

Advances in Aflatoxin B₁ detection in food commodities:

An adventurous story of devil Aflatoxin B₁ and detective Aptamer

Here, Let's start the story of Aflatoxin in his own words.

My introductory

Hello everyone; I am **Aflatoxin B₁**. You don't know who I am? Cool, I know you don't know about **me** and **my family**. Me and my siblings are very **powerful**, but you know what? I am the **most dangerous** and **deadly one**. I can move everywhere in your food, like in your agricultural crops, your dried fruits, your storage food, and I can even survive in your cooked food also, and finally, I move into your body and cause **liver cancer**. Now, let me tell you my exciting story.

My family and household

So, my parents are *Aspergillus flavus* and *Aspergillus parasiticus*, and my siblings are **Aflatoxin B₂**, **G₁**, **G₂**, **M₁**, and **Aflatoxin M₂**, etc. So, as I told you, we all live in all over the world and grow in various agricultural crops and love to live in warm and humid climates and survive in your food commodities at every stage, like before harvesting, after harvesting, storing as well as food processing. When your lovely domestic animals feed their food, my brothers Aflatoxin M₁ and Aflatoxin M₂ pass in your **milk, egg, meat**, etc.

My escaping looks

I am the most harmful carcinogenic, teratogenic, and immunosuppressive toxin for all kinds of animals like **poultry, trout, cattle**, and **rats** in every stage of life, but in you (**humans**), my toxicity level is extreme. In your body, I can move in every organ, but my first and foremost target is your loving "**Liver**," where my mechanism of action initiates. In your liver, I change my look from one chemical form to another form in multiple times and bind to biomolecules like DNA and protein.

So, in your liver, At First, I meet with an innocent enzyme **Cytochrome P450**, and with his help, I Convert into my most reactive and genotoxic form AFB₁-exo-8,9-epoxide (AFBO). After that, I bind to your liver cell DNA and change my look in DNA adduct. If your DNA repairing process cannot repair my this form before DNA replication, I start interacting with

the **Guanine** base of the DNA and start causing a mutation in the **p53 tumor suppressor gene** and become responsible for liver cancer:) Ultimately, I fulfill my job.

Apart from this, I have another way to cause toxicity in your liver. My **AFBO** form is also converted into **AFB₁-8,9-diol** that binds to the **lysine** amino acid of your **Albumin** protein and forms **lysine adducts** and finally causes **hepatotoxicity**, which increases the risk of liver cancer in the presence of **hepatitis viruses**.

Now you understand me; I'm not going to leave you and your food without causing liver cancer to all of you... **ha ha ha...**

My limitations in your food and feed

I have contaminated your food during plantation, crop maturation, harvesting, and storage. To prevent my toxicity and carcinogenicity, the government of various countries set my maximum permissible limit in food. According to the government of **European countries**, the maximum permitted limit in foods and feeds set to **2 ppb** for me and **4 ppb** for us (total aflatoxins). In **India**, our (total aflatoxins) maximum permitted limit is **4-30 ppb** in food commodities and **0.5 ppb** in milk.

Current detection techniques for recognizing me

I am very small in size, so it isn't easy to detect me. Although, this is very serious for you to ensure your food safety. Consequently, your researchers developed several conventional analytical techniques for the detection of me and my siblings, such as Thin Layer Chromatography, Gas Chromatography, High-Performance Liquid Chromatography, Mass spectrometry, etc., but all these techniques are very expensive and laborious, so all of you are not able to recognize me by using these techniques.

Meanwhile, some of your researcher friends also developed some antibodies-based techniques for determining me, like Radioimmunoassay, Enzyme-linked immunosorbent assay, Immuno-dipstick assays, Immunosensors, etc. Moreover, these all also have some disadvantages for you, like high cost, required skilled persons, and some are still laborious.

So now, you are not fully capable of defeating me because your various developing countries are still poor and cannot afford these techniques for my recognition and quantification. So, I am very happy and enjoying my life in several countries all over the world.

My new enemy, “Aptamer,” coming to destroy my life

As I wrote above.. My life was perfect. I was very happy because I enjoyed my work and my work of contaminating your food was going well. But.. we all know that life is all about ups and downs, and this time, the down part came into my life as an enemy to destroy my plan and me. Huh..!... **Awwwwwww.... Noooooooooo...**

To overcome the limitations of conventional techniques and to remove me from my house, **researchers** from **IIT Delhi** discovered a new diagnostic tool that is called “**Aptamer**,” a single-stranded oligonucleotide (DNA or RNA). He is very smart and intelligent, folds himself in a **3-dimensional conformation**, and binds to their **target** with high affinity and specificity. The Aptamer has all good features, like antibodies. Also, it has more advantages over antibodies, like very low cost, easily modified, reused properties, high stability in every temperature, etc. He is a non-immunogenic and non-toxic compound in *in vivo* conditions.

