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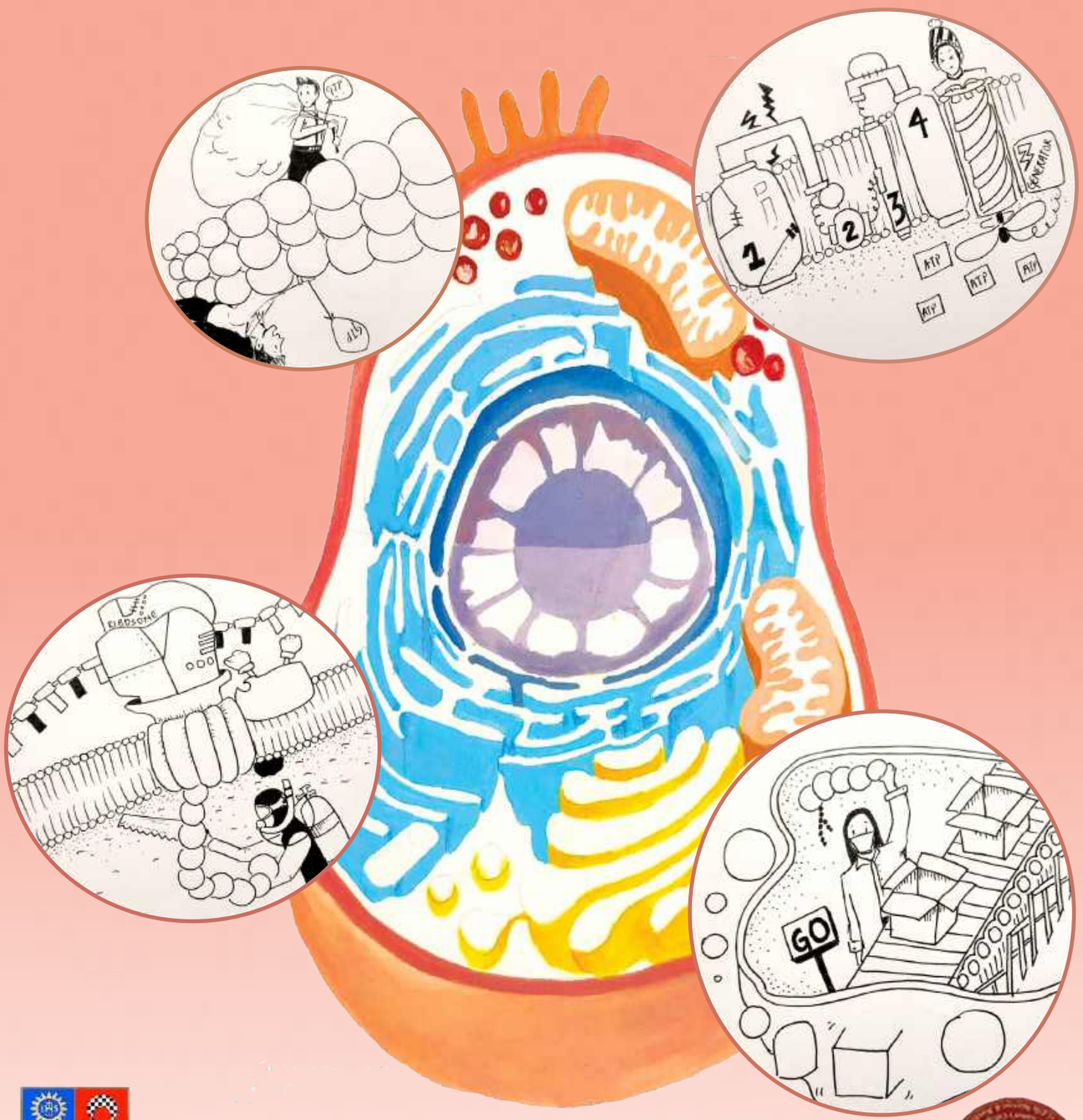
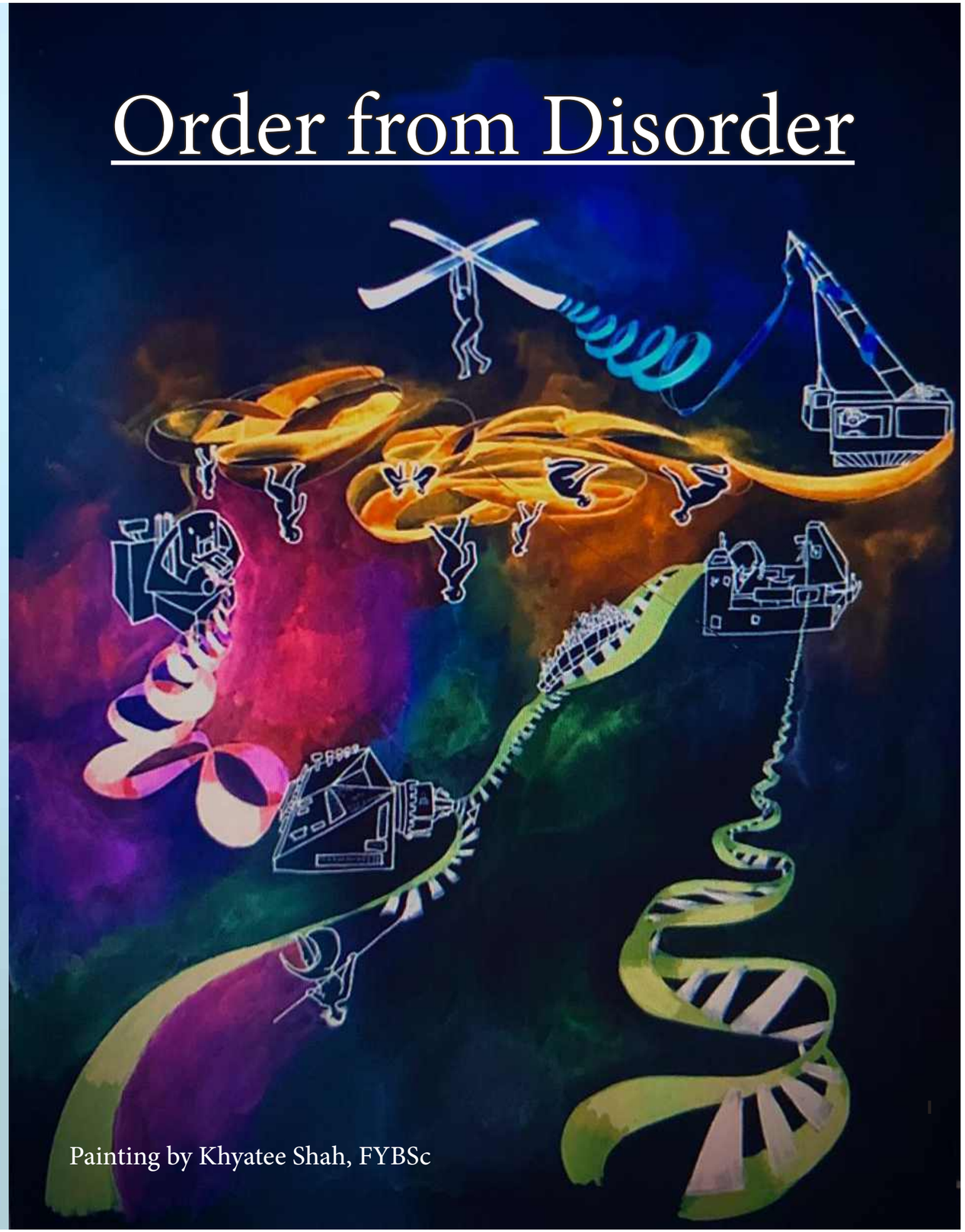
LIGNUM VITAE



The Department Of Life Science and Biochemistry
St.Xavier's College (Autonomous), Mumbai

Order from Disorder



Painting by Khyatee Shah, FYBSc

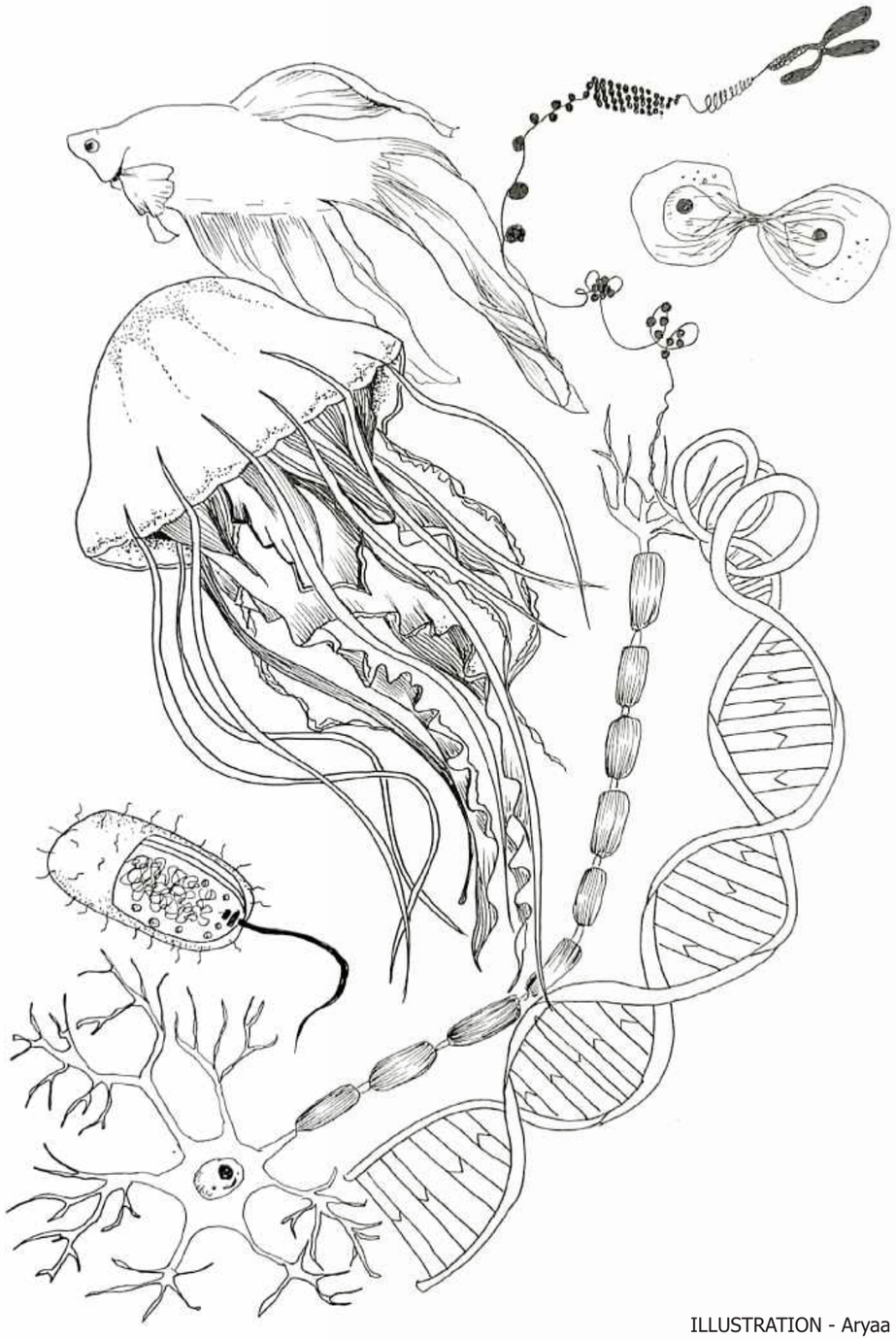


ILLUSTRATION - Aryaa Apotikar

EDITORIAL

All systems have the innate tendency to move towards disorder and yet somehow, every organism on this planet has some level of inbuilt order and predictability in the way it functions. Conventionally, disorder is thought to be the spontaneous degeneration of symmetry – the phenomenon of established systems being wrecked. However, decades of research indicate that it is this disorder that comes together to form precise, ordered and regulated processes for survival.

Every biological system can be considered to be an ensemble of individual microscopic entities-each of which exhibit simple and distinct behaviour- that collectively form a complex and dynamic system. Essentially, these systems arise from the chaotic interplay of a variety of individual units and not from the synchronised behaviour of identical units. Be it evolution, driven by spontaneous mutations, asymmetry during embryonic development, complex neuronal networks or the existence of self-sustaining microbial ecosystems, they all thrive on the disorder in nature. This paradigm of thought has not only provided an impetus to interdisciplinary collaboration, with fields like quantum biology and computational biology gaining rapid popularity, but also encouraged the entire scientific community to conduct research with a more holistic and contextual approach rather than studying phenomena in isolation.

With this year's theme of Lignum Vitae, "Order from Disorder" we intend to explore the importance of inherent disorder at various levels of life, ranging from the biomolecules within a cell to entire ecosystems, along with mathematical and physical perspectives on the same. We are also honoured to have eminent scientists like Dr. Vidita Vaidya and Dr. Maitheryi Narasimha shed light on some of the intricate biological systems described above as well as share with us experiences from their inspirational journeys in science.

Just as none of the systems mentioned above can function in isolation, this magazine too would not have been possible without the efforts of each and every member of the team of Lignum Vitae 2020, the talented writers and the unwavering support and guidance from all the teachers of the Department of Life Science and Biochemistry. I would like to sincerely thank them all for their contributions.

