with the numbers of electrons involved, at ambient conditions.

Electron transfer	Reaction	Potential (V vs SHE)
e^-	$CO_2 + e^- \rightarrow CO_2^-$	-1.9
$2e^-$	$CO_2 + 2\ H^+ + 2\ e^- \rightarrow CO + H_2O$	-0.53
	$2\ CO_2 + 2\ H^+ + 2\ e^- \rightarrow HCOOH$	-0.61
	$2\ CO_2 + 2\ H^+ + 2\ e^- \rightarrow H_2C_2O_4$	-0.913
$4e^-$	$CO_2 + 4\ H^+ + 4\ e^- \rightarrow HCHO + H_2O$	-0.48
$6e^-$	$CO_2 + 6\ H^+ + 6\ e^- \rightarrow CH_3OH + 2\ H_2O$	-0.38
$8e^-$	$2\ CO_2 + 8\ H^+ + 8\ e^- \rightarrow CH_4 + 2\ H_2O$	-0.24
$12e^-$	$2\ CO_2 + 12\ H^+ + 12\ e^- \rightarrow C_2H_4 + 4\ H_2O$	-0.349
	$2\ CO_2 + 12\ H^+ + 12\ e^- \rightarrow C_2H_5OH + 3\ H_2O$	-0.329
$14e^-$	$2\ CO_2 + 14\ H^+ + 14\ e^- \rightarrow C_2H_6 + 4\ H_2O$	-0.27
$18e^-$	$3\ CO_2 + 18\ H^+ + 18\ e^- \rightarrow C_3H_7OH + H_2O$	-0.31

A more recent trend in this field of research is the utilization of single atom catalysts or sub-nanometer cluster catalysts for electro-catalytic CO_2 reduction.[4] Single atom Catalysts (SACs) [5, 6] is a growing area in the field of heterogeneous catalysis where electronic properties (for example, charge, coordination etc.) of an atom are tuned by modifying the support. This makes SACs quite an attractive material to utilize for such processes to understand binding behavior of CO_2 and further hydrogenation to valuable products like CO, methanol, or formic acid. Moreover, SACs serve as a common platform to bridge the knowledge between homogeneous and heterogeneous catalysis.[5]

Molecular catalyst for electro-catalytic CO_2 reduction: For the past few decades, Rhenium (I) molecular complexes are shown to bind CO_2 effectively and further hydrogenation of CO_2 to valuable products like formic acid, CO, methanol etc. is already possible.[7]

However, there are quite a few open questions to answer. (a) Can one design a set of efficient solid catalysts that serve as alternatives to the molecular analogues that have similar precursors to the Re complex? This would be ideal because solid catalysts are easy to separate and regenerate, which is beneficial for industrial applications. (b) Is it possible to combine a conducting matrix (for example N-doped graphene) and a metal center that can bind CO_2 in close proximity to have efficient proton-coupled multi-electron transfer for CO_2 reduction? (c) Will solid catalysts, being rigid in nature compared to flexible molecular entities, favor a particular M-CO_2 binding mode that follows a specific reaction pathway for a specific product?

From molecular catalyst to supported catalyst: To answer the above-mentioned questions, we propose a series of solid single atom catalysts of 1st row transition metals incorporated into a host matrix such as N-doped graphene as shown in **figure 1**. This strategy utilizes the electron transport properties of graphene matrix and CO_2 binding abilities of transition metals. For this purpose, the molecular entity will be first anchored

over support via electrostatic interaction. Research based on the molecular Re complex will be used as a guide to synthesize a new series of new catalysts. A knowledge driven approach from homogeneous catalysis to heterogeneous catalysis will help us to understand the details of the mechanistic pathway. For example, (a) Is the flexibility of molecular complexes mandatory to drive the reaction? (b) What is the role of the CO ligand in molecular complexes? (c) Will there be a competing hydrogen dissociation reaction over the supported single atom? Single atom catalysts will have at least three nitrogen neighbors in the graphene pockets available for bonding and three vacant coordination spheres. Hence, there is enough room for CO_2 to fill that vacancy.

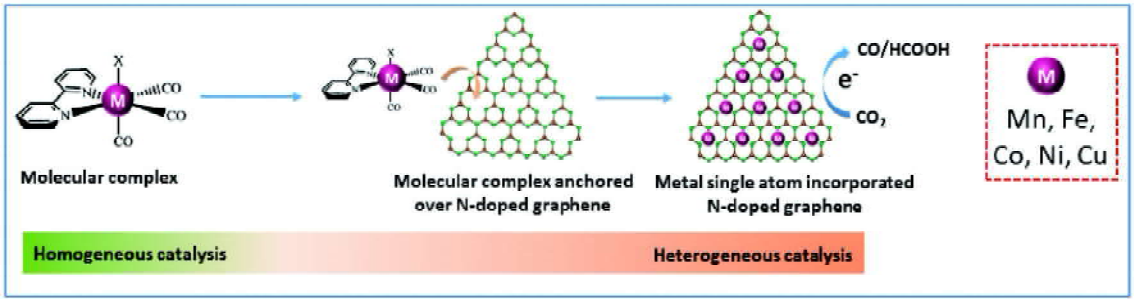


Figure 1. Bridging the knowledge between homogeneous and heterogeneous catalysis for electrochemical conversion of CO_2 over 1st row transition metals

Single atom catalysts (SACs) and its dynamic behavior: SACs are attractive materials and has already been proved to be useful for many catalytic applications as shown by many researchers.[6, 8, 9] However, the fate of the single atoms under the operating reaction conditions remains a question especially under harsh environments. A supported single atom possesses high surface energy and tend to form clusters or nanoparticles if the bonding interaction between atom and support is too weak. To tackle this challenge, a series of catalysts with different nuclearity (atom, cluster, and nanoparticles) can be synthesized and tested in combination with in-situ spectroscopic techniques (such as X-ray absorption spectroscopy (XAS) at synchrotron light source, FTIR spectroscopy etc.) as schematically represented in **figure 2**.