My Jobless future

Due to numerous advantages, Aptamer is now becoming a “**Superhero**” for all of you. Reserchers are now designing a **new onsite detection assay** for recognition and quantification of me by using Aptamer as a **diagnostic probe** which is cost-effective and easy to use by **laymen** also.

Huh..!! Now, I am very scared and counting back.. because in future, you are going to remove me from your food, and I am afraid that I am no longer capable of causing liver cancer in you.

Maybe in future, I will become **homeless** and **jobless**.... You are going to make me cry... Oh God Why Life is so hard..... **sob**

India's Solar Success with Cleaner Air: A Candid Conversation

Newspaper and my curious nephew

It was a Sunday morning, 7 o'clock. A sudden shout woke me up: "Uncle, your name is on the newspaper; come see." I couldn't believe myself. Still, I entered the living room hesitantly. Meanwhile, Bodh, my curious nephew had taken the newspaper from my father and shown it to me.

The line "... a study carried out in IIT Delhi" appeared before my eyes. That was an amazing day, and my research transcended the confines of the laboratory and reached to society.

It was 8:30 in the morning. I was in a hurry to have breakfast.

Before I left for the lab, Bodh exclaimed, "Why don't you have a holiday?"

To avoid his sincere objection, I proposed, "Okay, let's come with me today." He was excited, as I could see.

On our way to IIT, he asked, "Uncle, what are you doing at IIT Delhi that brings you to the lab even on Sunday?"

I replied, "I am doing PhD and re-searching how air pollution impacts India's solar energy goals."

He looked at me and asked with fervent interest, "How does it go, and why are you finding these questions?"

Before responding, I recalled Sir Mark Walport's sayings, "*Science is not finished until it is communicated,*" and decided to share my PhD journey with him.

"Let me tell you how all these started.", I replied.

Photo shoot to Photovoltaic: My Eureka Moment

It was mid-March of 2019; my supervisor had organised a workshop on atmospheric monitoring. After the training, we gathered on the roof for a group photo with various monitoring instruments. Suddenly, my colleague found a dusty spot on my shirt and pointed to

the dusted solar panels. I was upset and we were discussing what steps we should take to clean the panel. After a while, my supervisor called me into his room.

"What were you talking about the dusted solar panels?", Professor inquired.
"No sir. It was a casual discussion," I quickly replied.

However, he clarified that he had overheard our discussion and questioned, "Could we estimate the loss a photovoltaic panel experiences due to dust? What do you think?"
"Certainly!" I nodded.

"A photoshoot to photovoltaic. What a remarkable start!" Bodh cheered.

Looking at his face, I asked, "Are you familiar with $PM_{2.5}$?"

"Yes, but it will be great if you could explain briefly," Bodh responded.

"Sure! $PM_{2.5}$ are fine particulate matters of diameter 2.5-micron suspended in the air. However, these particulate matters can be coarser also, depending on their diameters. Particulate matters are also known as aerosols.", I replied.

"Understand," Bodh concurred.

"This is not the end. These tiny particles can enter our lungs, increasing the risk of cardiovascular disease. You often hear about the poor air quality in Delhi," I added.

"Yes, our school declares holidays on pollution days," Bodh said, annoyed.

"Let me tell you the impact of aerosols on photovoltaic panels," I stated.

"What is that?" Bodh inquired.

Aerosols: Casting Shadows on Solar Potential

"Aerosols block incoming radiation either by absorption or scattering. I am sure you are familiar with these two terms from your textbook", I said.

"Hmm," Bodh nodded.

"As a result, solar panels installed in the ground or on roof receive less solar energy than intended; even some coarse-sized particles are often deposited over the panel surfaces," I explained.

“Scientists call the first phenomenon as "atmospheric attenuation,” and latter one as “soiling effect,” I continued.

"Wonderful! Soiling was the culprit for you”, Bodh related with confidence. Further he asked, “But where does this aerosol come from?"

“They originate from human activities (such as household emissions, fumes from industries, vehicle exhaust, and road dust) and natural processes (like forest fire, desert dust),” I elucidated.

"But how can you measure them?" Bodh wondered.

"I relied on satellite remote sensing and in-situ measurements," I replied.

"Why do you need satellite remote sensing?" he inquired.

“Satellite provides data at global scale. Initially, we focused on Delhi, but aerosol pollution and its impact on photovoltaics are global issues, especially in Southeast Asia. So, we started focusing on Indian subcontinent," I said.

Bodh nodded his head and asked, “What do you find from all your analysis?”.

"Well! If the daily solar radiation is greater than 5 kWh/m², panel works effectively. Our finding says 60% of India's land is suitable for that. However, air pollution costs to \$245-835 million loss in generation. But, if India had avoided air pollution, it could have emerged with 89% of its regions suitable for efficient photovoltaic electricity, enhancing its resources by 29%," I stated.