In the words of Erwin Schrodinger, *"The task is not to see what has never been seen before, but to think what has never been thought before about what you see every day."* With this year's issue of Lignum Vitae we hope to have enabled you to think about something you had never before thought of.

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THE ORIGIN OF LIFE AND OUR PLACE IN THE UNIVERSE

-By Hetanshu Bharadiya, SYBSc

"The Earth is a very small stage in a vast cosmic arena."- Carl Sagan

What we call home, is one of eight planets orbiting one of a hundred billion stars in one of a hundred billion galaxies in the observable universe. Despite such unfathomable numbers giving a faint idea of the sheer scale of our universe, it seems to us, as of yet, that our pale blue dot is the only hotspot in this vast cosmic arena to be teeming with life. What do we owe this to? Mere chance? A soupy origin? In 1952, Stanley Miller and Harold Urey bubbled ammonia, methane, hydrogen and water through a tube, sparking the mixture with electricity and heat, replicating conditions similar to that of a primitive Earth. The result was the formation of amino acids, the building blocks of life as we know it. The idea of life originating in such a primordial soup dates back to Charles Darwin, when he considered tracing our origin to "a warm little pond". A more fitting approach to deducing the origin of life is by starting at defining life itself.

The Second Law of Thermodynamics says that the universe works to maximise entropy, maximise disorder. Matter and energy are inching towards equilibrium. But life, even at its most primitive, is so intricate, so complex. Erwin Schrödinger described life as "matter evading decay to equilibrium." In the words of the former president of Czechoslovakia, Vaclav Havel, it would appear that the birth of order from disorder seems inevitable; "Just as the constant increase of entropy is the basic law of the universe, so it is the basic law of life to be ever more highly structured and to struggle against entropy,'' Factoring that with evolution, it could be said that life consists of matter working to avoid disorder, where molecules of information in a closed system, evolve by natural selection.

In this approach towards defining life in a universe prone to increasing disorder and chaos, the high complexity and order we observe in life may be a necessity demanded by the laws of physics themselves; birth of order from disorder, so to speak. This tendency of particles in the universe to orient themselves in random, disordered arrangements, that is, to be in a high entropy state, starkly contrasts the ever increasing complexity in our biological systems, which is, to be in a low entropy state. Now, life has very low entropy, because the structures we observe are extremely intricate, ordered, non-random. Inside a single cell, there are 6 billion base pairs of nucleotides unpacking, transcribing, and splicing this data stored in the DNA to maintain the functioning of life. How can life head towards states of decreasing entropy, as is evident in the form of evolution, while the universe supposedly heads towards a state of increasing entropy? The Second Law of Thermodynamics appears to be violated here. This seeming Catch-22 situation can be avoided by looking at the statement of the Second Law itself. It states that the total entropy of an isolated system increases over time. An isolated system is that which is unable to exchange energy with the outside environment. But it would be incorrect to call living organisms as closed systems, given our interaction with the environment. Life may act to reduce its own entropy, but it increases the entropy of its surroundings, just like what is observed in a refrigerator. Case in point: thermal radiation. Thermal radiation is one of the most random forms of energy dissipation. Absorption of low entropy UV light and emission of high entropy infrared light, by living matter is an example of the same. Self replication leads to more randomisation of the environment, thereby increasing the entropy of the surroundings, just in accordance with the Second Law of Thermodynamics. As the universe approaches a higher entropy state from a lower entropy state, substructure develops. Substructure of high complexity, that is life, ultimately serves to increase entropy. Life feeds on energy gradients, the flow of energy from its higher density to lower density.

This would help pinpoint the hotspots on the planet where life could have originated, be it tidal pools, deep sea hydrothermal vents or polar ice caps. These hotspots have steep energy gradients. The flow of energy from higher density to lower density sparks chemical reactions that go on to form increasingly complex molecules, until equilibrium is reached. In large reservoirs of energy like the ocean, for example, equilibrium is never reached, (which is to say, it takes indefinitely long to reach equilibrium), and complexity goes on increasing as a byproduct of the system redistributing the gradient in energy. This is followed by self catalysing molecules, and the process of self replication initiates. Evolution takes over, and you eventually, ultimately end up having life.

This leads to the speculation of whether such an approach can be employed to find life elsewhere. This could also lead to a possibility that our so apparently Earthly origins might not be so Earthly after all, in a theory known as panspermia. Could this idea, that life originates at pools of steep thermal gradients, with large energy reservoirs, help pinpoint extraterrestrial hotspots that could potentially harbour life and be the answer to "Are We Alone In The Universe?", and as a result make us understand our place in this vast cosmic arena? This helps narrow down the region of interest to such hotspots like water. Water on Mars is a good place to start. Other non-planetary, possibly habitable extraterrestrial bodies like the Jovian and Saturnian satellites could be another place to look for life. Despite being so far away from the sun, these moons undergo tremendous frictional tidal forces, leading to water plumes on moons like Europa, and Enceladus, and enormous pools of liquid methane on Titan. These are clues for searching for extraterrestrial life just within our solar system. Taking into account the billions of star systems, within the billions of galaxies in our observable universe, it wouldn't be incorrect to assume that such large energy reservoirs with steep energy gradients could exist elsewhere, where life, in whatever form it may be, could exist, may have existed in the past, or might exist in the future. Life elsewhere may not necessarily even be carbon based, and might not even appear to us as we know it. However, the question is, what are the odds of encountering extraterrestrial life? The famous Drake's Equation tackles exactly that. The variables in the equation are quite abstract and even Carl Sagan's very favourable-case assumptions, while plugging the variable values in the equation only led to an underwhelming 10 planets as the result. Ten planets among billions of billions of possible planets. These are quite literally astronomical odds stacked against us. If we indeed have such a staggering number of potentially life harbouring bodies, and such infinitesimal odds of ever finding said life, can we actually detremine if we are or are not the only living beings out there?

"Two possibilities exist: Either we are alone in the universe or we are not, both are equally terrifying."- Arthur C. Clarke

IILUSTRATION - Hetanshu Bharadiya

With Love, The Brain

- By Bhumi Davda, SYBSc

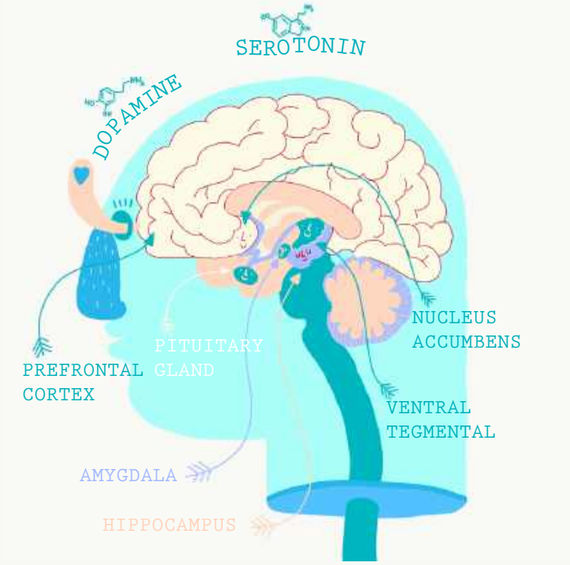


ILLUSTRATION - Aryaa Apotikar

Dalai Lama once said, “Ultimately, the reason why love and compassion bring us the greatest happiness is simply that our nature cherishes them above all else.” According to him, no one is born free of the need for love and the reason why instances of mental illness and depression are increasing in the world is not a lack of material necessities, but a deprivation of the affection of others. This idea does not only have Buddhist philosophical grounds, there are scientific pieces of evidence which prove it true as well. Science has given its nod to the idea that order and harmony in our life are forged by the feelings of love, loving someone and being loved, which is a state manifested by the disorder and the chaos created by the tiny molecules in our brain, the neurotransmitters.

The chemical messengers involved in elevating us to the exhilarating state of mind are many and not all have been identified yet. Also, the amount of these neurotransmitters present in the brain differs in different states of love, which are classified as lust, attraction, and attachment.

Lust is a state-driven by sexual desires, in almost the entire animal kingdom by the need to reproduce. The two hormones primarily involved here are testosterone and estrogen. The levels of testosterone heightens in males in this phase and goes down in females in this state.

The attraction is the phase that enhances blood flow to pleasure areas of the brain. This is associated with an increase in dopamine. Dopamine is the hormone that makes one feel overwhelmed and excited. There is an increase in cortisol, also known as the stress hormone that makes one nervous and gives one the sensation of butterflies in the stomach ie. anxiousness. Serotonin levels decrease that causes loss of appetite and makes one obsessive. These hormones have particularly potent effects in the brain’s pleasure centers which are spread across the brain but mainly include the amygdala, which is linked with emotional responses and the nucleus accumbens- found in the area of the basal forebrain which meditates reward behavior. But what stimulates the secretion of hormones in our brain in the first place? These events are initiated by stimulation of our five senses and all five senses play a role in budding attraction. The eyes are first components in attraction; they detect visual inputs and thus help to perceive a human being as beautiful, however many beauty standards vary between cultures and eras, and signs of fertility and good health. Long lustrous hair or smooth curvy skin are associated with reproductive fitness. And when the eyes spot something they like the next instinct is to move closer, where the nose plays an important role. It picks up natural chemical signals known as pheromones which activate a physiological response in the recipient. In an experiment, it was shown that there was an increase in testosterone levels in males when they were asked to smell the clothes of women who were ovulating. Female noses are especially attuned to major histocompatibility molecules. The major histocompatibility complex (MHC) is a large genomic region in vertebrates and an important component of the acquired immune system. It helps in the detection of macrophages which have

ingested microorganisms. A hypothesis suggests that, attraction of humans with opposite MHC molecules takes place in order to avoid inbreeding that increases the probability of expression of undesired recessive traits, which otherwise might be masked. Hence having evolutionary roots and avoiding homozygosity favors offsprings with better immunity.

Ears play an equally important role. Men prefer women with high pitched and breathy voices which correlate with smaller body size, while women prefer males with low pitched voices that are associated with a larger body size. Once the attraction is confirmed the bloodstream gets flooded with norepinephrine which activates the fight or flight system. It causes our heart to beat faster and our pupils to dilate and cheeks to flush. This is an involuntary response of the nervous system leading to widening of the capillaries of the skin. It is then paralleled with an increase in dopamine which creates a feeling of euphoria.

Another important hormone that regulates human emotions is oxytocin. Oxytocin surges are linked to maternal love and the love we feel for our family and friends. However, some scientists speculate that this hormone is not responsible for establishing a long term relationship in men. Why? There have been experiments conducted that suggest testosterone inhibits the facilitating effects of oxytocin. This has been hypothesized to have evolutionary significance. With oxytocin suppressed, activities such as hunting and attacking invaders would be easier as oxytocin is strongly associated with empathy. So the primary bonding hormone in males is thought to be vasopressin. Interestingly, vasopressin inhibits the synthesis of testosterone. This correlates with other evidence which shows that during attachment love, testosterone increases in women making them more aggressive while in men it decreases making them more passive. In a study conducted by Harvard University, it was shown that testosterone levels drop in men with committed relationships. What is more interesting is that monogamy is also linked with decreased levels of testosterone. A prolonged duration of low testosterone levels leads to an increase in oxytocin which in turn further increases vasopressin levels and their receptors in the reward centers of the brain. It is the activation of these reward centers that gives one the sense of well-being and security which are key for the formation of healthy long-lasting relations that create the much-desired order in our lives.

The amounts of these neurotransmitters differ in different people and in different stages in one’s life. However, too much or too little of these neurotransmitters can cause major mental illnesses. For instance, very low concentrations are thought to cause obsessive compulsive disorder (OCD). It is also linked with depression. On the other hand, an excess of serotonin can cause a deadly condition called serotonin syndrome. Serotonin syndrome is a potentially life threatening condition that results in the hyperactivity of the neuromuscular and autonomic system. Low levels of dopamine in certain regions of the brain result in apathetic behaviour and in parkinson’s disease, dopamine secreting neurons themselves steadily degenerate. On the other hand, in Schizophrenia some regions of the brain receive too much of this hormone leading to hallucinations and delusions. Some scientists also consider obesity and eating disorders as neural, where the brain’s reward systems are affected and overeating provides satisfaction. Consumption of drugs like cocaine cause a huge and quick increase in dopamine levels in the brain which heavily stimulates the brain’s natural reward system. Though these drugs make the consumer “feel good’, it’s continuous intake also raises the threshold levels for reaching those happy moments in the future. This makes one feel emotionally distressed in the sober state.

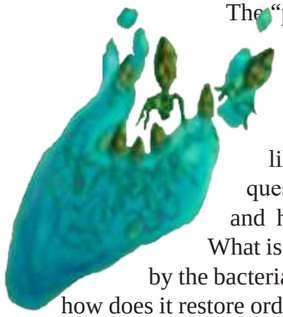
All these instances boil down to one serious conclusion: Our ability to feel emotions and perceive the world does not depend only on the world around us but rather more on the intricacies of our brain, whose functions are orchestrated by neurotransmitters. Indeed, neurotransmitters are dynamic and changes in their concentrations enable us to experience the highs and lows of life.

THE FIGHT AGAINST THE PHAGES

- By Sonia Varghese, FYBSc

A war ensues between two ancient organisms wherein one organism aims to create chaos within the other thereby killing it while the other aims to bring order within itself by applying primordial knowledge. But what are these two organisms involved in the fight of disorder and order? What is the "primordial knowledge" that is spoken of ?