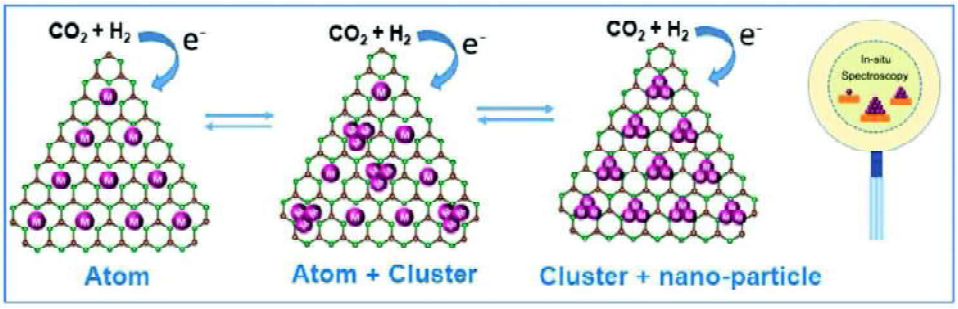
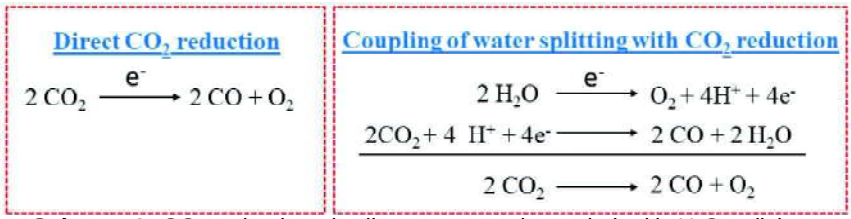


Figure 2. Schematic diagram of catalysts (with different nuclearity) that will be investigated under the electrochemical reduction of CO_2 with in-situ spectroscopic tools.

It is also important to mention in this section how the proposed work goes beyond the state-of-the-art research. Draw equations such as in scheme 1, figures, tables to get the attention of the reviewers. Some reviewers get 10 proposals to review within 4-5 weeks and this means 2 proposals per week which is very tedious work. Most of them are senior scientists and professors and will not have time to read every sentence. They also have to look at your CV.



Scheme 1. CO_2 reduction via direct route and coupled with H_2O splitting

Reaction mechanism and in-situ spectroscopic studies: Explain in this section about the reaction mechanism for electrochemical CO2 reduction and how you envision implementing in-situ spectroscopic tools to find out the mechanism. Highlight the innovative points.

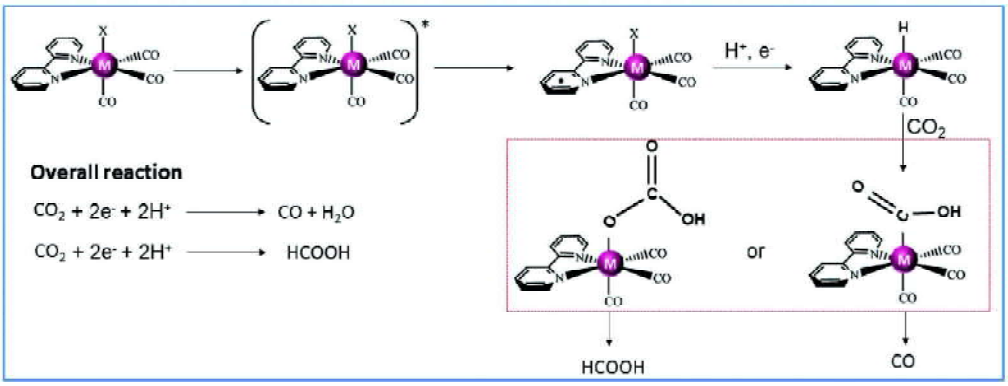


Figure 3. A hypothetical CO_2 reduction pathway with molecular complex (analogues to well-known Re complex)

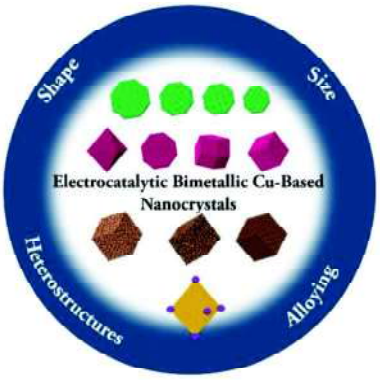
The proposed research concept brings a few innovative points:

(a) A knowledge driven approach between homogeneous and heterogeneous catalysis to understand a highly challenging electrochemical reduction of CO_2 will pave the way for designing a new set of materials in the future.

(b) Single atom catalysts, a well-established concept in heterogeneous catalysis; questions remain unanswered about the dynamic behavior of single atoms under operating conditions and this research proposal addresses this point very thoroughly.

(c) Artificial photosynthesis, a holy grail for many researchers, the proposed research concept will investigate combining H_2O splitting to produce electrons and protons, and then transfer the electron to reduce CO_2 with a metal incorporated into a host matrix such as N-doped graphene.