“Wow! But how do we clean our atmosphere?”, Bodh’s pondered.

"For cleaner atmosphere, air pollution mitigation is must. Our research shows implementing clean air policies (*Pradhan Mantri Ujjwala Yojana* and the *National Clean Air Programme*) not only improves human health by reducing air pollution but also boosts solar energy, yielding \$325-845 million annually, equivalent to the policies' budget," I stated.

“Commendable!”, Bodh exclaimed.

Meanwhile, we reached the IIT metro station. On the way to the lab, he asked, “Does the cleaner air help to achieve India’s 100 GW solar target?”

“Yes indeed. Our analysis suggests that India could achieve its solar goal on time if current installation continue along with air pollution mitigation," I responded.

Immediately, Bodh questioned, “How?”

“Under polluted conditions, solar panels generate less electricity. However, in a clean atmosphere, the same panels can produce more. We estimate that with 76 GW of capacity and effective clean air policies, India could generate as much electricity as 100 GW does. This would save the cost of an additional 24 GW installation," I responded.

“One last question. What do you think about cleaner air and clean energy?” Bodh asked.

"We need a Memorandum of Understanding (MoU) between clean air and clean energy", I concluded.

We arrived at the lab, everyone welcomed him and showed our experimental solar panels.

“Thank you for Scientific Sunday," Bodh greeted, with a smile.

Guardian of the Fields: How Tiny Techies revolutionizing the agriculture

Do plants feel unwell?

As everyone knows, Plants are the significant foundation of our existence; they provide us oxygen and daily calorie requirements. However, this crucial ecosystem is in danger, and much is at stake. By 2050, with the population rising, world food production must increase by 50% just to keep pace with our needs. Surprisingly, in spite of developments, hunger persists, with the number of people affected rises from 811 million in 2020 to 828 million in 2021. Even more alarming is the silent battle going on in our fields. Plant diseases destroy about 40% of the crops cultivated worldwide annually. Thus, yes. **"Plants also gets sick"**, just like us.

But exactly how terrible is the situation? As it turns out, plant diseases cost us a huge \$220 billion worth of crops in 2019. And by 2021, the number had increased even more, to \$250 billion (as reported by FAO). This massive loss shows the constant **fight for survival** within the complex ecosystem, where pathogens adapt and evolve with the host plants. Coming from a family of an agricultural background, I always had an overwhelming sense of connection to the land and an in-depth awareness of the need to protect our crops. The year 2019–20 had been rough. The COVID-19 pandemic showed how uncertain existence can be, and the **locust attack** on the fields threatened food security globally, including India. Regardless of the struggle, plants and pathogens have managed to establish a delicate balance for millions of years. We were mesmerised by the complex interface that kept life going on in the fields. It was evident that by exploiting the underlying equilibrium between infection and defense mechanisms, a strategy could be devised to protect crops. Furthermore, **Power dynamics** can be seen in plant pathogen coaction wherein the ability of either of the two actors to influence the outcome of their interaction is hidden. As everyone knows, **no fair battle exists** in the ecosystem, so we had to be strategic to exploit limitations and strengths to build on.

As we explored further into the realm of plant infection and defences, we discovered a plethora of potent molecules called **bioactive agents**, which plants employ to protect themselves against pathogens. But the hegemonic nature of highly virulent pathogens gain control over the plant defences via hijacking their immune systems, thus limiting the production of these biomolecules. Therefore, providing the plants with these bioactive agents externally, can arm plants with **nature's own weapons** against plant pathogens, highlights the transformative impact of nature-inspired solutions in revolutionizing plant disease management practices.

Though, there was a disclaimer: effectively delivering these biomolecules to plants presented a difficult challenge. Our attempts have been shackled by the plant cell wall, which serves as a hard barrier. In addition to the aforementioned challenges, the plant cuticle, which acts like a raincoat, prevents biomolecules to stick on the plant surfaces, further complicating our objective. But the pursuit to use the potential of plant defences persisted, driven by an urgent need to protect crops against constantly evolving pathogens.

In our quest, we found **Nanotechnology** as an ally. These tiny techies empowered us with the efficient delivery carriers for bioactive agents, increasing their ability to cross the plant cell wall and dispensing the cargo precisely to the **core of the infection**. Moreover, the future of

sustainable agriculture depends on genetic modification. As many plant species that we eat everyday such as rice, wheat, or maize, are very challenging to transform. Despite their important role in feeding the global population, they remain resistive to our most attempts to improve them for their disease resistance, productivity, and ability to adapt to changing climates. Innovative nanoparticle approaches improve delivery by altering size, surface properties, and adhesion capacity depending upon plant species and infection severity.

Though, our adventure does not stop here. What's waiting for us tomorrow? Oh, the possibilities are infinite! Imagine growing plants that can fight off diseases or refining their nutrient profiles. It's like entering into a brand-new era of agriculture where **sustainability, innovation, and abundance** taking centre stage.