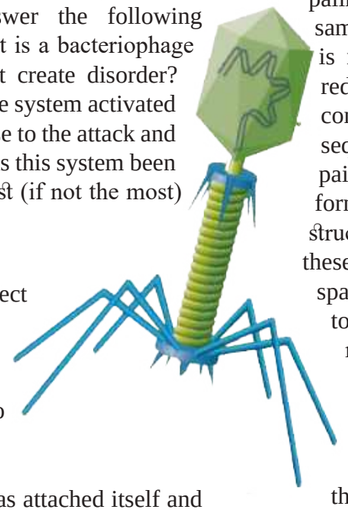
The two organisms are bacteria and bacteriophages. The "primordial knowledge" refers to the immune system activated by the bacteria in response to the bacteriophages.



Through this article, I would like to answer the following questions: what is a bacteriophage and how does it create disorder? What is the immune system activated by the bacteria in response to the attack and how does it restore order? How has this system been utilized to develop one of the most (if not the most) powerful gene-editing technique?

The Bacteriophage's attack:

Bacteriophages are viruses that infect bacteria. But how does the phage create disorder within the bacterium and ultimately kill it? The answer lies within the two types of life cycles of the phages: the lytic and lysogenic cycles.



In the lytic cell, after the phage has attached itself and has injected its genetic material into the bacterium, rapid production and assembly of new phages take place within the bacterium. This leads to the lysis, that is, the rupturing and ultimately the death of the bacterial cell. On the other hand, in the lysogenic cycle, the genetic material of the phage, after getting injected into the bacterium, recombines with specific regions of the bacterial chromosome thereby creating disorder within the host genome. This cycle does not lead to the death of the bacterium.

The bacterium's response:

The bacterium's adaptive immune system responds to the viral attack. This type of immune system can recognize and memorize certain characteristics of the pathogens.

Background Illustrations: Pearl D'Souza

The bacterial adaptive immune system is based on a specific region of its genome called the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR). The CRISPR system was first identified in the cells of Escherichia coli. Let us first understand the components of this system.

In the CRISPR system, there are segments of 20-30 DNA sequences that are identical to each other and palindromic in nature, that is, they read the same irrespective of the end from which it is read. For example, 'murder for a jar of red rum'. This palindromic nature provides complementarity to the two halves of the sequence thereby allowing them to base pair. This property helps the sequences to form hairpin shaped stable RNA secondary structures after they are transcribed. Now, these repeated segments are interrupted by short spacer DNA. These spacers are non-identical to each other. It was a long time before the role of the spacers was identified.

It was the spanish microbiologist Francisco Mojica, who discovered the palindromic identical repeats in the 90s. His further research helped him conclude that the spacer DNA matched with the genetic material of many of the bacteriophages.

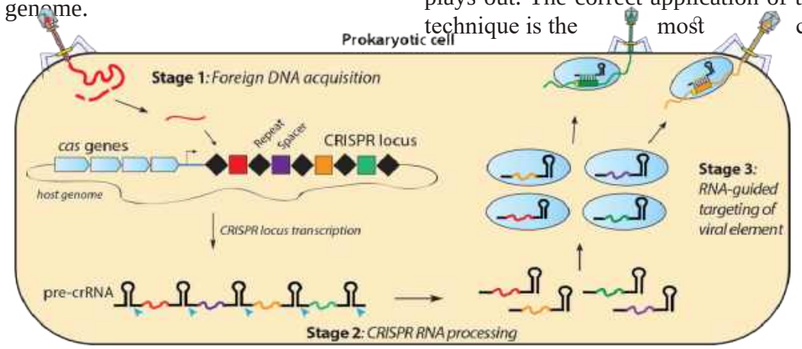
There are several genes linked with CRISPR. They are called the CRISPR-associated genes abbreviated as the cas genes. These genes produce proteins by the process of transcription (conversion of DNA to RNA) and translation (RNA is converted into proteins). The proteins are mainly of two types: Helicases and Nucleases, they unwind and cut DNA respectively.

Now, let us understand the process by which the bacterium uses this CRISPR system to fight against the bacteriophage and, hence, avoids its imminent death thereby restoring order. The process begins after the bacteriophage has injected its genetic material into the bacterial cell.

The first stage, known as Adaptation or Spacer Acquisition, begins with the incorporation of a DNA sequence from the invading viral genome also known as "protospacer" into the CRISPR array thereby creating a new spacer. Two main proteins- Cas1 and Cas2, both of which are nucleases, are mainly identified to be involved in the spacer acquisition process. There are also two types of spacer acquisition processes- Naïve, when there is no previous encounter between the bacteria and the invader, and Primed, when there is a record of a previous attack of the virus on the bacteria.

The second stage, known as Biogenesis or Expression, involves the transcription of the CRISPR array into a precursor crRNA (pre-crRNA) which is long. The pre-crRNA is processed by Cas proteins and other accessory factors and consequently forms the mature guide crRNA (CRISPR RNA). This contains the memorized sequences obtained from the invading bacteriophage at the beginning of the process. These memorized sequences help in the identification of future invading bacteriophages.

The third stage, that is, Interference, involves a complex formation, comprising the mature crRNA and the Cas proteins, which targets the invading nucleic acid (can be DNA or RNA) and strategically degrades it. It also has to be highlighted that different CRISPR-Cas systems employ different types of Cas proteins combined with the crRNA. For example, Type I system uses Cas3, Type II uses Cas9, etc. The mature crRNA acts as a guide molecule and binds to a specific Cas protein (mostly a nuclease). This complex then searches the entire bacterial cell for sequences that match those of the bound crRNA. Once it finds the requisite invading nucleic material, the Cas protein strategically and precisely cleaves the viral nucleic material thereby rendering it ineffective. Hence, the infection ends before it can lead to lysis of the bacterial cell or cause disorder in its genome.



http://doudnalab.org/research_areas/crispr-systems/

The CRISPR system resembles a telephone dictionary. However, instead of telephone numbers, the system has the entire history of old infections. The best part is that not only new viruses infecting the bacterial cell can be recorded, but also the system with the information of new infections can be passed onto the progeny.

Is the CRISPR-Cas system more than just an immune response?

Nature has varied and even unique ways to restore order in its children. The CRISPR-Cas system is a prime example of this. However, soon after the role of this system was discovered, by 2008, speculations about wider implications had begun. These speculations culminated in the realization that the spacer DNA is, in fact, programmable, that is, the spacers can be replaced with a desired similar segment, and the matching DNA segment will be cut out of the genome.

Further research work conducted by Emmanuelle Charpentier, Jennifer Doudna, and Feng Zhang, with the former two being the pioneers of CRISPR as a gene-editing technique, resulted in the understanding that the CRISPR-Cas system could be the key to programmable gene editing.

Nessa Carey, in her book 'Hacking the Code of Life', had stated, "The ability to hack the code of life had truly arrived." Truer words could not have been written for this context.

Through this beautiful story of the bacteriophage creating chaos within the bacteria and the bacteria's attempt to restore order within itself, humans have developed the revolutionary technique of gene editing. Soon enough, Liberal Eugenics might not just remain an ideology but would become the reality and 'designer babies' would become the norm as portrayed in the futuristic movie, 'Gattaca'. We have the joint responsibility of deciding how our collective future plays out. The correct application of this gene-editing technique is the most crucial.

Rainforests: A Universe of Interactions!

- By Rene Zachariah, FYBSc

Tropical Rainforests are comprised of tall evergreen trees and experience continuous heavy rainfall. They are considered natural reservoirs of genetic diversity as they are home to more than half of the earth's plant and animal species even though they cover only around 6% of the total land surface.Tropical rainforests are exposed to intense sunlight moderated by humidity that together results in an overall warm temperature that provides the necessary energy to power the forest via photosynthesis.

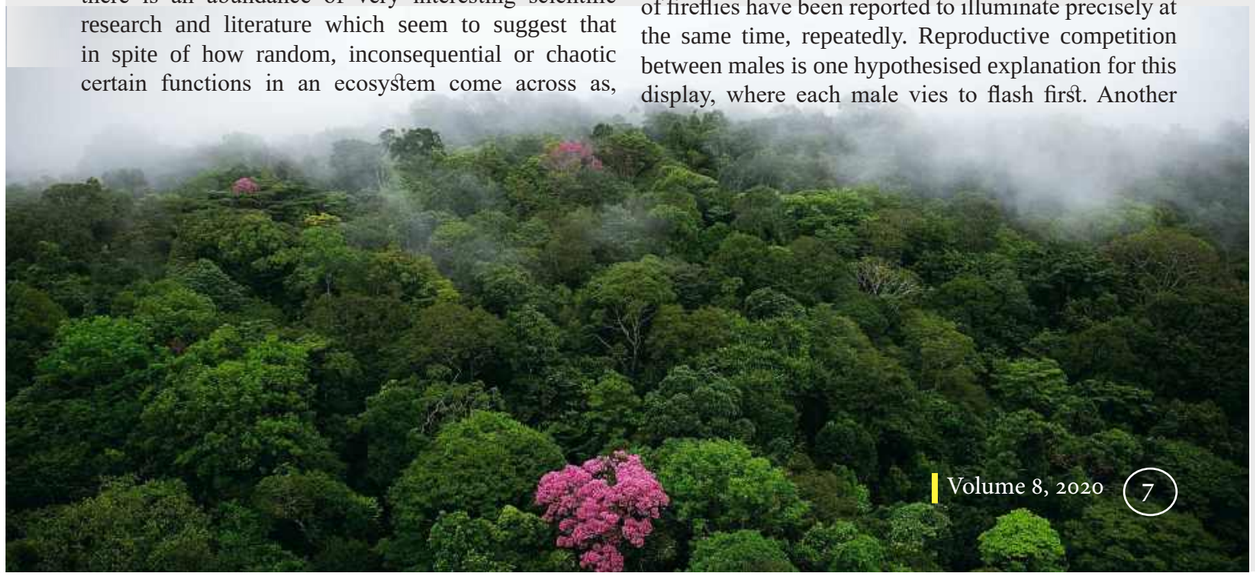
An ecosystem is the sum of interactions between organisms and their surrounding biotic and abiotic factors. In a healthy ecosystem, the key factor is the establishment of balance or a sense of homeostasis. The concept of a healthy ecosystem therefore is inherently at odds with the idea of 'disorder' which comes about due to an imbalance or lack of organisation.

In the past, the existence of the concept of an 'ecosystem' was in fact up for debate as some scientists were of the opinion that 'change' in the natural world is directionless, indefinite and not geared towards attaining any stabilization in biomass or greater cohesiveness in plant and animal communities or further success in environmental regulation. While some components of this argument may hold true, there is an abundance of very interesting scientific research and literature which seem to suggest that in spite of how random, inconsequential or chaotic certain functions in an ecosystem come across as, all natural processes and relationships seem to be highly interrelated and interdependent. Diversity in an ecosystem leads to resilience of an entire community, hence of the planet itself. This is due to the fact that a multi-layered community will be more resistant to a particular pathogen or infestation. Agriculture has utilised this phenomenon via multiple cropping.

In a rainforest ecosystem, almost all species are dependent on each other (directly or indirectly).These relationships (between plant and pollinator, prey and predator, symbiotic relationships etc.) between species have been evolving over millions of years and form the basis of the complex ecosystem.

An interesting and beautiful example which embodies behavioural complexity and unusual predation can be found in fireflies. Fireflies are winged beetles belonging to the family Lampyrdidae. Fireflies are bioluminescent and have light organs that are located under their abdomens; they take in oxygen and, inside special cells, combine it with a substance called luciferin to produce light.

A fascinating phenomenon exhibited by a large number of fireflies in certain parts of the world is synchronous flashing or 'simultaneous bioluminescence'. Thousands of fireflies have been reported to illuminate precisely at the same time, repeatedly. Reproductive competition between males is one hypothesised explanation for this display, where each male vies to flash first. Another



analysis states that the simultaneous luminescence takes place for females to make better comparisons between the flashing males in order to choose the fittest mate. (Fitness being determined by the male's signalling/ flashing ability).

Another tool which leads to a greater sense of order in a community in a forest is the ability to 'communicate'. While one might expect the more sentient mammals or insects to be the only beings which communicate in a rainforest, it has been known for a while that plants too, have the ability to communicate with each other through 'signalling' by the release of certain Volatile Organic Compounds (VOCs).

Plants secrete primary and secondary metabolites. Primary metabolites (molecules such as carbohydrates, lipids and proteins) are responsible for growth and metabolism in plants while secondary metabolites (diverse chemicals like terpenoids) are the end products of primary metabolism. VOC'S represent 1% of the known plant secondary metabolites. VOCs are used to perform a variety of tasks, one such task is plant communication for defense against predation.

For example, when a herbivore begins to feed on a plant, it may respond directly or indirectly. A direct response would include the transmission of an electrical impulse to the rest of the plant which triggers the undamaged parts of the plant to start producing defensive chemicals that have a toxic or repellent effect on the herbivore. These chemical signals are picked up by neighbouring plants which immediately secrete their own defensive toxins making them less susceptible to predation,whereas an indirect response of a plant would be the release of a blend of volatiles that specifically attract natural enemies of the particular herbivores and /or by providing food (e.g., nectar) and housing to enhance the effectiveness of the natural enemies.

For example, a part of a plant damged by caterpillars secretes a VOC which attracts parasitic wasps that lay their eggs in or on the caterpillar. When the eggs hatch, the offspring consume the caterpillar. This species specific response suggests that plants have the ability to recognize different herbivorous species and respond accordingly. It is said that this is done by a plants perception of chemical cues generated through the saliva of the herbivore. Some plants produce trichomes, sugary appendages which grow from the epidermis of the plant. They are eaten by caterpillars. However, trichomes mark the caterpillars with a strong odour which makes them susceptible to predation.