The catalytic activity of CO_2RR over supported nanoparticle depends on the morphology of nanocrystals, size, shape, coordination number and the number of dangling bonds. Lower the coordination number, higher is the number of dangling bonds and hence higher is the reactivity. The population of low coordination site increases with decreasing the particle size.[10] However, decreasing particle size does not necessarily always increase the activity of CO_2RR, but also sometimes increases the competing HER. Therefore, for an efficient catalyst design, it is necessary to increase the CO_2RR active site over HER active sites.[11]



1.2 Soundness of the proposed methodology (including interdisciplinary approaches, consideration of the gender dimension and other diversity aspects if relevant for the research project, and the quality of open science practices, including sharing and management of research outputs and engagement of citizens, civil society, and end users, where appropriate)

Methodology: The proposed research involves synthesis of molecular complexes, supported transition metal complex over N-doped graphene and single atom and cluster/ nano-particle catalysts. On successful synthesis of catalysts, catalytic tests will be carried out in an electrochemical cell (figure 4) that is already available at the host group. Catalyst characterization will be performed by various complementary techniques such as ^{1}H-NMR,^{13}C-NMR in liquid phase, N2-physisorption, powder X-Ray diffraction, Scanning Transmission Electron Microscopy (STEM), UV-Vis, FTIR and X-ray absorption spectroscopy (XAS). The host group has some of the facilities available in his/her laboratory and the others can be accessed via the service department or in collaboration with other groups at the University. For identifying short-lived intermediate in-situ spectroscopic techniques based on XAS and FTIR will be used. The reactor set-up for the most conventional CO_2RR is as shown in figure 4 wherein H-cell is used, cathodic and anodic compartments are separated by an ion-exchange membrane to avoid product crossover. The cathodic compartment contains working (WE) and reference electrodes (RE), and the anodic compartment contains the

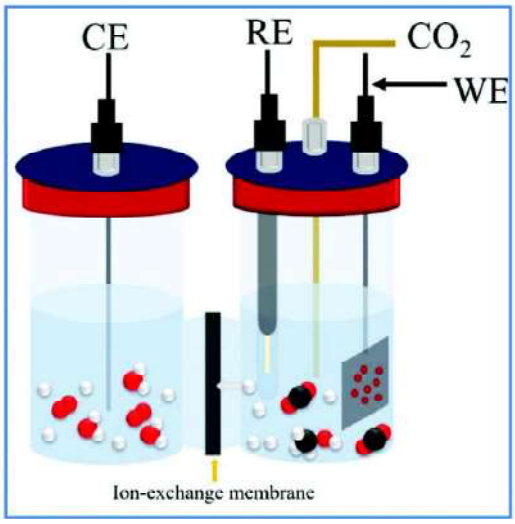


Figure 4. Schematic diagram of an electrochemical cell for CO_2 RR.

counter electrode (CE). The reduction of CO_2 and H_2O occurs in the cathodic compartment, whereas oxidation of H_2O to O_2 takes place in the anodic compartment.

Interdisciplinary approach: It is imperative to state how your research is inter-disciplinary. Interdisciplinary and collaborative work has higher chances to receive funding.

Open science practices: The research funding is often coming from taxpayers. At the end if you publish your results in a journal that common public will not be able to read, obviously it is not appreciable. However, many universities have now open access policy agreements with most renowned publishing agencies.

1.3 Quality of the supervision, training and of the two-way transfer of knowledge between the researcher and the host

In this part, it is crucial to describe the qualifications of the host and training of the researchers in detail and how a two-way knowledge transfer between them is expected. For example, where the supervisor got education, training, some soft skills, publications, organization of conferences, editor of journals, public outreach program etc.

Qualification and experience of the supervisor: Education, citations, h-index, how many former PhD/post-doc supervised until now, what are the competitive research grants got so far, award and achievement starting from his/her independent career etc.

Training of the researcher: How the applicant will receive training on various facilities in the host group. For example, the researcher will receive training on NMR, STEM, XRD, FT-IR etc. during the funding period. Moreover, the researcher will participate in workshops on career development such as writing grants, project managements, building up leadership quality.

Two-way transfer of knowledge between the researcher and the host: Explain how the proposed research will help the researcher (the applicant) explore a new field and how you will bring new knowledge to your host group. It must be two-way gain of knowledge.

1.4 Quality and appropriateness of the researcher's professional experience, competences, and skills

Quality and appropriateness of the researcher's professional experience: The applicant needs to elaborate on the skills you have learned and milestones you have achieved in your scientific activities so far. Mention what you have done in all your first author articles in one sentence. Explain in brief what you have done in your MSc and PhD thesis. The invited talk, selected talk and if you already received some awards related to your research topic, thesis, university rank etc.

2. Impact

2.1 Credibility of the measures to enhance the career perspectives and employability of the researcher and contribution to his/her skills development

Expected skill development of the researcher: In this sub-section, you need to explain how the proposed research will help you in further development of your career. For example, apart from research, you are also willing to explore a new culture and language and expand your scientific network. Mention what are your plans once you finish the funding period.

2.2 Suitability and quality of the measures to maximise expected outcomes and impacts, as set out in the dissemination and exploitation plan, including communication activities

Plan for the dissemination and exploitation activities, including communication activities: In this sub-section, explain where you want to publish your research work. Mention important conferences that you want to attend related to this topic in next two years. If you have your own twitter, YouTube, Facebook, and other social media platform to communicate science you can also highlight here.

Strategy for the management of Intellectual property, foreseen protection measures: Any invention related to the project will be intellectual property of the host institution and need to be stated here.

2.3. The magnitude and importance of the project's contribution to the expected scientific, societal, and economic impacts