So next time you enjoy a tangy salad or the sweetness of a ripened banana, remember the undercover agents that work nonstop behind the scenes 24/7 for the set of flavours dancing on your taste buds.

Together, we protect our plants, paving the way for a green and sustainable tomorrow,

A gift for our future generations, a promise of prosperity that knows no sorrow.

Metal Air Batteries: The Catalyst of Change and Curiosity

Gone were the days when lighting a Diya with water seemed miraculous. Who could have imagined that water could be used as fuel to power cars? From the tiny button batteries found in hearing aids and watches, to the high energy ones in phones and E-rickshaws to the powerful ones in the generators, these devices are the topic of interest in my laboratory. Yes, being a Ph.D. student, I am in a habit of explaining my work to the experts in the field through seminars and presentations. However, whenever asked by my family I always end up just saying, “I work on battery technology”. Once, on the festival of Diwali my whole family was gathered at our home for the *Diwali Poojan* followed by a family dinner. During the dinner, once again the topic of my research came and as always, I vaguely replied about my work. But this time, a series of questions were waiting for me.

“Oh, Batteries! My phone’s battery discharges very fast. Do you know what I can do about it?”, my mother asked. I replied, “No Mom, I don’t work on the phone batteries. “So, do you work on the ones in the remote control?”, enquired my mother. “No Mom, it’s the metal-air battery I work on. It’s different than the conventional Lithium-ion battery in phones and the dry cells in remote controls. It was first developed in 1970s and uses the oxygen from the air to generate the energy and has much higher potential than the generally used ion batteries.”

“Better than the ones being used? then why aren’t we using them instead of the Li-ion batteries?” Asked my father curiously. “Because their efficiency is still low because of the slow chemical reactions. The metal air batteries have a metal anode (like zinc or lithium) and an air cathode. When the metal reacted with oxygen from the air, it produced electricity. But this reaction of oxygen is very slow, hence a suitable catalyst material (a substance that speeds up a chemical reaction) is needed. The existing materials such as Platinum have high cost and low durability that increases the cost of these devices 10 folds than the conventional batteries. That is why their commercialisation is still a hurdle. My work is to find a cheap and stable material to catalyze the oxygen reduction process in these batteries.”

“It sounds quite interesting, using the oxygen from the air just as we breathe in oxygen and energy is produced. But how would we be able to recharge them?” asked my mother. “This is indeed one of the problems with this battery. To recharge them the water in the electrolyte has to be split to form oxygen. It’s like breaking the H_2O in water to H_2 and O_2 using the electrical energy. But this process is again very slow and requires a catalyst. The bigger problem is that a single catalyst is difficult to catalyze both oxygen reduction and oxygen evolution reactions during the discharging and charging of a metal-air battery. Thus, my next goal of the thesis is to develop a material in my lab which can catalyze both the reactions with equal efficiency.”

My uncle who was listening to the conversation silently suddenly asked “So, how far is your progress? Have you found a material yet?” “Yes, Uncle and the material is very old and well known. It is called as Prussian Blue; it was found in the 18th century and introduced the world with the blue indigo (royal blue) colour for dyeing clothes and making paints. I read about it and found the suitable structural and chemical properties for the battery application. In addition, the material is low in cost and shows promising results in catalyzing the reactions. Though previously used for other applications, it was still unexplored in the oxygen electrocatalysis field. By using various strategies, I have optimised the property of Prussian

Blue material and found the enhanced activity and have even published my results in journal and presented my work at an international conference in Germany.” I explained in detail.

“This seems great *beta*”, chuckled my mother and continued, “Do you mean in future, we can use these batteries in cars and other big devices?”

“This is the question we all are trying to find the answer to Mother” I said, everyone started laughing. I continued, “With the advancement in Science, I believe we would be able to achieve this in future. Electric vehicles powered by these batteries could travel much farther on a single charge, reducing the need for frequent recharging and making them more practical for everyday use. Moreover, the environmental benefits will be significant. As metal-air batteries became more prevalent, they could help decrease reliance on fossil fuels, reduce greenhouse gas emissions, and combat climate change. Their role in renewable energy storage further supported a cleaner, more sustainable energy infrastructure.”

The Power of captain of death: RNA regulation, a promising target

Around 3 million years ago, Humans evolved from Australopithecus. This story began to unfold in late 1974 in Ethiopia when the skeleton of a Hominin, Lucy, was discovered. Of course, the TB-causing *Mycobacterium tuberculosis* (MTB) was also evolving. It has been immortal since then and has maintained its fame in the history of a devastating human disease known as *Consumption or Great White Plague*, or “**Captain of all these men of death.**”

Initially friendly but humble, living peacefully inside the lungs without harming our ancestors. Long co-evolution resulted in a brilliant, powerful, and successful bacterial pathogen nobody knew until 1882. An estimated 30% of the world’s population carries inactive MTB, which can cause a disease on reactivation. According to the WHO Global TB Report, there were 1.5 million deaths and over 10 million new cases last year. Currently, MTB drug resistance and co-occurrence with HIV are significant issues. That’s why TB is a major public health problem and the leading cause of death worldwide.