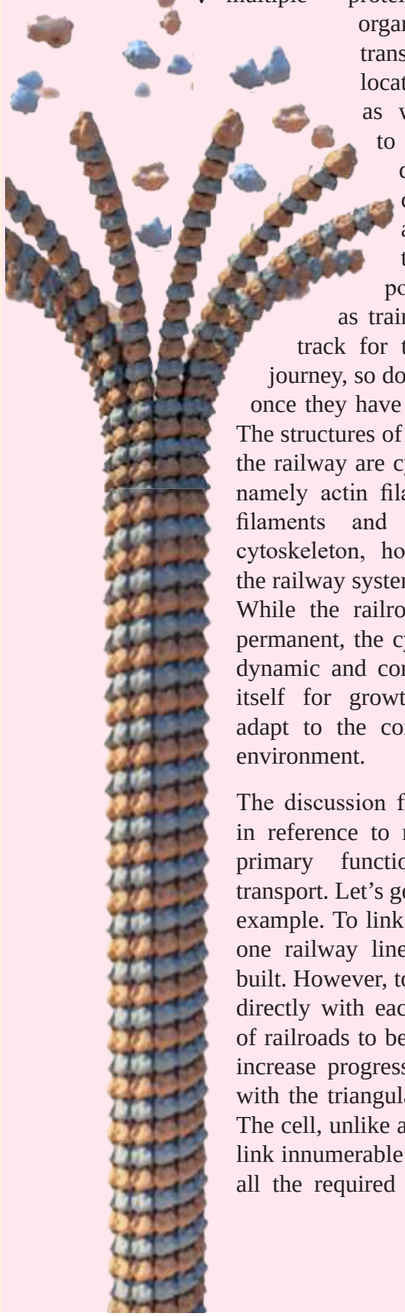
A more recently discovered fact is that plant communication takes place even underground through a complex network of mycorrhizae fungi which colonize plant roots forming a symbiotic relationship. Some studies have proven that plants are able to adapt to situations such as defending themselves against herbivores or parasitic infestations (a quality which was thought to be demonstrated only by animals) and have even been observed to exhibit a supportive nature towards other plants (e.g. younger plants in need of nutrition). The existence of this kind of 'behavior among plant species has led researchers to question whether a forest might be better imagined as a single superorganism rather than a grouping of independent individualistic ones. And within a single organism, is immense order.

In this article one gets a glimpse into the complexity that exists within a rainforest ecosystem. Complexity, as a concept seems to have a negative connotation as we associate it with 'entanglement' or heterogeneity, something which is not simple and from which problems arise. But it is imprudent to judge and dismiss ecosystems just because their complexity is incomprehensible to us. The sooner we are able to accept and respect the fact that diversity exists within, among and outside of us the better. And hopefully we will soon realise that we are just components of a larger ecosystem, just as our bodies are ecosystems for microorganisms.

Once they are established, living systems must function within the context of the environment they are a part of, else, they are selected against. Newly adapted living systems will be generated with the demise of poorly adapted ones and in response to the continually changing environment.
Order from disorder indicates the generation of life and greater order from pre-existing order ensures its continuation.

The Railway of Life

-By Pooja Mehta,SYBSc



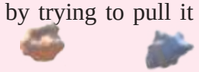
Visualise the cell to be a city, where multiple proteins, vesicles and organelles are to be transported from one location to another. Just as we use the railway to travel from one destination to another, cellular components also use direct paths to travel from one point to another. Just as trains traverse the same track for the entirety of their journey, so do cellular components once they have begun their journey. The structures of the cell analogous to the railway are cytoskeletal elements, namely actin filaments, intermediate filaments and microtubules. The cytoskeleton, however, differs from the railway system in one crucial way. While the railroads of the city are permanent, the cytoskeletal system is dynamic and constantly reorganising itself for growth, division and to adapt to the continuously changing environment.

The discussion further is specifically in reference to microtubules, whose primary function is intracellular transport. Let's get back to the railway example. To link two points in a city, one railway line would have to be built. However, to link multiple points directly with each other, the number of railroads to be built would need to increase progressively in accordance with the triangular number sequence. The cell, unlike a city, has the need to link innumerable points to ensure that all the required cellular components reach their desired location. To have permanent microtubules linking all these locations would be detrimental in two major ways. Firstly, building these networks would be extremely resource intensive and since these paths would not be used at all times, this would not be economical. Secondly, the destruction of one path would mean, that no components can be transported between the two points that the path connected. The alternative to connecting all the locations directly would be to create junction nodes through which cargo can be routed. This however, would require a central intelligence to control the complex flow of cargo.

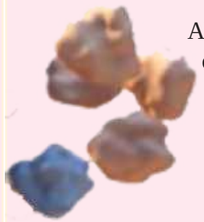
Our cells however, have developed a brilliant mechanism to overcome all these challenges. The existing cytoskeleton within a cell can spontaneously dissociate into its constituent subunits (tubulin in the case of microtubules) which dissolve in the cytoplasm and can diffuse to a region of the cell where they are required to build another microtubule. In this way, the constituent building blocks of the cytoskeleton are very efficiently recycled and utilized. This also solves our second problem, as the dynamic behaviour of the microtubules relieves the cargo's dependence on a single fixed path. Finally, as we shall see ahead, the assembly and disassembly of microtubules can be regulated locally, by proteins as well as the concentration of cytoplasmic tubulin, as opposed to being controlled centrally, which would require a complex routing algorithm. To expand the railway analogy, this would be like dismantling and reconstructing the railroad in the desired direction every time we needed to travel between different destinations.

But what enables microtubules to have this dynamic nature only at its ends, thereby ensuring that the transport of cargo is not disrupted by the breakage of the tubule in the middle? The answer to this question lies primarily in the microtubule structure. Microtubules are composed of thirteen parallel protofilaments linked non-covalently to form a cylinder. Each of these protofilaments are polymers of a heterodimer called

tubulin which itself is composed of two globular proteins (alpha and beta tubulin) tightly bound to each other by non-covalent bonds. Now, if subunits from a microtubule are to be made available as free cytoplasmic subunits for use elsewhere, there are two possible ways this can be achieved. The removal of a single subunit from each end requires the breakage of just two lateral and one longitudinal bond. In contrast, if a subunit were to be removed from the middle, this would require the simultaneous breaking of longitudinal bonds in each protofilament at that level to free that subunit, ie in a complete microtubule, to free a subunit in the middle thirteen longitudinal bonds would need to be broken at once! The difference in energy requirements between the two, make the former option the most viable. As a result, the flexibility of the ends of the microtubule is maintained while ensuring resistance to thermal breakage. This process is analogous to a Velcro, which has to be peeled apart from one end to another and cannot be separated directly by trying to pull it apart from the centre.



Now, we come to the mechanism behind the assembly and disassembly of a microtubule. The alpha and beta subunits of tubulin each contain a binding site for GTP (Guanosine Triphosphate). The dimers are arranged in the protofilament in a manner that traps the GTP bound to the alpha subunit at the alpha- beta interface, while the GTP binding site of the beta subunit remains accessible for hydrolysis. Hydrolysis of this terminal GTP to GDP spontaneously occurs leading to the dissociation of the subunit from the microtubule, as GDP bound subunits have lesser affinity for neighbouring subunits than their GTP bound counterparts. This would result in the continuous depolymerisation of the microtubule. However, this is not the case as the addition of a new GTP bound subunit on an existing non-hydrolysed subunit of the microtubule can trap the subunit, protecting it from hydrolysis. Thus, if the rate of binding of new GTP bound subunits to the exposed, terminal subunits of a microtubule exceeds the rate of hydrolysis of the GTP on these subunits, polymerisation occurs, otherwise depolymerisation continues.



Although, what determines these rates? The of polymerization is directly proportional concentration of tubulin subunits in the surrounding cytoplasm. As the subunits get utilized, the concentration falls and consequently so does the rate of polymerisation. At one point, the concentration of the subunits is so low that it is unable to maintain the rate of polymerisation high enough to prevent hydrolysis of GTP and at this stage the rate of loss of subunits is equal to the rate of addition of subunits, that is, the system is in equilibrium. At concentrations below this, hydrolysis takes over and the microtubule begins to depolymerise.

An interesting consequence of the association and dissociation of microtubules is the generation of energy. When the concentration of subunits exceeds the critical concentration, polymerization occurs spontaneously and hence yields a high amount of free energy. This energy is often used by the cell to carry out energetically unfavourable processes like pushing and pulling of loads. In fact, it is the shrinking of microtubules that facilitates the pulling apart of sister chromatids during anaphase.

Up till this point we have explored the importance of the dynamic nature of microtubules. However, in terminally differentiated neurons microtubules form the architectural framework that enables axons to elongate and form networks over long distances in addition to transporting cargo. Hence, a higher proportion of microtubules in the axons of neurons are stable rather than labile. Although, recent studies demonstrate that the transient polymerisation of microtubules in dendrites lead to the formation of dendritic spines. These are small protrusions of the dendrites that receive an impulse from an axon. They play a key role in maintaining synaptic plasticity which is found to be essential for learning and memory formation. This highlights the importance of both stability and instability of microtubules necessary for the maintenance and proper functioning of neurons.

Decades of studies on microtubules have revealed a crucial link between impaired microtubule dynamics and neurodegenerative disorders and it is this link that will help scientists better understand several neurodegenerative disorders as well as design therapeutic agents for the same in the future. To conclude, it is this seemingly chaotic dynamic instability of the cytoskeleton that is responsible for the highly efficient utilisation of resources, shape and function of cells that bring order within an organism.

SYMMETRY AND ASYMMETRY

- By Shannon Rodriquez, SYBSc

Image Courtesy: Ernst Haeckel - Kunstformen der Natur (1904), plate/planche 49: Actiniae

In 1788 medical students from the Hunterian School of Medicine were dissecting a cadaver wherein to their shock they discovered that the organs of the cadaver were a mirror image of what is generally observed. The liver of the cadaver was on its left, its heart was tilted towards the right, not the left. The condition was later known as situs inversus and was found to occur in only 1 out of 20,000 individuals.
We all know that in life there exists symmetry. In biology symmetry can be classified as point symmetry, that is, any straight cut through the central point of an organism can divide the organism into two equal or two mirroring halves. The second classification of symmetry being radial symmetry found in organisms like starfish, sea anemone, etc. The last class of symmetry is bilateral symmetry wherein a body can be divided into two equal halves which are mirror images of each other.
In organisms displaying bilateral symmetry like humans, the body can be divided into the left half and the right half. But internally it is a completely different situation and asymmetry reigns. Now the question that arises is ``how do cells differentiate between the left half and the right half of the human body?' "how does your body direct the positioning of your liver to the right side of the body, why is your stomach placed on the left side of your body?". "How does the body prevent abnormal conditions of asymmetry such as dextrocardia (a rare condition in which the heart points to the right instead of the left)?"
This process is established during the early stages of development. The ball of cells formed after fertilization which is symmetrical in nature develops into a head and a tail end. The left-right axis of the embryo is laid down only after the anterior-posterior and dorsal-ventral sides have been identified. An occasion known as the left-right symmetry breaking occurs when the embryo determines its left and right sides. Experiments performed suggest that the event of left-right symmetry breaking occurs due to the leftward flow of extra embryonic fluid (left of the embryo). This leftward flow occurs due to the beating of cilia on a region called the node. The node is filled with liquid and lined with monocilia or primary cilia wherein the motor is of the nature 9+0 rather than 9+2. The latter is typical of most cilia and flagella. The nodes are responsible for the leftward flow of extra embryonic fluid, a process known as nodal flow. It was observed that the cilia has a slight tilt which points away from the head and it is due to this tilt that the left and right sides can be distinguished. The tilt of the cilia helps in the flow of the fluid towards the left side and experiments showed that if the direction of the flow of fluid was reversed, the positioning of the organs also reversed.
Genes involved in crucial developmental pathways express asymmetry and activate subsequent morphogenesis pathways. The major players involved are NODAL, activin receptor IIB and sonic hedgehog. The first two belong to the transforming growth factor beta (TGFB) family while the last one belongs to the hedgehog family. Activin receptor IIB gene is expressed on the right hand side such that it inhibits the expression of SHH, thereby restricting SHH expression to the left hand side. This restricted expression of SHH causes expression of NODAL in the left hand side which then leads to development of organs asymmetrically via inducing expression of LEFTY2 and PITX2, the latter plays an essential role in left-sided morphogenesis. These proteins known as morphogens are factors which influence development. Often this is via gradients of the protein or gene expression in specific regions.