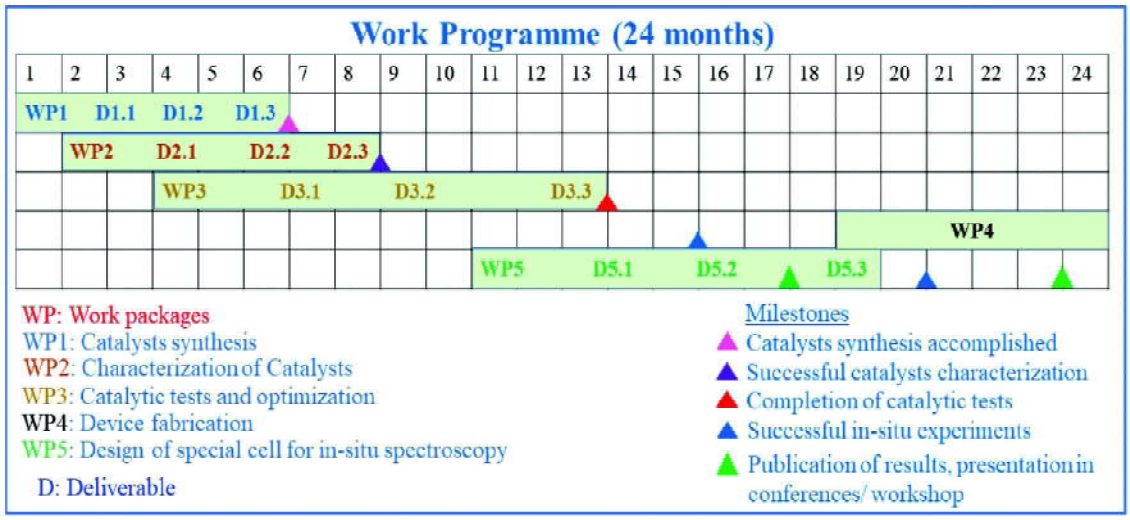
Expected scientific impact: The proposed research bridges the concepts between homogenous and heterogeneous catalysis with in-situ spectroscopic investigation to find the active center during electro-catalytic reduction of CO_2. CO_2 hydrogenation has already been practiced in industry to produce methanol and formic acid. However, all these processes require high temperature (523-623K) and high pressure (20-40 bar). An alternative way is to utilize electricity for this process. Electrochemical conversion of CO_2 has been achieved with molecular catalysts where stability and recyclability are always issues. This research proposal systematically addresses these issues with in-situ spectroscopic investigation. Single atom catalysts, a growing topic in heterogeneous catalysis, will be investigated in this proposal, for instance single atom catalysts of transition metals (Fe, Co, Ni and Cu) for electro-reduction of CO_2. A successful outcome of this study will inspire the development of a sustainable process for the electrochemical reduction of CO_2.

Expected societal impact: In summary, there are several strategies for efficient CO_2 conversion to valuable chemicals, such as designing of optimum catalyst, use of suitable electrolyte and CO_2 flow avoiding CO_2 mass transport limitation. Therefore, we suggest the newcomers in this topic to rigorously screen through each parameter for a successful CO_2 conversion. Increase in CO_2 in the atmosphere is a global threat to humanity and urgent steps are necessary to slow the increase in the global rise in temperature, which stems from the steady increase in greenhouse gases like CO_2. Design of an efficient catalyst for this process will inspire many others to solve the urgent need for this process.

3. Quality and Efficiency of the Implementation

3.1 Quality and effectiveness of the work plan, assessment of risks and appropriateness of the effort assigned to work packages

Here a summary of work plan preferably in the form of a Gantt chart for a 24-month plan is expected. Please highlight millstones, deliverables, and any other relevant information.



Once you have the work programmed planned, then explain each work packages. For example, (a) catalyst synthesis, (b) catalyst characterizations, (c) catalytic tests, (d) in-situ experiments, (e) device fabrication etc. If there are specific risk involve mention here so that the project looks challenging, and you already identified those.

3.2 Quality and capacity of the host institutions and participating organisations, including hosting arrangements

Quality and capacity of the host institution: In this section, you need to write about the details of the department where you want to apply. What are the facilities that will be available to you? For example, (a) Brucker 400 MHz Avance Nuclear Magnetic Resonance (NMR) spectrophotometer is available at the chemistry department. In the host group 4 gloveboxes, UV-Vis and IR Spectrophotometers, electrochemical station, spin-coating device are available.

Conclusion: Applying for a prestigious grant or fellowship needs significant amount of time and devotion. Starting from finding a host until submitting the proposal it might take up to 6-8 months and then 5-6 months for the evaluation process. I highly recommend my fellow junior researchers to prepare for such a prestigious fellowship at least once in their research careers. Since most of the fellowships have a similar format if you apply for one of them, you will not be afraid of writing any research proposal in the future. Also, keep in mind that these grants have less than 10% success rate on average. Therefore, failure to get it will not mean that your proposal was bad but the score will tell you how the proposal was written. Finally, some reviewer's comments (weakness) from a proposal that received more than 85% score but failed to get the grant are mentioned below so that the readers know in addition to your research proposal what other things play a significant role (apart from scientific part) for successful funding.

(a) The researcher does not have adequate experience in supervising students at various levels considering the current track record.

(b) This research will produce results of potential industrial and commercial interest. It is not sufficiently discussed what kind of industrial applications are envisioned.

(c) The proposal insufficiently justifies the possibility to accomplish the important workload foreseen in work package 4 within the short, allocated time schedule.

(d) The methodology is not presented in sufficient detail.

(e) Most of the proposal is focused on synthesis. The mechanistic and kinetic studies are not described in adequate detail, even though the need for such a multidisciplinary approach is evident for reaching the project objectives.

(f) Insufficient details are provided about how participation in the proposed research project will open the best career possibilities for the researcher.

(g) The implementation plan is described in a too generic way and lacks specific details.

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The Chemical Axis 2022, Vol. 21, No.1 ■ ISSN 2249-8842

Students' Section

Solar Cell Technology : New Records

Pragyan Jyoti Goswami
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A team of researchers from the National University of Singapore (NUS) has set a new record in the power conversion efficiency of solar cells made using perovskite and organic materials. This technological breakthrough paves the way for flexible, light-weight, low cost and ultra-thin photovoltaic cells which are ideal for powering vehicles, boats, blinds and other applications.

"Technologies for clean and renewable energy are extremely important for carbon reduction. Solar cells that directly convert solar energy into electricity are among the most promising clean energy technologies. High power conversion efficiency of solar cells is critical for generating more electrical power using a limited area and this, in turn, reduces the total cost of generating solar energy," explained lead researcher Presidential Young Professor Hou Yi, who is from the NUS Department of Chemical and Biomolecular Engineering and also leading a "Perovskite-based Multi-junction Solar Cells group" at the Solar Energy Research Institute of Singapore at NUS.