One day in 1905, Robert Koch got the Nobel Prize for MTB discovery on 24 March 1882, celebrated as World’s TB Day. He smartly caught the **bacteria** and understood its hide-seek game. He collected some clues about infectious diseases spreading among humans by coughing and sneezing, resulting in chest pain, weight loss, fever, night sweats, and chills. Our body’s immune system treats an invader. Bacteria are encountered by eater cells called Macrophages, while virus neutralization is the task of T-cells. MTB prefers to live in the lungs (pulmonary) and other organs (extrapulmonary) like the brain, kidney, and spine. This greedy guy doesn’t want to spare any part. Scientists became alert after knowing the intentions of MTB **hiding inside macrophages.**

Since 1921, the BCG vaccine has been given to infants where TB is more common. Still, there was no proper treatment for TB in adults. In 1943, Hope was enlightened with the discovery of streptomycin to defeat TB—a cocktail of 4 antibiotics: Isoniazid, Pyrazinamide, Ethambutol, and Rifampin was approved for 6-9 months. *But fools always start celebrating before winning! TB patients skip the pills once they feel good and encourage the MTB to pump out all drugs in the meantime. ‘One that doesn’t kill you makes you stronger’. MTB has come back as more powerful and ready for justice. Even scientists made the mistake of digging potholes in its way; clever MTB took the longest jump in its style to become multi, i.e., MDR or extreme drug resistant, XDR with time. It successfully established the condition where drugs are not effective at all.*

In this MDR/XDR establishment, However, all drugs in the market can only target protein synthesis, not RNA (ribonucleic acid). DosR and PhoP serve as MTB Trojan horses. Our research mainly focuses on these significant bodyguards and lifesaver proteins for MTB. Their primary role is to bind DNA and control the production of **small regulatory RNA (sRNA)**, which is only found in disease-causing mycobacteria, essential to its survival, i.e., adaptation, reactivation, and causing the disease. **sRNA production leads to MTB entering an inactive, dormant state** where it is immortal, and nobody can harm it. *Still, MTB was enjoying the supreme life, knowing people were scared. However, one day, MTB was surprised while browsing its favorite Times magazine, which covered recent RNA research highlights. Researchers have been able to dig out the secrets of the detoxification of reactive oxygen species, and they have already gained pace by publishing their research in science journals to spread awareness.*

MTB: Let's not overthink; they will not be able to kill me. I'm immortal!"

The king MTB was still enjoying the high status but was bothered by the questions of other MTBs... "Highness! Humans know DosR-regulated sRNA. What will happen now? We will die..."

King replied, "There is nothing to worry about. PhoP..., works better under acid.

However, after a few years, again reading TB magazine "FEBS Research," the sky collapsed when MTB got the news that his confidential information had been leaked and was used against it. Researchers have isolated its genomic DNA, made copies using a PCR machine, and purified DosR and PhoP in the lab.

In research, there have been numerous cutting-edge advancements. We have taken a biochemical approach to investigate how DosR controls the sRNA biosynthesis. We performed point mutations to find out if the sRNA gene differs from protein-encoding genes!

- Since MTB DNA has two regions (boxes), DosR can bind even after weak DosR box deletion or mutating 3-4 nucleotides within the strong proximal box.

We also investigated whether PhoP, which is responsible for MTB virulence, interacts with MTS1338!

- We identified that DosR can bind to the DNA. Although PhoP did not directly bind, binds to the DosR-bound DNA. This study substantially highlights the regulation of MTS1338 expression in *Mycobacterium tuberculosis* and helps design novel drugs that can target the sRNA promoter, specifically, to kill and eradicate MTB.

We learned about the trump card of the MTB: the **saver sRNA is regulated by DosR and PhoP**. MTB regretted his old days as the "*Captain of death*." But why? Scientists are especially researching RNA targets for small RNA regulation. MTS1338, *Mycobacterium tuberculosis* small RNA, is required to survive during the infection to counter macrophages. It works as an **energy-saver** by inhibiting protein synthesis and degrading non-essential RNA. *MTB's end is very near; already, MTB had a headache with the Government's TB eradication programs!* MTB was able to manage protein-inhibitory antibiotics, but we continued to spy on him, and his savers were well-reported. Unsure of what to do! MTB feels hopeless. RNA Biologists are dedicated to finding RNA regulation by growing MTB cells in the lab and studying their effects on mouse infection models. I think the researchers won't remain silent until they have killed MTB. But for now, All I can say is, 'Eat good, Exercise more, and Stay Healthy!'

Moral: TB will remain Dormant if Human immune system is robust.