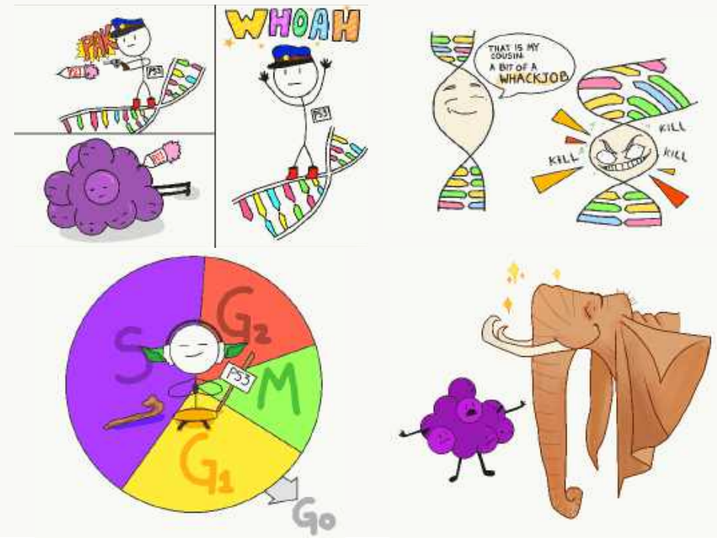
Human beings have evolved with such asymmetry in their internal organs because the existing placement of organs allows for the formation of a more compact organism with more efficient utilisation of space than an internally symmetrical organism could allow. In fact, the asymmetry in our bodies is organised in a specific fashion to facilitate the seamless functioning of different processes and damage to this asymmetry wrecks havoc in our bodies.
The research carried out to explain left right asymmetry in embryos is just the tip of the iceberg and many questions such as "what process does an embryo carry out to orient the L/R symmetry in tandem with the other axes?", "when does this occur at what stage in embryonic development can the embryo differentiate it's right from the left?" are yet left to be answered.
As every individual may have experienced for oneself, external symmetry is crucial for humans to be able to interact with the outside world, however organic asymmetry in human bodies is equally important, if not more, for carrying out life sustaining physiological processes.

GENE IN FOCUS :

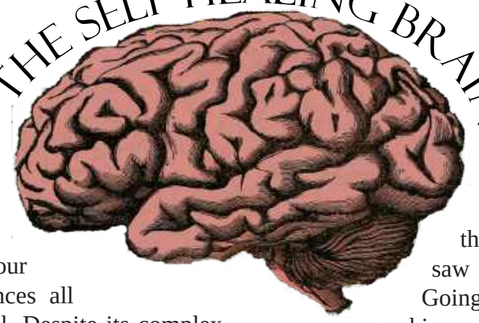
p53 gene

A gene that codes for TP53 or tumour protein. It regulates the cell cycle and fuctions as a tumour suppressor.

ILLUSTRATIONS - Aryaa Apotikar



THE SELF HEALING BRAIN



By Lianne Fernandes,SYBSc

Our brains are quite remarkable, a 1.4 kg mass controls everything we do! What's striking is our brain's sheer physicality to create our thoughts, dreams and experiences all formulated from neural material. Despite its complex anatomy, the human brain is a commodious place with an estimated count of more than 200 million neurons and a total cell count that exceeds the number of stars in the the milky way!

One of the most common phrases that echoes in emergency rooms among neurosurgeons and medical attendants who exchange what they call "war stories" when it comes to Traumatic Brain Injury (TBI) is that brain injuries do not discriminate, implying the plausibility that this invisible wound could occur to anyone. Traumatic brain injuries are best described as a calamitous hit to the head, almost punching the brain from inside leading to long term disabilities. According to empirical studies, TBI left patients exceptionally vulnerable to stroke, a sudden interruption to the blood supply in the brain affecting the frontal and temporal lobes. Till now any form of recovery was viewed merely as a compensation and never a solution.

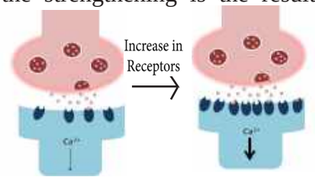
Going back 60 years ago, the brains hitherto unexplained capability to transform was anathema to the field of neuroscience. Scientific literature at the time heavily presumed the human brain to be fixed in nature. With the functioning of the brain often metaphorically compared to that of a machine, with many parts adapted for a singular function. However, unlike a machine where parts can be replaced once they are damaged the brain cannot grow new parts to compensate for those gone.

Recent studies, however, suggest that the brain can be rewired for love, sleep, procrastination and even for traumatic brain injuries. If these studies are to be trusted we have the capability to consciously change our brains. But what is rewiring? It essentially refers to neuroplasticity: the catch all term used to describe how the brain reorganizes itself to form new neural connections. Orthodox neuroscience held that only immature brains were malleable and morphable, that is highly plastic. While the transition into adulthood saw neuroplasticity fade steadily. Going back to the metaphor of a machine, neural circuits were essentially considered to be "hardwired". However, landmark experiments performed by a rather tiny constellation of neuroscientists proved otherwise.

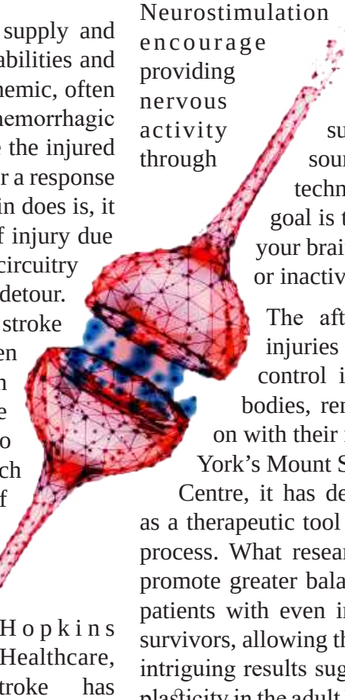
In 1959, Paul Bach-y- Rita was one of the neuroscientists who pioneered the theory of adult neuroplasticity and rehabilitation through its wilderness years. His interest in this field was piqued by his father Pedro, who suffered a stroke leaving him paralyzed and speech deficient. Doctors considered any treatment implausible due to the dogma that persisted in the medical community at the time. However, rather than watch his father succumb in a nursing home, he was put through a self-rehabilitation program to the dismay of his neighbors who watched the 78 year old man struggle to perform chores after a stroke but in the mind of a neuroscientist the rigorous motor training was reinforcing basic skills like walking. Miraculously, Pedro made an astonishing recovery and even returned to his job as a professor for two years. This discovery was one of the most daring applications of neuroplastic rehabilitation in the adult brain.

Developments in technology today have facilitated neuroscientists to map the brain's labyrinth of links between neurons known as the connectome. The connectome aims at visualizing the many neural circuits in the brain, almost symbolic of a road map. This neural map helps to perfectly illustrate neuroplasticity.The roads that are well travelled represent your habits and have well established neural routes controlling your actions. However, when something as catastrophic as traumatic brain injuries occur, it results in the damage of some of these neural circuits. One of the principles of neuroplasticity is "If you don't use it, you lose it" ,thus rehabilitation focuses on the continuous practice of utilizing a specific cognitive process to carve a

a road that was once damaged. Therefore, the persistent stimulation of a neural connection helps strengthen it. On a synaptic level, the strengthening is the result of an increase in receptors in the postsynaptic neurons which governs several processes crucial for neuronal responses.



Stroke has a tight stranglehold on blood supply and thereby oxygen to the brain, leading to disabilities and crippling of the mind. Most strokes are ischemic, often beginning with a blood clot and the rest are hemorrhagic caused by ruptured blood vessels. Imagine the injured brain to be a wound, the immune cells trigger a response leading to healing on its own. What the brain does is, it essentially reorganizes itself in the event of injury due to there being a roadblock in the neural circuitry thus post stroke neural circuits take a detour. This period of brain plasticity after a stroke lasts for one to three months and is often frittered away by medieval rehabilitation programs. The opportunity for repair once missed is what turns rehabilitation into compensation. However, with more research done into neuroplasticity, new methods of rehabilitation now focus on cell enrichment and neurostimulation as ways to enhance post injury plasticity.



John Krakauer, a professor from John Hopkins Malone Center for Engineering and Healthcare, stressed upon the impact that stroke has on the hundreds of people that it devastates, yet current treatments for therapy and rehabilitation are either too late into recovery or too driven by economics rather than scientific research.
Through his extensive experiments with mice, Krakauer learned that on receiving therapy in a rather stimulating environment by housing mice in larger cages, providing interaction through toys or other rodent friends. An enriching environment appeared to show evidence of functional recovery: the brain's unique way of transferring functions from the area damaged by trauma to other areas that are not afflicted. This enhanced plasticity was stimulated by sensory experience and well accounted for positive effects on the brain. Current data even suggests that on a cellular level an enriched environment increases the proliferation of glial cells as well as neuroblasts promoting recovery by the release of regenerative factors.

After a stroke has possibly done its worst, slaughtering cells or reducing their blood supply to dangerously low levels, healthy cells fill in but what would be the best way to restore or induce them?

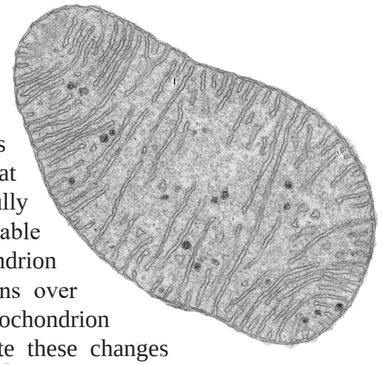
Neurostimulation could be part of the solution to encourage the formation of healthy cells by providing a stimulus to activate the nervous system, whether it be physical activity such as walking, or stimulating through sound by listening to music or even technology based games: the main goal is to wake up the various circuits in your brain that may have become dormant or inactive in response to trauma.

The after effects of traumatic brain injuries often include the loss of motor control in various parts of the patients' bodies, rendering them unable to continue on with their routines. A great example is New York's Mount Sinai Hospitals Abilities Research Centre, it has devised ways to use video games as a therapeutic tool to supercharge the rehabilitation process. What research tells us is that video games promote greater balance as well as independence for patients with even improved arm function in stroke survivors, allowing them to perform daily tasks. These intriguing results suggest the effect of neurocognitive plasticity in the adult brain. The possibility that gaming increases attention spans as well as concentration, stimulating the brain over time, helping to rewire the brain, thus helping improve motor skills that were lost.

At present, stroke is a public health issue, with advances in neuroplasticity paving the way for rehabilitation programs.What was once thought to be a completely heretical theory can now be used in the post stroke recovery process. These ambitious visions on neuroplastic rehabilitation will take time to be accepted, however with research providing solace to those affected by this catastrophic neurological disorder there is hope.

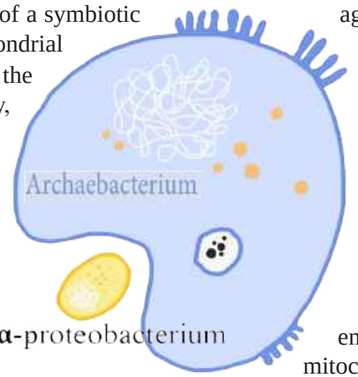
The Greatest Invasion of All Time

-By Arjun Udupa,SYBSc



Eukaryotes, true nucleus containing organisms. Their complexity is bewildering and worthy of awe. But, how did this complexity arise? What led to the evolution of quintessential eukaryotic characters like splicing, nuclear membranes, split genes, apoptosis among others to arise? This article highlights a number of reasons and primarily hints at one particular hypothesis mentioned later. Considering this concept is yet to be understood completely, as a reader you are encouraged to ponder over the theories provided and come up with your hypothesis.

One of the most critical events in the history of life on Earth has to be the development of a symbiotic relationship between the mitochondrial ancestor, an **α**-proteobacterium and the host cell being an archaea. Obviously, various theories have been proposed but this one seems most plausible. Eukaryotes are wonderful hybrids that are considered to have genetic homologues of various archaeal and bacterial genes as they are derived from these groups. It is considered that once the endosymbiont (hereon, mitochondria) was incorporated, there was a significant invasion of mitochondrial DNA into the host genome. Over time this loss of mitochondrial DNA has been immense with as much as 99% of the mitochondrial genome being lost in comparison to its closest relative. The mitochondrial DNA transfer to the nucleus can happen if the former disintegrates and leaks DNA into the cytoplasm.



But, why should mitochondria lose DNA? How does it happen? Mitochondria have an obvious advantage of losing DNA, that being, faster replication as well as energy conservation. The reduced amount of DNA present ensures that DNA replication is faster, hence lesser time is required for the mitochondria to divide. It must be noted that though an endosymbiont, the mitochondria is also an organism caught up in the race for survival. Faster replication allows the mitochondria to fully colonize the cell. Additionally, reduced DNA content leads to a lesser energy requirement for gene expression, translation, transcription, repair and maintenance among others. Thus, the overall output of ATP increases. The loss of genes is enhanced by the fact that the cytoplasm is carefully regulated and remains stable while the mitochondrion genes undergo fluctuations over generations. If the mitochondrion survives optimally despite these changes and loss of genes, these genes may not be required again. Prokaryotes on the other hand, due to the flux of the niche lose some genes but eventually gain certain other genes to adapt.

The transfer of essential mitochondrial genes like those that form the Complex I, did not really cause a large variation in cell characteristics,but made the mitochondrial membrane complexes mosaic as they contained proteins encoded by both the nuclear and the mitochondrial DNA.This is also an important reason why two different sexes arose and why only one parental gamete passes on its mitochondria. (I deliberately leave the reader hanging here as the details are beyond the scope of the article, the book in the references would be a useful starting point)

But, some mitochondrial genes, when transferred to the nucleus, transformed to form families of genes with novel and useful functions. The energy saved by the elimination of mitochondrial protein synthesis (due to mitochondrial gene loss, no gene - no protein synthesis) could now be used in developing novel characteristics out of the newly formed gene families such as the building of a dynamic endoskeleton network which has tremendous benefits.