New Trends in the Solar World

Solar cell technology has achieved tremendous growth in recent years as a sustainable energy source. The reliability, efficiency, durability, and price of solar cells have a crucial impact on the commercial potential and large-scale implementation of solar energy projects around the world.

The conventional solar cells being used in solar power plants are based on a single-junction architecture. The practical power conversion efficiency of single-junction solar cells is limited to about 27% in industrial production. To push the frontiers of solar energy production will require novel solutions for solar cells to perform better in power conversion.

In order to raise the power conversion efficiency of solar cells to go beyond 30%, stacks of two or more absorber layers (multi-junction cells) are required. Tandem solar cells, which are made using two different types of photovoltaic materials, is a hot area of research.

In their latest project, Assistant Professor Hou and his team break new ground in the field of perovskite/organic tandem solar cells. Their discovery opens the door to thin-film tandem solar cells that are light and bendable, which could have wide-ranging applications such as for solar-powered blinds, vehicles, boats and other mobile devices.

Breakthroughin power conversion efficiency

A tandem solar cell comprises two or more subcells electrically connected using interconnecting layers (ICLs). The ICL plays a critical role in determining the performance and reproducibility of a device. An effective ICL should be chemically inert, electrically conductive and optically transparent.

Although perovskite/organic tandem solar cells are attractive for next-generation thin-film photovoltaics, their efficiency lags behind other types of tandem solar cells. To address this technological challenge, Asst Prof Hou and his team developed a novel and effective ICL that reduces voltage, optical and electrical losses within the tandem solar cell. This innovation significantly improves the efficiency of the perovskite/organic tandem solar cells, achieving a power conversion rate of 23.6%.

"Our study shows the great potential of perovskite-based tandem solar cells for future commercial application of photovoltaic technology. Building on our new discovery, we hope to further improve the performance of our tandem solar cells and scale up this technology," said Asst. Prof Hou.

Reference:

Wei Chen, Yudong Zhu, Jingwei Xiu, Guocong Chen, Haoming Liang, Shunchang Liu, Hansong Xue, Erik Birgersson, Jian Wei Ho, Xinshun Qin, Jingyang Lin, Ruijie Ma, Tao Liu, Yanling He, Alan Man-Ching Ng, Xugang Guo, Zhubing He, He Yan, Aleksandra B. Djuriši, Yi Hou. Monolithic perovskite/organic tandem solar cells with 23.6% efficiency enabled by reduced voltage losses and optimized interconnecting layer. Nature Energy, 2022; DOI: 10.1038/s41560-021-00966-8

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Students' Section

Plastic Waste Management

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India generates 15 million tonnes of plastic waste every year, but only one-fourth of this is recycled due to lack of a proper solid waste management system. This ultimately burdens the landfills and poor socio-economic conditions of waste pickers.

Here I would present 3 solutions to this plastic menace. First is to mix plastic with bitumen for the constructions of roads. Roads made with mixing plastic would consist of 6-8% plastic, while 92-94% bitumen. Construction of every kilometer of road this way requires nine tonnes of bitumen and one tonne of plastic waste. This means for every kilometer of road constructed it would save 1 tonne of bitumen which costs around Rs 30,000.

The waste plastic used is polyethylene, polystyrene, polypropylene. The waste is shredded and coated over aggregate and mixed with hot bitumen and the resultant mixture is used in the construction of roads and pavements. This will not only increase the strength and durability of the roads but will also provide solution to various defects like pot holes, corrugation and ruts.

Secondly, plastic could be used to make affordable bricks that are even stronger than concrete. A Kenya based entrepreneur and inventor, Nzambi Matee, has created a start-up that recycles plastic waste into bricks. She was successful in creating a prototype machine that turns discarded plastic into paving stones.The product is almost five to seven times stronger than concrete.

A wide array of plastic wastes could be used for the production, like starting from high density polyethylene, used in milk and shampoo bottles, to low density polyethylene, often used for bags for cerals or sandwiches, and even polypropylene, used for ropes, flip-top lids and buckets. The plastic waste is mixed with sand, heated and then compressed into bricks. Matee's start-up is an inspiration for others to take up similar works and create solutions to the plastic waste problem.

Thirdly, plastic wastes could be used as a partial substitute for sand in concrete. When plastic waste specifically Polyethylene Terephthalate (PET) was used in place of sand in

concrete and the effect of this material on the physical and mechanical properties of concrete were studied it was found that reusing waste plastic as a sand-substitution aggregate in concrete gives a good approach to reduce the cost of materials and solves some of the solid waste problems posed by plastics.

Recycled PET bottles can be used in the concrete production at certain replacement rates. This approach reduces the self-weight of concrete in structures and helps conserve natural resources such as sand. Although the mechanical properties of concrete decreased by increasing the replacement ratio of PET and plastic had a negative effect on the fire resistance of concrete, plastic particles can be encapsulated with other materials and produce environmentally safe concrete. In addition, recycled PET bottles can be used in many applications such as highway medians, sub-bases for highway pavements and various structures where strength is not the most important factor.

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International Conference on "Progress and Challenges in Modern Day Science" (PCMDS 2021)

An international conference was organised by The Department of Chemistry, B. Borooah College in association with Assam Science Society. Spanning over two days the conference was organised on the topic "Progress and Challenges in Modern Day Science" on June 17 and 18, 2021 in the virtual mode. Honourable Vice Chancellor of Gauhati University, Prof. Pratap Jyoti Handique, set the conference to motion by delivering the key-note address. Three plenary lectures were delivered during the course of the conference by Prof. Thalappil Pradeep (awarded Padma Shri in 2020) of IIT Madras, Prof. Tomislav Friscic of Mc Gill University, Canada and Prof. William Jones of CambridgeUniversity, UK.