"Discussing Cancer Research Over Ice Cream with My Curious Sister"

On a hot summer evening, me and my sister, an 8th grader, went for an ice cream stroll. She jumped and asked me, "Appi" (used to address elder sister), "What are you working on in your PhD?"

Me: I told her, "I use spatial transcriptomics to understand lung cancer pathogenesis."

Her: English, please!

Me: I laughed and asked her, "What will you get if you put a car in a giant blender?"

Her: Mostly metal

Me: Exactly, I go on to explain, 'So, when a person is diagnosed with cancer, usually a biopsy is done.

She interrupts and says, "What is a biopsy?"

Me: It is just cutting and taking out some part of the cancer tissue to characterize the type of cancer, what stage it is, what treatments to give, etc. Now, the techniques we currently use to understand cancer tell us the average composition of the cancer tissue. Like in the case of a car, you can only tell that metal would be found. Currently, the techniques just blend the cancer tissue.

Her: But I read in my textbook that tissues are made of different types of cells. How will you know what type of cells are there if you just blend them up? For example, how will you know if a car has engines, wheels, doors, and seats if you just grind it? She smirks and asks "Are you even sure of what you are doing?"

I look at her with an understated pride in my eyes!

Me: Interesting question! To understand the cell type composition in the cancer tissue, researchers are currently using a technique called single-cell transcriptomics where you dissociate the tissue cell by cell. This allows them to tell the cell types present in the tissue.

Her: What will you benefit from it?

Me: For example, we can tell if the cancer tissue has B-cells, T killer cells, T helper cells, Macrophages, NK cells, etc. All these cells fight against cancer. There are many cases where some crucial cells might be absent! Such a discovery helps in decoding what is lacking in a patient's defense against cancer.

Her: But every cell looks like muscle only. How do you know what cell type it is?

I laugh out loud and say, “You’re absolutely right”. To label a cell type, we do ‘transcriptomics’- that is, we sequence genes active in a cell type to know what cell it is. To understand better, all cells in our body have the same DNA, but our heart is different from our lungs, kidneys, liver, etc that is because there is a specific set of genes active in various cells that make different organs.

Her: Interesting! She rolls her eyes and says, “But you haven’t come to the point yet! Is this what you work on?”

Me: Partly, yes. I use single-cell transcriptomics but majorly use spatial transcriptomics to investigate cancer. I ask her, “ Now you know that if you blend a car- you get metal. If you get the dissected car pieces one by one, you will know about the different car components, that is, the different cell types in the cancer tissue. But what are you still missing?

Her: I think there is nothing left.

Me: No, there is very crucial information left undiscovered yet! I explained to her, "How will you assemble the car? How will you know which part goes where? If you put the brakes in the trunk, the car will malfunction, and accidents might happen. Or if you remove the accelerator, you will be late to reach anywhere!"

Her: Interesting! By that analogy, you are saying you can also tell the location of the cells and their neighbors.

Me: Yes! (Being proud of my work)

Her: She says with eyes sparkling with curious excitement, "My mind is bursting with fireworks right now." But again, you have explained your working technology. But what have you found so far?

Me: So, I have found that in the case of lung adenocarcinoma, which is one of the most commonly found lung cancers in India, the tumour cells are majorly surrounded by cancer-associated fibroblasts (CAFs), which form a mesh-like matrix in the tissue. I also observed that the CAF-enriched microenvironment is also found in the normal tissue adjacent to the cancer (NAT).

Her: Okay, but what is the importance of these CAFs?

Me: CAFs help in tumour invasion to other areas and tumour progression; they work as car accelerators for cancers. But what's really interesting here is that the normal tissue (NAT) is also exhibiting the presence of cancer-associated fibroblasts, which means it's not just the tumour that dictates or controls its invasion to other sites in the body, but the normal tissue in the body might also be helping to do so.

Her: Wow, meaning normal ain't really normal. It's just pretending to look all regular and cool!

Me: Yes! (I smiled, knowing she did not even realise she had given conclusive remarks about my study.)

Her: Okay. I am curious if there are so many lung cancer patients, no one else observed this before you?

Me: Only a few preliminary studies have reported this, and even fewer have observed the presence of CAFs in normal tissue. Numerous independent studies are required to establish a particular finding as a hallmark or marker of cancer. This robust body of evidence is necessary for official bodies like the FDA to approve drugs targeting the reported marker. Ensuring sufficient statistical power is crucial in these studies to validate the findings and support regulatory decisions.

Her: Appi, just one last thing. How will it help doctors?

Me: The doctors can administer therapies and drugs targeting CAFs to improve patient response. Every discovery fuels my hope and commitment to make a difference in people's lives.

Our ice creams had melted, a testament to how engaging our conversation had been. After a brief silence, she suggested we buy another round.