The introns in eukaryotic genomes are considered a relic of mitochondria's bacterial past. Bacteria have self-splicing Group II mobile introns which cut (splicing) and paste (reverse transcription) themselves in various parts of the genome, wreaking havoc by causing genomic instability. Eventually, these mobile introns were tamed down either due to selection of those bacteria where the introns were positioned in a non harmful part of the genome or because the introns could not survive without being a part of the host genome that replicates and yields organisms that survive. It's in the intron's interest to position itself in regions that result in minimal interference and this could be an important selection pressure. Hence, bacterial introns are seen in groups in intergenic regions rather than in the middle of protein coding genes. Over time, the introns from the early mitochondrion entered the host genome; this was advantageous for the host because now, the exons could be rearranged to provide a whole new set of proteins as in the case of the variety of antibodies produced in spite of a limited sequence. The ribozymes that form the spliceosome have a mechanism of action that is very similar to that of splicing by mobile introns. Hence, it is considered that spliceosomes and eukaryotic introns are derived from self-splicing Group II mobile introns. The need of spliceosomes arose because mutations eventually withered the self-splicing ability of the introns. Moreover, energetically, eukaryotes could afford this due to the mitochondria providing an abundance of ATP as compared to ATP available for the prokaryotes.

ATP must constantly be used because accumulation of ATP reduces respiration, leading to the accumulation of electrons in the membrane that reduce the membrane lipids and make them reactive with oxygen, as a result forming destructive free radicals. Thus, the excess ATP now available due to the mitochondria was used to increase genome size, build an endoskeleton network and increase cell size among others.

One problem that spliceosomes pose is that they are slow in performing the task at hand compared to ribosomes. In the early eukaryote, this would have resulted in the ribosomes starting translation before splicing, resulting in redundant proteins. However, this was prevented by the formation of the nuclear membrane that prevented the ribosomes in the cytoplasm from accessing the pre-spliced mRNA.

Presence of introns could have helped guide the formation of the nuclear membrane as mitochondrial genes in the host genome promote lipid synthesis and back then, it would have been uncontrolled. This is further supported by the fact that eukaryotes have bacterial lipids, a clear result of mitochondrial gene transfer. Moreover, because of increased lipid synthesis and the tendency of lipids to form vesicles and clump together, the clumped lipid vesicles would have formed internal membranes that would have eventually formed the nuclear membrane. This can be seen during cell division wherein the nuclear membrane forms smaller vesicles.

From cell division, we go to the other extreme, that is death. All eukaryotes trigger the process of apoptosis wherein the loss of cytochrome c from the membrane is an essential factor. Why should cytochrome c play such a crucial role? Considering that one of the most essential functions in a cell is ATP synthesis, it is absolutely necessary to have optimally functioning mitochondrial membrane complexes. As we saw earlier, mitochondrial membrane complexes are mosaic, implying that the mitochondrial and nuclear proteins should perfectly synchronize and even a slight change can greatly vary electron transport. Subsequently, the membrane gradient gets disrupted due to lack of proton pumping. We have seen earlier that electron accumulation can lead to the formation of free radicals that react with membrane lipids like cardiolipin and subsequently release cytochrome c, a peripheral protein. Hence, the role of cytochrome c in triggering the very ordered pathway of apoptosis is crucial as it limits the extent of damage to the affected cell, thereby selecting cells that have mitochondrial and nuclear proteins acting in perfect harmony.

Thus, it is now evident that disorder at multiple steps, in terms of incorporation of an endosymbiont and subsequently its DNA into the host has led to various essential adaptive features of eukaryotes. To quote the renowned geneticist Theodosius Dobzhansky, "Nothing in biology makes sense except in the light of evolution''.

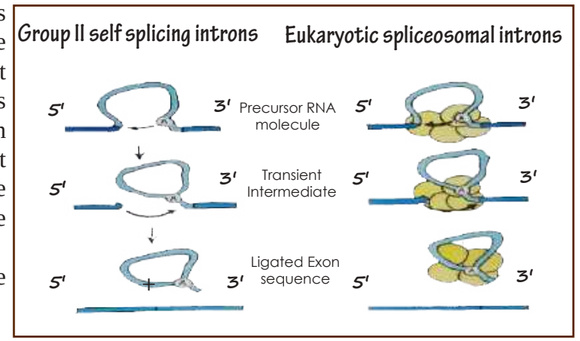


Diagram By: Austin Varughese

A PASSAGE TOWARDS ANTIFREEZE

- By Kabeer Nadkarni, SYBSc

Antarctic Icefish

https://www.quantamagazine.org/icefish-study-adds-another-color-to-the-story-of-blood-20190422/

Antarctica, the land of cold and harsh waters. In these waters lies a nutrient-filled ecosystem. The unpredictable nature of the ocean foreshadows its unstable and turbulent past. The Antarctic wasn't always in the state that we see it as today.

About 50 mya, the waters around it were similar to temperate regions with temperatures of about 100° C. During this period, the Antarctic shelf itself was connected to the tip of South America. But then about 34 mya, the Antarctic separated from the tip of South America which resulted in the formation of the Drake's Passage. This had repercussions on the circulation of water on a global level. It resulted in a change in the direction of warmer waters coming from the tropics and simultaneously a deepening in the Drake's Passage that further led to the formation of a continuous current called the Antarctic Circumpolar Current (ACC). The ACC formed a barrier between the waters of the Antarctic and the incoming warm waters. This allowed the water near the continent to always remain cold. The order was regained.

This entire geographical exercise led to the evolution of something extraordinary on a molecular level in a suborder called *Nototheniidae*. This sub-order includes a family called the *Channichthyidae*. A type of fish called the 'Icefish' belongs to this family. The Icefish thrives in these icy cold waters. Predominantly, it is found in the Southern Ocean and the shores of Antarctica where the waters are capable of getting as low as -20°Celsius, a temperature at which the blood should freeze. The question which arises is, how does a fish survive in such extreme conditions?

To answer this question, let us take a look at *Nototheniidae* as a whole and then come to *Channichthyidae* which took it a step further.

The *Nototheniidae* evolved something called Antifreeze Glycoproteins (AFGPs). In 2011, a paper published by three German biologists used phylogenetic techniques to prove that the cooling of the Antarctic coincided with the development of AFGPs in the *Notothenioids*.

Because the Antarctic had cooled down, there was an immense nutrient-rich region that had formed and remained untouched. To exploit these resources and colonise these waters, the *Notothenioids* needed something to overcome the blood-freezing temperatures that existed. The "linchpin" in this process were the AFGPs.

In the 1960s, Arthur DeVries found out that the *Notothenioids* had come up with AFGPs to prevent themselves from freezing. Generally, in the absence of AFGPs, ice crystals would infiltrate through the skin and the gills and begin to grow in size. Once large enough, it would allow them to pierce through sensitive tissues and nerves, killing the fish in minutes.

AFGPs are produced by the fish in their pancreas, esophageal tract, and stomach. The function of AFGPs is to bind themselves to the ice crystals present in the blood and prevent their further growth. At the same time, they divide the long and crystal-like structures into small and curved ones. A team of researchers from the University of Auckland, ascertained that the particles formed from the binding process of the AFGP onto the ice crystals are engulfed by phagocytic cells and moved into the spleen. The purpose of moving them to the spleen could be to wait for warmer conditions to melt the ice. The function of AFGPs on a molecular level is still unknown.

AFGPs are made of two amino acids: alanine (Al) and threonine (Thr). It consists of a varying number of repeating units of (Al-Al-Thr)n, with minor variations that comprise the protein backbone. To the hydroxyl oxygen of threonine, a disaccharide, beta-D-galactosyl(1,3)-alpha-N-acetyl-D-acetylgalactosamine is attached.

The AFGPs are produced by a gene which actually evolved from a gene that encodes for pancreatic trypsinogen, making it an ancestral gene. When a gene arises from a pre-existing gene, which in this case was the pancreatic trypsinogen producing gene as a result of gene duplication, it is referred to as *De Novo*.

The change in function occurred when the ancestral gene underwent accidental duplication. While one copy of the gene remained the same, the other copy underwent further mutations. These mutations gave the gene its antifreeze properties.

When seen from a molecular perspective, the shake-up happened between the first intron at the 5' end and second exon towards the 3' end of the trypsinogen gene. After the duplication, the region between them underwent mutations resulting in the production of 41 tandemly repeated segments, which were responsible for the production of antifreeze proteins. The two ends of the gene remained the same, while the disturbance only took place between the ends. The retention of the ends was quite important as the 5' end of the trypsinogen gene codes for a peptide used for secretion from the pancreas into the digestive tract. The fact that the AFGPs are produced in the pancreas also supports this explanation on the evolution of AFGPs in *Notothenioids*.

Channichthyidae took it to a whole new level. They did this by completely eliminating haemoglobin and red blood cells (RBCs) from their blood. Normally, red-blooded fish have a linked pair of alpha and beta-globin genes. This is what gives them proper haemoglobin. A study carried out by William Dietrich and his colleagues at Northeastern University found that in 15 of the 16 species of Icefish, the adult beta-globin gene has been completely scrapped, while there is a truncated alpha-globin gene that is retained.

The loss of haemoglobin and RBCs was initially thought to be a beneficial adaptation, biologists assumed that not having RBCs made the blood thinner, and hence, less energy would be required to circulate it in the body. Conserving energy would make a huge difference considering the animal's extreme habitat.

This was considered to be logical until further research showed that it wasn't a beneficial adaptation. Instead, it created even more disorder.

Icefish blood can only transport as much as 10% of oxygen when compared to typical fish blood. To compensate for this, the physiology of *Channichthyidae* changed. As compared to the other *Notothenioid* families, Icefish have larger hearts and blood vessels. Due to the loss of haemoglobin and erythrocytes, their blood became unusually thin, but they still had a circulatory system that could handle huge volumes.

Kristen O'Brien and Bruce Sidell described the aforementioned uniqueness of the Icefish physiology in their paper. Also, they proved that they spend a large amount of energy in circulating the extra blood present in their large vessels. Generally, a fish in the temperate region would delegate about 5% of its resting metabolic rate to the heart. An Icefish goes the extra mile by designating 22%. We now know that the majority of oxygen exchange in an Icefish takes place through its gills, with a small amount taking place through the skin.

The loss of haemoglobin also created a new problem. The function of breaking down nitric oxide is overshadowed by its oxygen transfer function. Now, because nitric oxide wasn't being broken down, something had to change. The icefish underwent physiological changes to overcome this hurdle. The presence of nitric oxide increases mitochondrial biogenesis, the process by which cells increase in mitochondrial mass; muscle hypertrophy, the increase in the size of skeletal muscle, and angiogenesis is the physiological process through which new vessels form from pre-existing ones.
Apart from these three processes, higher levels of nitric oxide also led to an increase in tissue vascularisation, and more importantly, an increase in the lumenal diameter of the blood vessels. All these characters already exist in the Icefish, indirectly allowing it to compensate for the loss of haemoglobin and its low capacity to carry oxygen.

The evolutionary process of an Icefish began with an imbalance of such a magnitude that it sent ripples across on a geographical as well as molecular level. Conclusively, it ended in the calmness that once initiated it.
James Ivory once said, "When you least expect it, Nature has cunning ways of finding our weakest spot." Be that as it may, nature does show a way out, and brings order to its own chaos. It settles the unsettled, and more importantly, always finds a way to survive.

Image retrieved from: https://pxhere.com/en/photo/949663

AN ABIOTIC BASIS OF BIOLOGY

-By Satchit Chatterji
The University of Groningen, The Netherlands

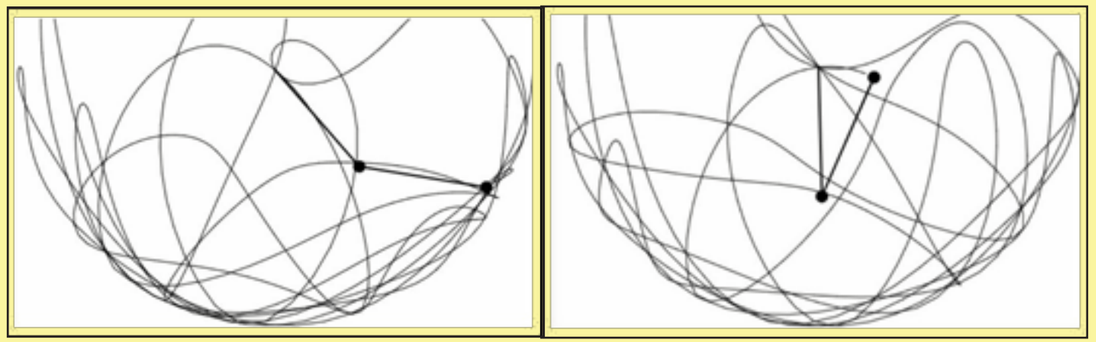
Life is complex. That fact does not need to be stated twice, especially since the reader of this article is perhaps already well-versed with several sub-aspects of life, be it from experience or academic review. Biology, being an ancient domain of research, has been trying to break down this equally ancient question with some, but incomplete, success. Alongside, it has influenced (and been influenced by) other disciplines in science, most recently, and of importance to this article, the field of *artificial intelligence*. AI is still in its infancy, being only around 70 years old. However, its contributions are growing exponentially in volume and consequence, thus may prove invaluable even to one of the oldest of the sciences.

Several techniques in machine learning had been originally inspired by biology (even if they are significantly different now), for example genetic algorithms and neural networks[1]. In this article, I would like to touch upon two important, and marginally related ideas - chaos theory and emergence. I would also ask the reader to take analogies as indeed imprecise, however they will, with some hope, form a solid conceptual foundation in the reader's mind.