The conference had nine invited lectures, delivered by researchers and scientists from around the globe. One session of the conference was earmarked especially for women scientists, and the session was held in honour of Dr. Sutopa Raichoudhury, the then Head of the Department of Chemistry, B. Borooah College. Apart from the plenary lectures and invited lectures, short invited lectures, oral presentations and poster presentation were also held during the conference.

The conference saw the successful participation of scientists from various prominent institutions of the globe viz. StanfordUniversity (USA), Karlsruhe Institute of Technology (Germany), Rowan University (USA),Technion-Israel Insitute of Technology (Israel), State University of New York (USA), Bengurion University (Israel), Virginia Commonwealth University (USA), Humboldt-Universitatzu (Germany), University of California (USA), University of Sharjah (UAE), University of Gottingen (Germany), Universitat Stuttgart (Germany), Uppsala University (Sweden), North western University(USA), National Yang Ming Chiao Tung University (Taiwan),Universitat Autonoma de Barcelona (Spain), JNCASR (India), Cotton University, Shiv Nadar University, IIT Guwahati, Gauhati University, IISER Kolkata, Presidency University, Kaziranga University, Assam Don Bosco University, IASST, Tezpur University, Bhattadev University, North East Hill University, Nowgong College, Behala College, Sipajhar College, Tinsukia College, Morigaon College, Cachar College, DKD College, Assam Engineering College, B. Borooah College, etc. There were participants of industries as well viz. Unimax Medical Systems Inc. (Taiwan), Futur Ceuticals Inc. (USA) etc.

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News in Focus

DNA to Build the World's Tiniest Antenna :

Researchers at university de Montreal have created a nanoparticle to monitor the motion of protein. Reported this week in nature in Nature methods, the device ia new method to monitor the structural changes of protein over time and may go long way to helping scientists better understand natural and human-designed nanotechnologies. The result are so excited that they are currently working on setting up a start-up company to comercialize and make this nanoantenna available to most researchers and the pharmaceutical industry. An antenna that works like a two-way radio, over 40 years ago, researchers invented the first DNA synthesizer to create molecules that encode genetic information. "In recent years, chemists have realized that DNA can also be employed to build a variety of nanostructures and nanomachines.

Inspired by the 'Lego-like' properties of DNA, with building blocks that are typically 20,000 times smaller than a human hair, we have created a DNA-based fluorescent nanoantenna, that can help characterize the function of proteins. Like a two-way radio that can both receive and transmit radio waves, the fluorescent nanoantenna receives light in one colour, or wavelength, and depending on the protein movement it senses. One of the main innovations of these nanoantennae is that the receiver part of the antenna is also employed to sense the molecular surface of the protein studied via molecular interaction.

Blood Test Offers New Hope to People With Depression

A blood test using RNA maker is offering new hope to people with mood disorders such as depression in could be what a significant breakthrough in the diagnosis of mental condition. A team from US Indiana University School of Medicine launched the blood test in April, claiming it be psychiatry's first ever biological answer to diagnosing a mood disorder. This work will help to avoid years of trial and error, hospitalization, and side effects. Every system of body the brain, the nervous system, the immune system has a common route is the principal of research. When the body is depressed psycho-neurological mechanism, hormones etc are released that effect our blood and immune system. Rna biomarker were identified that could track the mood stages over a period time, 26 such biomarkers was identified and worked with. More research will add more pieces towards a definite outcome.

Super Enzyme Eats Plastic Six Time Faster

A super enzyme that degrades plastic bottles six times faster than before has been created by scientist and could be used for recycling within a year or two. Plastic is a concern for whole planet and organism residing on it. People are known to consume and breathe microplastic particles. Plastic bottles are very difficult to break into their chemical constituent in order to make the new ones from the odds.The super enzyme derived from bacteria that naturally evolved the ability to eat plastic, enables the full recycling of bottles. Scientists believe that combining it with enzymes that break down cotton could also allow mixed-fabric clothing to be recycled. Today million tones of clothing is either dumped in landfills. The newly developed enzyme break down plastic in few days which is six times faster and work in room temperature.

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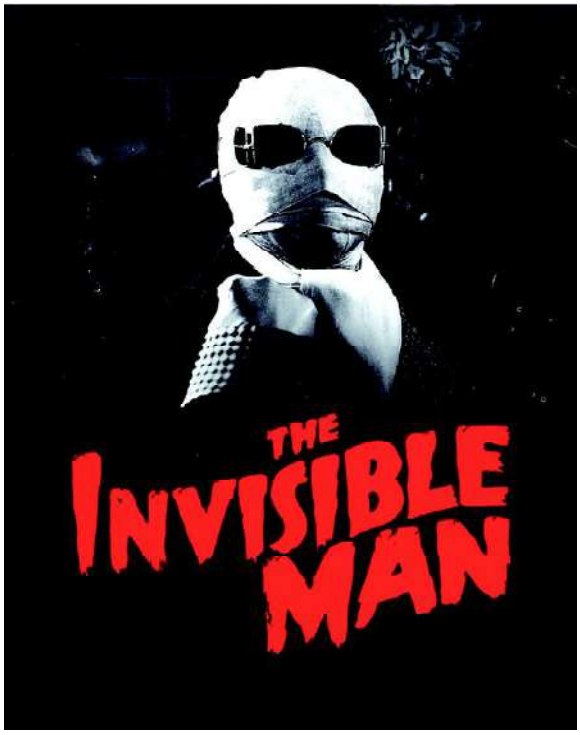
CHEMISTRY IN MOVIES

THE INVISIBLE MAN (1933)