Optimum Design of Hybrid Vibration Control Systems for Lifeline Structures Subjected to Earthquakes and Winds

Earthquakes are dangerous: a 7.2-magnitude earthquake occurred in Taiwan this April, strongest in 25 years, claiming at least nine human lives (source: CNN news report). Twenty days later, 200 aftershocks to that earthquake followed, which were not that strong however people experienced the tremors throughout the night. This is indeed worrisome because in India, the only earthquake over magnitude 7 occurred on January 26th, 2001, almost 24 years ago. The 7.7-magnitude Bhuj earthquake in 2001 claimed almost 25,000 human lives, a million people were left homeless (source: BBC news report). Needless to mention, the devastation to the society from such an event was enormous at those times. Post the Bhuj earthquake, infrastructure in India has improved considerably. Now, the building design standards (codes of practice) have been developed to incorporate significant earthquake-resistant characteristics in (civil) structures. Therefore, the obvious questions at this stage are: what will be the current consequences of such strong earthquakes in India, and what more is required to ensure adequate safety of people and also the civil infrastructure against these disastrous earthquakes? Globally, civil infrastructure has become much more resilient to earthquakes, especially in regions of high seismicity. India, being not so prone to severe earthquakes, has been slow in adopting the state-of-the-art technologies to protect structures from earthquakes, however the current building standards in India are top-notch and are adequate to ensure human life safety under the strongest of earthquakes. Interestingly, my PhD research is regarding the second question, i.e., what further needs to be done, not only in India but also across the world.

To understand the need of the hour with more clarity, let us imagine a scenario where a doctor is performing a critical operation on a patient and an earthquake occurs. Alternatively, think about those physically impaired patients on the eighth floor of a hospital during an earthquake. What should they do under these circumstances, do we expect everybody to vacate the hospital? Under these situations, is it fine to only think about life safety and forget about the hospital building itself or the crucial life-supporting equipment inside it? Obviously no, right? Therefore, we can reach at a consensus that structures of severe importance such as hospitals, bridges, nuclear powerplants, and so on (also known as lifeline structures) must remain functional even during earthquakes. To achieve such supreme performance from structures during earthquakes, conventional civil engineering techniques are not efficient or even practical. Therefore, various vibration control strategies are often implemented to improve the performance of structures under earthquakes.

The major damages to structures under earthquakes arise from relative deformation of the structure in the lateral direction (sway of the structure) and the high acceleration response (vibration) of the structures. Base isolation is a popular vibration control mechanism, wherein flexible rubber-based engineered devices are installed at the ground level under the structures. Essentially, these devices decouple the structure from the ground. This could be easily visualized by imagining a solid block placed on rollers, thus when the ground shakes, the solid block moves like a rigid mass (i.e., without sway) and additionally the vibration experienced by the mass reduces. In fact, more the flexibility of the isolation device, lesser are the structural vibrations. Importantly, the base isolation devices are designed sufficiently to carry the heavy weight of the structure as well as provide flexibility in the lateral movement of the structure. Now, in order to ensure continued functionality in lifeline structures, these base isolation devices naturally need to be extremely flexible. However, very high flexibility of the base isolation devices in turn attracts other complexities. For instance, a structure standing practically on rollers will no doubt move as a rigid block however the movement at the level of the rollers will be too large, and its response to small lateral loads will become pronounced. This is the exact reason why the base-isolated structures become vulnerable to wind excitations too. Interestingly, one tenth of the world's tropical cyclones occur in India, which imply frequent windstorms affecting a significant region across the country.

Therefore, in my doctoral thesis, I have proposed a novel hybrid vibration control device consisting of base isolators and tuned mass dampers (TMDs). TMDs are another genre of vibration control devices which are efficient for tall structures subjected to strong winds. TMDs are basically certain added mass to the structure connected by the means of spring and dashpot systems. TMDs can be visualized as two mass blocks connected in series with springs, whenever the support of the connection shakes, the smaller mass moves extensively absorbing all the vibrations of the larger mass. Thus, the smaller mass here signifies the TMD which absorbs the vibration of the larger mass, i.e., the structure. Notably, the design of this TMD is very crucial for obtaining better performance of the base-isolated structure. Here, the TMD plays a dual role: first, to reduce the excessive base displacement of the base-isolated structure under earthquakes, and second, to diminish the unwanted vibrations of the base-isolated structure under winds. Now, earthquakes and winds are fundamentally different in nature. Therefore, the optimum selection of all the design parameters of the hybrid control system is supremely important, especially because it needs to cater both the hazards, earthquakes and cyclones.

In the first three years of my doctoral study, I have proposed this new hybrid control system. I have numerically tested the performance of the hybrid system on an existing hospital located in New Delhi, India, when the structure is subjected to site-specific earthquake and wind hazards. Further, I have utilized emerging machine-learning based optimization techniques to obtain the design parameters of the hybrid system. Moreover, I plan to experimentally verify the efficacy of the developed hybrid control system. Through my doctoral study, I aim to introduce this state-of-the-art hybrid vibration control system to the civil engineering fraternity; this technology can then be implemented in planned (new) structures, as well as retrofitted in existing (old) structures.