Chaotic Systems

Chaos theory is a fairly recent field of mathematics that talks about complex systems, especially of particles, which are likely to *decend into chaos* relatively quickly. In more precise terms, a chaotic system is one that can have immensely different outcomes over time, given almost exact initial conditions. Thus, these are also called nonlinear systems, since the variance of outputs and inputs do not have a linear relationship.[2]

To illustrate further, we may look towards its early days. In 1961, meteorologist Edward Norton Lorenz was experimenting with computer simulations of weather-prediction models[4]. Within the set of experiments were two simulations where one of the initial variables was set to 0.506, a relatively precise approximation of the original 0.506127. This seems like a minor change, and indeed it seemed so to Lorenz as well. He expected perhaps a small difference in the weather patterns predicted in both models, but the actual results found were significantly different. Thus evolved a common metaphor used to describe chaos theory - the flap of a butterfly's wing in the Amazon is enough to cause a hurricane in Texas. This is also



(a) Mass of lower weight = 10.0 (b) Mass of lower weight = 10.1

Figure 1: Path traced by the lower mass of a double pendulum setup, with minor differences in initial settings. This is a chaotic system. Code influenced by Shiffman1.

colloquially known as the *Butterfly Effect*.
How does this relate to biology? Well, ever since the existence of the field, biology has been treated mainly as an *observational* subject, whereas for hundreds of years, the other natural sciences - physics in particular - transitioned to have a more *predictive* outlook[5]. It is only in recent years that biologists are looking towards prediction and verification, especially in the interdisciplinary fields of computational and quantum biology. Chaotic systems have been studied quite thoroughly in mathematics, and predictive machine learning models have been built, mainly focused on short-term prediction.

One of the main realistic interpretations of chaos theory is that it might as well be impossible to measure every particle that can influence a system accurately. Using an earlier example, weather patterns cannot be predicted far into the future, as so many variables are responsible for overall behaviour - humidity, air temperature, the rotation of the earth - just to name a few. Financial markets are inherently chaotic as well; stocks are influenced by a large chain of factors that make prediction just *slightly* better than random in the short term, and *wholly unreliable* in the long term[6].

In terms of fundamental biological systems, some suggest that chaos may play a role in genetics, but feedback loops exist to regulate this[7]. If a system-state is going too far off-course with respect to an optimal operating state (analogous to the body temperature of a warm-blooded animal), then correctional measures exist to bring it back. Over time though, chaos affects genomes too. The environment that a gene is replicated in affects the properties and probabilities of its mutations. Think of other, traditionally 'random', variables that are responsible for variation and survival - randomness in this sense is a pillar that holds up the temple of mutation and crossover. If one starts with our last universal common ancestor, and attempts to measure it and predict what future cells would look like, it is near-impossible to predict a giraffe. The amount of genetic diversity in the living world right now is a testament to the importance in understanding how chaotic systems evolve and grow over time[8].

Emergence

Emergence is quite a tricky phenomenon to describe. Essentially, when a system consists of simple beings ('agents') making decisions based on simple rules, the most unexpected behaviour might arise[9]. For example, there are no rules in a single water molecule that dictate the shape of snowflakes, yet they are all 6-sided. Ants follow a set of simple reactionary rules, yet somehow are able to build large nests, intricate tunnel systems, and even find optimal places (furthest from the entrances) to relocate dead bodies outside their nests[10]. A good visual example of this in the animal kingdom is flocking. A system has a set of birds, and they only follow a set of three personal rules, described first by Reynolds[11]:

1. Don't crash into neighbouring birds.
2. Try to align your direction of flight with birds neighbouring you.
3. Try to fly towards the centre of neighbouring birds.

This dogmatic set of rules are enough to approximate real birds flocking[2, 9, 11]. Figure 22 shows one frame of this simulation. Other creatures show flocking as well, for instance, bees, ants and fish. Each may have its own variation of guidelines, or may follow a different doctrine altogether. A more abstract, and perhaps more controversial example of emergent behaviour is *consciousness*. Many cognitive scientists believe that consciousness is just an emergent property of neurons that follow well-described and well-understood physical and chemical laws[12, 13].

The main point here is that simple rules acting on simple agents can have unreasonably complex results. Note that in all these cases, the agents act independently. We call these types of agents *autonomous*. Despite no rules dictating direct interaction or decision-making with other members of the population, the group as a whole displays

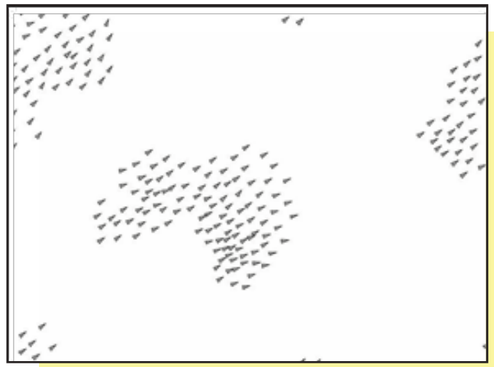


Figure 2: A simulation showing how artificial birds called boids form flocks using three simple rules. The agents' flight-paths were randomly initialized. Image self-made, based on open source code by Shiffman[2, 3].

complex, intelligent behaviour[9]. The *purpose* of the group is only apparent to an outside observer, and the rules followed by each autonomous agent is not enough to explain this purpose – one needs to consider many other variables, including other agents and the environment that they exist in. Some even would not call this *purpose* inherent to the beings or the rules, since it is only a by-product of something less significant.

A Coalescence of the Sciences

One of the earliest studied and most complex ideas within genetics is that of *morphogenesis*, or the processes during which an organism acquires its physical patterns and shapes. Zebras all have stripes, but they are all unique. Tigers have stripes, similar to zebras, but the patterns are very different indeed. What dictates this?

In 1951, mathematician and computer scientist Alan Turing, known also as one of the fathers of modern AI, wrote his only biological paper, *The Chemical Basis of Morphogenesis*[14]. In it, he describes in detail a system of deterministic, non-linear different equations (a chaotic system) that may dictate pattern formation. This paper is still being cited today as an important landmark in genetics. In my opinion, stripes, and generalised patterns, are indeed an *emergent* property of the set of cells from which it grew. Nowhere in the cells are there information to form specific patters - this is a byproduct of inter-cell interaction. One dark cell upon white does not form a pattern.

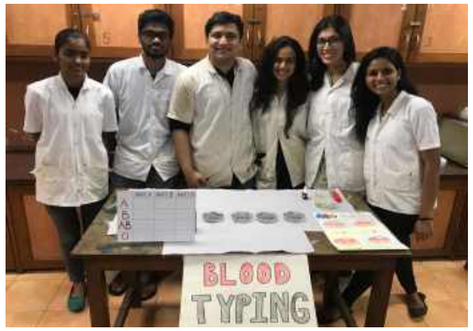
A unique problem with emergent properties is that it is always with respect to a set of internal deterministic rules, but also with respect to an outside observer[9]. Whether or not a particular group behaviour is *expected* from the rules is thus subjective. Biologists take for granted that the purpose of evolution and natural selection is the propagation of life, be it at a general-, or species-level. However, this purpose, might just be the by-product of the simple dictums of Darwinism (or any other evolutionary school of thought, for that matter). Amino acids know not the purpose of the proteins they build, they just fall into the most stable chemical configuration dependant on the environment. Whether or not *the propagation of the species* is the goal of evolution is not known to, and thus not directly followed by, the vast majority of those creatures who reproduce in the first place.

Thus it seems necessary to port our understanding of emergence and chaos into the wider reasonings of modern-day biology. Studies into the relationship of chaos and biology have already yeilded results, especially within the medical sciences[15]. Exploring phenomena in terms of different levels of perception is absolutely necessary in order to understand it as best we can. The volume of research humans are turning out year after year is astounding, thus it is definitely beneficial for the godfather that is biology to inculcate ideas from the one of the youngest members of the scientific family - artificial intelligence.

Department Activities

Orientation for First Year Students

Popularisation of Science



Popularisation of science was celebrated in college with the aim to fascinate and inspire young minds towards the basic sciences. A stall in the foyer and several live stations were set up in the life science laboratory by the department. Second and third year students of the department actively participated in the event by demonstrating and explaining a variety of experiments and models to inquisitive school and college students.

Khandala Seminar

MLP (Multiple Layer Packages) Drive

Social Outreach by SY's

SYBSc Life Science students conducted a science workshop for the ninth and tenth grade students of the BMC school at Worli Sea face in collaboration with Teach for India. Live demonstartions and exciting experiements were shown to the students keeping in mind their school curriculum. The event was conducted under the guidance of Dr.Radhika Tendulkar, Dr. Binoj Kutty, Dr. Nandita Mangalore, Dr. Bhaskar Saha and Dr. Sangeeta Shetty.

NOBEL

William G Kaelin Jr, Sir Peter J Ratcliffe and Gregg L Semenza jointly received the Nobel Prize for Physiology or Medicine "for their discoveries of how cells sense and adapt to oxygen availability."

Their findings have helped in understanding the basis of how the level of oxygen affects cellular metabolism and physiological functions. Our cells constantly need to adapt to fluctuations in oxygen levels by adjusting their metabolism rate. These events trigger an adaptive process called the hypoxia response. When a cell experiences a hypoxic environment, HIF-1α (a hypoxia inducible transcription factor) accumulates in the nucleus. This along with another protein, ARNT (Aryl Hydrocarbon Receptor Nuclear Translocator) regulates the expression of hypoxia-regulated genes. In normoxic conditions, on the other hand, the HIF-1α gets degraded. HIFs are known to promote angiogenesis and formation of blood vessels during development.

Their research has paved the path for understanding oxygen sensing which is absolutely paramount in order to study a large number of diseases. It has also influenced academic laboratories and pharmaceuticals in development of drugs that can interfere with different disease states by inhibiting or activating the oxygen-sensing machinery.

ILLUSTRATION - Khyatee Shah

ILLUSTRATION - Khyatee Shah

Albert Lasker Basic Medical Research Award

The two scientists that won the 2019 Albert Lasker Basic Medical Research Award discovered that the adaptive immune system is composed of two distinct cell types, B cells and T cells. They showed how the immune system distinguishes between self and non self and disproved the commonly held belief that lymphocytes are of a single cell type. Their discovery challenged the notion of the thymus being a vestigial organ that was prevalent at the time. They discovered that the thymus is a site of T cell production based on their studies of mice with lymphocytic leukemia. Cooper proposed that the adaptive immunity involved two cell lineages, i.e. B cells for antibody production and T cells for cell mediated immunity. They also identified that these cells have independent origins, while B cells arise from hematopoietic stem cells, T cells arise from the thymus. They added that, cooperation between these cells is crucial for the development of immunity.

The Lasker-DeBakey Clinical Medical Research Award

Winners- H. Michael Shepherd, Dennis. J. Slamon & Axel Ullrich received the Lasker~DeBakey Clinical Medical Research Award for their invention of Herceptin. Herceptin is a monoclonal antibody i.e. antibodies made by similar immune cells that have formed from one common parent cell. This drug is made via the formation of hybridomas using antibodies from the spleen of mice. In general, hybridoma technique involves fusing certain myeloma cells (cancerous B cells), which can multiply indefinitely but cannot produce antibodies, with plasma cells (noncancerous B cells), which are short-lived but produce a desired antibody. The resulting hybrid cells, called hybridomas, grow at the rate of myeloma cells but also produce large amounts of desired antibody.

It may be a potential form of therapy that could be performed along with conventional chemotherapy. The oncogene HER2 (Human Epidermal Growth Factor Receptor-2) is mostly responsible for cell division and regulation. If mutated, it causes tumor formation due to uncontrolled cell division. In mutations resulting in a malfunctioning receptor, the Herceptin antibody binds to such a receptor. As a result, the receptor cannot interact with its outer environment and receive signals by ligands like EGF. Thus, the chances of tumor growth and division reduce. Herceptin is particularly useful for breast cancer treatment.

ILLUSTRATION - Khyatee Shah

Bhatnagar

Kayarat Saikrishnan of IISER, Pune, and Soumen Basak of National Institute of Immunology, New Delhi, are the awardees of the Shanti Swarup Bhatnagar prize for the Biological Sciences, 2019.

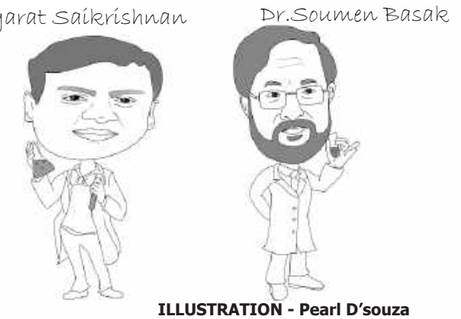


ILLUSTRATION - Pearl D'souza

Infosys

The Infosys Prize 2019 in Life Sciences has been awarded to Dr. Manjula Reddy for her discoveries regarding the structure of cell walls in bacteria. For a bacterial cell to divide, it must increase the amount of its cell wall. This would require the breaking of the cell wall to allow addition of new components of the cell wall matrix to expand it. Dr. Reddy's work involved deciphering the identity of the enzymes playing a role in breaking the cell wall. Proteases regulate these 'spacemaker' enzymes. The presence of an adapter allows the targeting of these enzymes to reach the protease. Lack of endopeptidases led to the cell wall becoming structurally unstable and subsequently led to cell explosion. Considering this process is crucial for bacterial growth and that these enzymes are conserved across pathogenic bacterial species, they offer new targets for antibiotic action. This novel target is different from that of beta-lactam antibiotics wherein the enzyme involved in linkage formation between peptides in the cell wall is targeted.