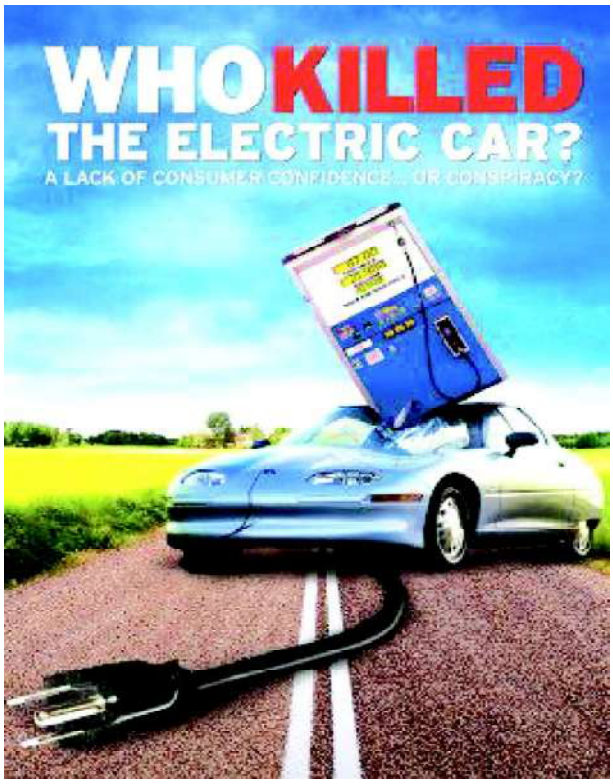
The film plot a story of a chemist ,who is involved in many series of experiments. Dr. Jack Griffin, the chemist who discovered the secret of invisibility while conducting one of such test involving an obscure drug called monocane. Dr. Cranley one of Dr.Griffin's employer and his other assistant, Dr. Kemp search Griffin's empty laboratory, finding only a single note in a cupboard. Cranley becomes concerned when he reads the note which had a list of chemicals, including monocane, which Cranley knows is extremely dangerous; an injection of it drove a dog mad in Germany. Griffin seems unaware of this, Cranley deduces Griffin may have learned about monocane in English books printed before the incident that describe only its bleaching power. As the story proceed the search of Dr Griffin continued as the number of crime committed by him increased such as murder. At last is body appeared when he was shot dead by police.



WHO KILLED THE ELECTRIC CAR ?

The film explores the roles of automobile manufacturers, the oil industry, the federal government of the United States, the California government, batteries, hydrogen vehicles, and consumers in limiting the development and adoption of this technology.

The film deals with the history of the electric car, its modern development, and commercialization. The film focuses primarily on the General Motors EV1, which was made available for lease mainly in Southern California, after the California Air Resources Board (CARB) passed the zero-emissions vehicle (ZEV) mandate in 1990 which required the seven major automobile suppliers in the United States to offer electric vehicles in order to continue sales of their gasoline powered vehicles in California. Nearly 5000 electric cars were designed and manufactured by Chrysler, the Ford Motor Company, General Motors (GM), Honda, Nissan, and Toyota. Which lead to increase in demand of lead rechargeable batteries for the electric cars. As lead batteries provide a large on road life for the car.The film also explores the future use of hydrogen fueled automobiles. The use of hydrogen as fuel can prove to the broadest feet in the path towards sustainable development.



Zeolite Nanotube Discovery

Zeolites have pores roughly the size of many types of molecules, and scientists and engineers have used the varied sizes, shapes, and connections of the pores to discriminate between molecules of different sizes, allowing for the production of chemicals suitable for plastic production, or for the separation of undesired molecules from desired ones.

The team was designing syntheses to assemble 2D zeolite materials, in an unexpected turn of events, some of the results indicated that a new type of assembly process was occurring. Indeed, one such case led to a novel 1D zeolite material that had a tube-like structure with perforated porous walls. This 1D material, termed a zeolitic nanotube, was unlike any zeolite ever synthesized or discovered in nature previously.

Zeolite nanotubes could be used to make entirely new types of nanoscale components that can control transport of mass or heat or charge, not only down the length of the tube the pipe, but also in and out through the perforated walls.

Resolving the detailed arrangement of the atoms in the zeolite nanotube was a challenging task, for which the Georgia Tech researchers teamed up with zeolite crystallography experts at Stockholm University and Penn State. They found that the nanotube walls had a unique arrangement of atoms that are not known in 3D or 2D zeolites. This same arrangement is also responsible for forcing the zeolite to form as a 1D tube rather than a 2D or 3D material. This is the first example of a new class of nanotubes, and its unique and well-defined structure provides exciting ideas and opportunities to design zeolite nanomaterials, Through further work, there is hope that different zeolitic nanotubes could be obtained with variations in pore size, shape and chemistry. Put plainly -- a nanometer-scale tube made from a 1D material with regular, perforated holes on the sides is now available for exploration. In addition to this being a fundamental scientific discovery that could change the way we think about designing porous materials, the researchers see potential for many practical applications.

The unique structural attributes of these materials will allow for an array of potential applications in membrane separations, catalysis, sensing, and in energy devices where mass or energy transport are crucial. The materials may have unique mechanical properties, as well, finding applications in composite materials, as carbon nanotubes have done. At this stage, the sky is the limit, and we hope researchers will look for creative ways to deploy these materials for the benefit of humanity.

AMAZING FACTS

- Spider webs are made of protein fibre.
- The rarest naturally occurring element on earth crust is astatine.
- Bee sting is acidic while the asp is alkali.
- Chocolate that we eat contain phenylethylamine.
- DNA is flame retardant.
- Every hydrogen atom in our body is 1.3 billion year old, as created art birth of universe.
- Car's airbags are packed with salt of sodiumazide, which is very toxic.
- 60 elements are found inside our body.
- Liquid and solid form of oxygen is blue in colour.
- Its possible to die from drinking too much water.