From Nature to Innovation: A Voyage through the Polymer Patterns in Thin Films

I used to assume all great stories had a beginning, middle, and an end. My great PhD adventure however consists of a beginning, plot twists, and surprises, all without an end. As I discovered, research never stops. There will always be more experiments, datasets, and literature to analyse. What I learned, however, is that at some point you just have to sit down and write. That is the hardest part, but it is also where everything comes together. If you do it just right, something good can happen. This story is an account of my floundering in the ocean of research trying to stay afloat and eventually gaining enough confidence that I wouldn't drown in it.

Finding my research topic was easy. Nature's most amazing material science miracles, if we can imitate even a portion of them, will lead to enormous technology advances. Have you ever wondered how lotus leaves slide water droplets off or where butterfly wings get their iridescent colours. I saw these and stepped into the exciting frontier of my research trying to create a patterned thin film that can be used as a scaffold in itself or as a coating to biomedical implants.

I began by reading scholarly articles on patterns and thin films, polymer blends, phase separation and dewetting, not necessarily in the most linear or organised fashion. In the beginning it was mostly random, cautiously reading each article and then gently trying to recreate the process, almost like a newborn stepping into the world for the first time. I read a lot about polymers and thin films made of it which were used seemingly everywhere. Over time, I began wondering, what will happen if instead of just one polymer, I take 2 and mix them together to create a film. Being from a biology background, my mind immediately jumped to the question of how can I use my newfound knowledge in tissue engineering, specifically in bone regeneration. I chose polystyrene and polydimethylsiloxane, both polymers known for their biocompatibility but with very distinct properties to each other. Polystyrene being very biocompatible, non-resorbable and hard, the other, polydimethylsiloxane being non-toxic, elastic, highly flexible. It is said that curiosity killed the cat, however satisfaction brought it back. So, to satiate my curiosity, I mixed these two and lo and behold, I got beautiful landscapes with spiralling columns, widespread islands dotted in a polymer sea, and so much more. With each changing parameter, a new structure was there and it became highly challenging to control how these polymers mix and separate.

I focused on using a technique called spin coating to create these polymer blend films. Spin coating resembles a high-tech pottery wheel where by placing a solution of polymers on a

spinning substrate, centrifugal force spreads the solution evenly, forming a thin film. The speed of spinning and the properties of the polymers determine how they separate and organize themselves within the film.

Early in my experiments, I faced a significant hurdle. The polymers did not always separate in the way I anticipated. Some blends formed uniform films, while others looked like a chaotic jigsaw puzzle. This was not good, I wanted to grow human cells on them, and for that I needed a good surface pattern with a high surface area, having nooks and crannies for little cells to hold on and grow and multiply. It was crucial to achieve controlled phase separation and make the blended films follow a predictable pattern.

This was the height of my frustration. I turned to my supervisor who asked me if I had actually read any of the theory and equations behind the principles of dewetting, phase separation and interfacial engineering. And somehow, in my eagerness to experiment, I had managed to overlook the fundamentals. So, back to my laptop, countless hours of literature and videos and discussions with my supervisor, and slowly, I started understanding my system. I experimented with different polymer combinations, tweaking concentrations, spinning speeds, and temperature. Countless hours spent analysing the films under microscopes, seeking patterns and insights. Slowly but surely, a picture began to form. I discovered that by carefully adjusting the concentrations used in the polymer solution, I could influence the phase separation process. This breakthrough was akin to finding the right recipe in a cookbook—a dash of this, a pinch of that, and voilà! The polymers would separate beautifully, creating a film with distinct, well-defined regions.

These phase-separated films have remarkable potential, especially in the field of biomedical engineering. I have found that these films can enhance the cell growth by more than eight times when compared to the blanks. Such kind of coatings on implants can provide a very effective means for enhancing the recovery of the patients from the trauma. Things such as invisibility cloaks, brain implants etc. that have only existed in science fiction are now being tested in real life.

This story is a journey of not just two polymers mixing and separating and swirling around to create beautiful patterns, it is also a tale of perseverance and curiosity. Each experiment, whether it succeeded or failed, brought new insights and deeper understanding. It reinforced the idea that scientific discovery is not just about the end result, but also about the process—the iterative cycle of questioning, testing, and learning.

Looking back on my research path, I realize that the real worth of scientific discovery is not just the results and innovations but also the never-ending quest for knowledge and new ideas. With their intricate patterns and potential applications, each spin-coated polymer mix film represents the convergence of curiosity and determination. Inspired by the wonders of nature and the possibilities of new technologies, my work shows how research may bridge the gap between imagination and reality and with each experiment and every challenge, we inch closer to a future where today's science fiction becomes tomorrow's everyday reality.