■ ■ ■

Chemistry Puzzle

EXTREME COMMON NAME WORD SEARCH

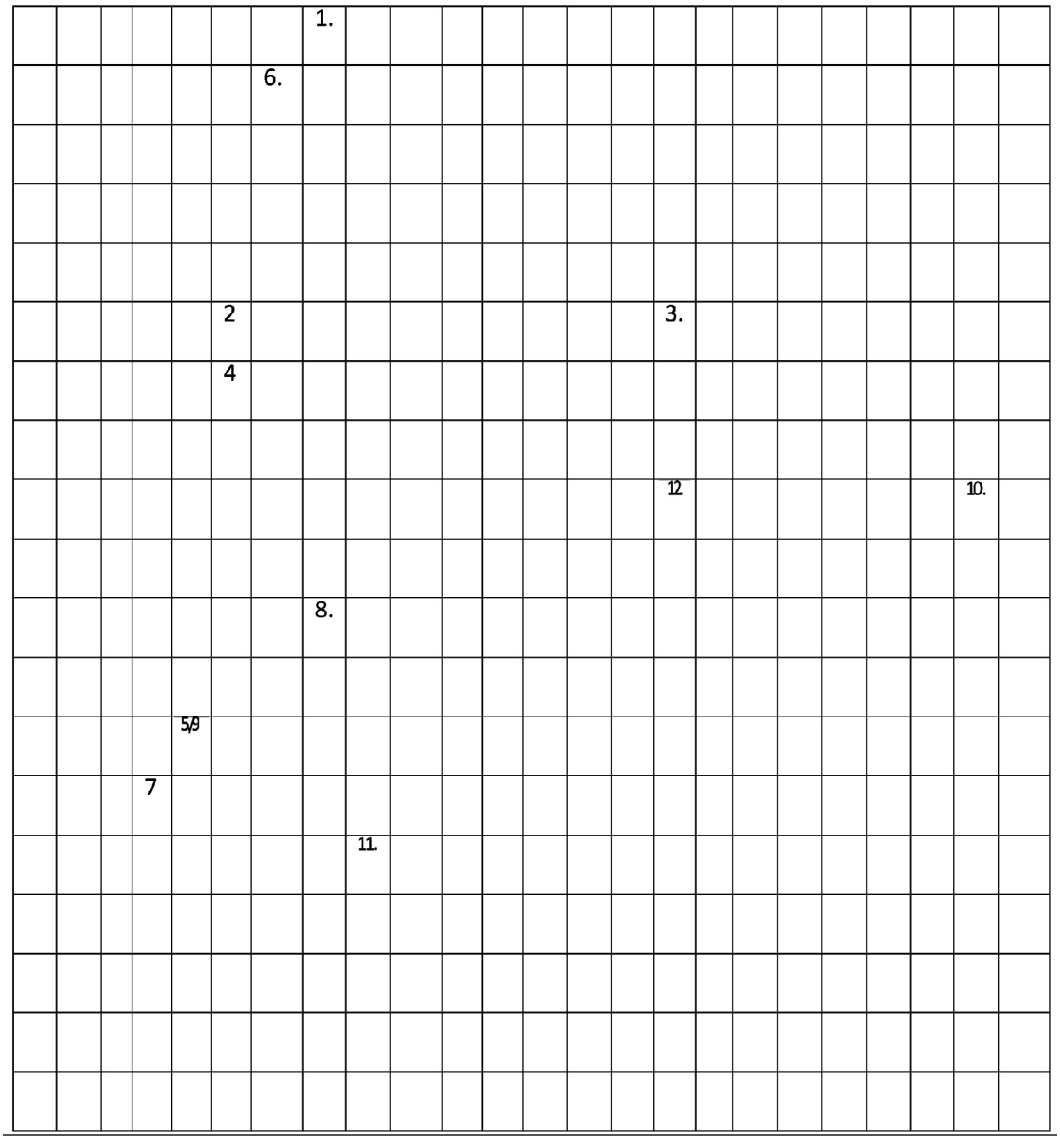
Listed here are the common names of few organic compounds. Find them in the grid below :

CATECHOL HYDROQUINONE RESORCINOL

ASPIRIN GALLIC ACID BENZYNE ATRAZINE

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

Chemistry Crossword



HINTS

Processes involved in Metallurgy

1. Extraction of Nickel with CO (DOWN)
2. Removal of Zn and Pb from Gold (ACROSS)
3. Removal of Lead (DOWN)

4. Production of ti from $TiCl_4$ (ACROSS)
5. Purification of Iron (ACROSS)
6. Ore heated in presence of air to remove impurities (ACROSS)
7. Ore heated in absence of air to remove volatile impurities (ACROSS)
8. Production of metal from ore (ACROSS : BACKWARDS)
9. Ore of aluminium (DOWN)
10. Ore of Silver (DOWN)
11. Separation process for cleaning suspension (ACROSS)
12. Diagram representing  G with Temperature (ACROSS)

N.B. Please send the answer to The Editor, 'The Chemical Axis', Department of Chemistry, B. Borooah College, Guwahati, Assam - 781007 on or before 05-03-2022

E-mail : thechemicalaxis@gmail.com

Any suggestion regarding the improvement of 'The Chemical Axis' will be solicited. Please send your suggestion to The Editor, 'The Chemical Axis', Department of Chemistry, B. Borooah College, Guwahati, Assam-781007.

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CHEMICAL FORUM

B. Borooah College
Guwahati - 7

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3. Address for correspondence :

4. Phone No. / Fax No./ e-mail :
5. Permanent Address :

6. Present Occupation :
7. Period of study :
8. Course of study (PG/UG/HS) :
9. Any suggestion regarding development of the Forum :

Date :
Place : Signature

N.B.

		Registration	Rs. 100.00
•	Registration Fees :	Life member	Rs. 2000.00
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- Fees should be preferably paid in cash/ cheque, drawn in favour of Chemical forum, B. Borooah College, payable at SBI, Chenikuthi Branch.

IDEA BEHIND THE *Chemical Forum*

- *To bring teachers and students to a single plat form including ex-teachers and ex-students.*
- *To develop the creative instinct of the students by various activities.*
- *To make necessary arrangement for beneficiary programme for the students.*

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