ILLUSTRATION - Aryaa Apotikar

Alumnus Speaks- Rewinding Dr. Vidita Vaidya's Journey into Science

Dr. Vidita Vaidya is a neurobiologist who studies the neurochemistry of emotions as well as molecular, cellular and epigenetic changes that contribute to long term behaviour in animals. She is currently a professor at the Tata Institute for Fundamental Research (TIFR), Mumbai.

Dr. Vaidya is an alumnus of St. Xavier's College (Mumbai), after which she pursued her Doctorate in Neuroscience from Yale University and Post Doctorate from Karolinska Institute and University of Oxford. Her distinguished academic career is decorated with awards such as the National Bioscientist award in 2012, the prestigious Shanti Swarup Bhatnagar Award in Medical Sciences in 2015 and most recently, in 2019, she was awarded the Sree Ramakrishna Paramahamsa Research Grant.

Q1. What inspired you to take up research?

If I look back, I found animal behaviour conceptually interesting. To some extent this was because I grew up in the Ciba- Geigy Research centre campus in Goregaon, an area where there were a lot of animals. We were frequently visited by leopards, foxes and lots of snakes including cobras. We often had conversations about wildlife and nature while I was growing up. Moreover, there was nothing that came on television at the time, except if you were lucky you had access to documentaries like Planet Earth. Every Wednesday evening though, there would be special talks that I often attended. One particular talk of these, I remember really well. It was by a couple who had gone to Africa to study hippopotamus' in the wild. Their study was about aggressive behaviour in the wild and they showed some incredible videos. I was very fascinated by the fact that this could be an official job. Then I started reading about Jane Goodall and Dian Fossey. I thought of this job of studying behaviour in the wild as the coolest profession on this planet. I did not end up doing anything like that, in that I now study more of cellular and molecular behaviour in laboratory conditions, but conceptually I was very enamoured by the job of an explorer. I also grew up on a campus with a lot of people who did science for a living. I found research very fascinating but I knew early on that I did not want to be a medical doctor. Becoming a scientist was like joining the family business for me because my parents were researchers and clinicians. I don't think I ever really diverted from wanting to become a researcher, unless you count the time when I was very young and wanted to become an archaeologist!

Q2. What has the role of St.Xavier's College been in building your passion for science?

When I joined Xavier's college, Father Lancy was the principal and also the one who lead the Life Science Department. We had wonderful professors who were all very easy to talk to. Although, I think a lot of my learning took place even beyond the classroom. When I was in the first year, four students including me were selected to be a part of the Caius program which was very exciting because we got to stay back after college hours. Now that I think about it, what we did was not that exciting but it felt like a big deal then. We poured plates (I must have poured some ten thousand petri plates!), autoclaved stuff, set a few things on fire and then later I moved on to a little bit of molecular biology for Sorab Dalal who is currently a faculty member at ACTREC. I keep telling him that he permanently put me off of molecular biology because he made me work on a whole lot of plasmid preparations and I discovered then that molecular biology was not where my heart was. Essentially, we did the grunt work and were like apprentices

but we thought it was the coolest thing because we got to work in this laboratory where all of the interesting work took place. Atmosphere wise, Xavier's was a place where a lot of people wanted to go ahead and do a PhD and were excited by what they were doing. Overall, it was a fantastic place with great teachers and a lot of available time to spend in the library. I spent most of my time between the library and the Caius laboratory, other than the woods downstairs.

Q3. Since your last interview for Lignum Vitae, are there any highlights from your research that you would like to share with our readers?

Last year, we made a very interesting discovery that we just published in May 2019. A large amount of glucose is used to run the nervous system and in fact a fair bit of glucose is consumed just to maintain the resting membrane potential. Action potentials are also highly energy demanding and hence there is a continuous requirement of energy by the brain. Additionally, these are cells that do not die and do not turnover, their bioenergetics have to be maintained throughout one's lifespan. While we know a lot about other metabolically important tissues like the liver and the muscle, we know very little about what manages to maintain the number of mitochondria within neurons and what regulates the function of the mitochondria. We stumbled upon a finding in collaboration with one of our colleagues Dr. Ullas Kolthur. We discovered that serotonin, which is normally thought of as the neurotransmitter that regulates mood and plasticity, also directly regulates the production of mitochondria in neurons and drives their function. So this is an old, conserved and unexpected role of serotonin. It is a very interesting discovery because one does not generally think of this neurotransmitter as being a metabolic energy maintenance molecule in the brain.

Q4. Neuroscience is a fast growing and attractive field. Based on your experience, what aspects of it will have maximum scope in terms of novel discoveries or unanswered questions?

You think about this as the blind men trying to describe an elephant. Up until now, everyone has been picking their favourite circuit and studying it as best as they can at all levels. The complexity with neuroscience is that you can start at a circuit level, you can go to the neurons, you can go within neurons and then you can even study how that circuit communicates with another part of the brain. Usually people study upto two or a maximum of three circuits communicating with each other. For instance, the prefrontal cortex talking to the amygdala or the hippocampus communicating with the hypothalamus. Nothing functions in isolation within the nervous system because it is a complex network. The difficulty with studying a network is that you have to zoom out and then zoom in for detail. The last several decades have been spent on zooming in on details, but the minute you zoom out it all becomes fuzzy because you do not know how all the details fit as you get to higher levels of organisation. That is the direction the field will now take. Scientists are now not recording from cells within one brain region but from a large number of neurons in distributed networks and trying to understand how this results in the emergent property of function. It will mean that we will inevitably drown in big data. This cannot be manually or even computationally solved in a simple manner. You will need algorithms, machine learning and large data analysis tools to analyse the scale of data you generate. However, there is still always room for detail because in detail you sometimes discover fundamental principles that apply to the entire nervous system. Another direction this field could be headed towards is more human related neuroscience, because imaging tools have begun to, and will continue to improve, giving us a better resolution into the human nervous system.

Q5. You have spoken about the hyperactive stress response condition in some of your previous talks. Has there been any scientific progress in developing methods to regulate this pathway in adulthood?

A5. The strongest programming of life long risk for psychiatric disorders does happen in the early window. The early

period has a massive influence on how you will respond to stress in adulthood. That is not to say you cannot attempt to increase resilience and decrease vulnerability to stress in adulthood, but all psychiatric disorders happen because of failures in distributed networks, multiple circuits in the brain simultaneously not working. A lot of the therapy today focuses on elevating levels of neurotransmitters. So we go after big hits, but this also has side effects and you cannot help it. I think we are better than the dark ages of psychiatry though. There is a lot more rational thought on new drug designs, and yet we are still skirting the edge of fundamental change, making discoveries that can shift the network into a functional state such that you get an immediate and rapid effect. Right now, the numbers are ridiculous and insights from neuroscience indicate that the first decade of life should be prioritised as a major public health initiative so that this burgeoning psychiatric crisis is not set up in the long run.

Q6. Considering biology has many facets, how does one narrow down one's choices and select the most suitable field for them?

I would not even worry about that at the undergraduate level. My general view is do not narrow down. This inbuilt desire we have to narrow down is very risky. I think it is inbuilt partly because we have been put into these tracks so early that the idea of jumping tracks causes a huge amount of trauma to everybody. Let undergraduate level studies be absolutely broad. You may have things that you particularly like and that can be defined by what you have been taught or who has taught you the topic or sometimes it can be defined by something as arbitrary as a small project you did for a short period of time. You might think you love a particular field, but that is because you have only had time to read or hear about that, you haven't had time to read about anything else. So wanting to hurry and label everything you like is in my opinion a slippery slope and so be open at least at the undergraduate level. I would advice you all to try out different kinds of projects so you get a sense of what fits your skin and there will be multiple things that will fit your skin. But do not define very quickly what precisely you want to do. Seeing the way things are going right now, you may want to diversify the courses that you take to give you the capacity to stay with the field as it grows. If a little bit of basic programming can be incorporated into your curriculum, it would help you all tremendously. Look at what you may need irrespective of where you end up and fill up those needs using courses online, summer courses etc where you learn something from scratch. I would do all that instead of worrying about nailing down what I want to do next.

Q7. What are some of the habits that you think can be inculcated at our stage to pursue a life in science and research?

I always believe that there are no characteristic traits you have to have to be a scientist. Fundamentally, you have to enjoy doing science. Different people will be different kinds of scientists. Some are stamp collectors and love making observations and there are some who are super reductionistic in wanting to understand mechanism in excruciating detail and that personality type will not want to go stamp collecting. You do not need to be one over the other. I think what is most important is figuring out what fits your skin. I am a phenomenologist. I enjoy mechanism, but if I had to study mechanism without discovering new phenomena I would get bored very quickly. Something you have to figure out for yourself is what you enjoy and what will sustain you. If I had to write papers about very similar things over and over again, I will get bored. That is my personality type. I am a 'big picture' creature so I like moving out quickly to the bigger picture and contextualizing, which means I may miss out detail.

Q8. Research in biological sciences can be strenuous and requires a lot of patience. How does one keep oneself motivated through the course of it?

The strenuousness is experienced the most when you are a masters and PhD student, because you have to sometimes repeat the same experiment over and over again and sometimes they fail, on a colossal level. That is when the pain of it is most acutely felt. Sometimes, you spend a month on something that flops. But even in that period of time, you realise that you learnt something. In academia, you are buffered from every single failure, because now you experience lab level failure which means that the failure is experienced by multiple people and then it is your job to partially buffer their pain. But failure is a part of the process, you cannot avoid it. I think part of the problem is that you are all very accustomed to practicals working and getting perfect data in your school and college years. But most experiments in reality do fail, that is the baseline and then every now and then they work. This mismatch causes a lot of trauma in the first few months after you first transition into a genuine research program where you do not know what your results are going to be. Secondly, you tend to idealise what a research environment should be like and so there is a mismatch between your expectations and reality. Personally, the reason I think I continued to remain motivated is that this is one of the few places of human endeavour, like art, which is beyond our lifespan. People have wondered about the conceptual idea of where thoughts and emotions originate from for hundreds of years. It is not a new idea. We just use new tools to answer these questions now. Three hundred years later people will still ask the same questions and think of our tools to be primitive. It's not just a job, you get to be a part of something larger than you and that is the magic element of science for me. There might be long periods of time when nothing great happens with your science, but that does not mean that for all that time you sit in a dry patch. You can always enjoy the creativity of somebody else's science. And that is what keeps sustaining you. Conceptually, you can be blown away by the magic of science and if you remove that, you will find it harder to sustain.

Q9. Conventionally, students tend to believe that the scope of research is better abroad. But what is the ground reality and how much scope does India have for biological sciences?

There are several factors that come into play when trying to define 'scope'. If you go to societies that have a more established culture of scientific research and academia, you will not have to build up anything, you will just have to focus on what you want do. At the same time, you will enter a far more crowded place where a lot more people are attempting to do the same thing as you. In India, inevitably there is a slight pioneering effect in terms of setting up something in a new environment which is something I find interesting. However, it can be a problem for some people because a lot of your time is spent in setting up than on your primary goal. People need to ask themselves where they see themselves happiest in all multiple dimensions of who they are as a human being.

However, I am also a firm believer in leaving your comfort zone and in the importance of seeing the world. I think travelling is essential to widen your mind and to think about what you want to do. All of the things I said are true, but I wandered the world myself and then came back. And I still keep travelling. So my general advice to people doing their undergraduation here is to do their masters program somewhere in the country that gives you a broad enough base and training for where you want to go and then the world is your oyster. Open up the possibility of doing your PhD elsewhere, even some place new to you in India. But generally, I would say, challenge your comfort zone and go a little broader than you planned.

Q10. What advice would you give your younger self that just entered the arena of research?

I would tell my younger self to retain a sense of humour. I do it now much more often and more effectively than my younger self did. The younger version of me got stressed about little things that I now tell myself to forget about. Have the ability to look at a situation, no matter how awful it is and laugh at the absurdity of the situation you find yourself in. That distance and attachment is so critical to buffer what life will send your way. A quote that I stand by is , "Take your work very seriously, but do not take yourself very seriously."

An Interview with Dr.Maithreyi Narasimha

Dr. Maithreyi Narasimha is a scientist working at TIFR as faculty since 2006. Her current research is on cell adhesion, epithelial morphogenesis and cellular reorganisation. Dr. Narasimha studied medicine as an undergraduate at St.John's Medical College, Bangalore. Her doctoral research was on Genomic imprinting in the mouse in Azim Surani's lab at the Wellcome Trust/Cancer Research UK Institute, Cambridge University (The Gurdon Institute). After a short postdoctoral stint in Maria Leptin's lab ,Germany studying cell shape changes during Drosophila gastrulation, she returned to Cambridge to Nick Brown's lab (The Gurdon Institute, Cambridge) to study cell adhesion in the context of epithelial morphogenesis. Join her as she explains some of the fundamental concepts of cell biology and delves into cutting edge research integrating various aspects of biology.

Q1. What are some of the aspects of genomic imprinting that you worked on during your PhD and based on your studies what determines which parental gene undergoes genomic imprinting ?

The genomes we inherit from each parent are not functionally equivalent on account of the fact that some genes, called imprinted genes, are mono-allelically expressed in a parent-of-origin dependent manner. The implication being that at some gene loci, only the paternal allele is actively expressed while the maternal allele remains silent, while at the other loci, only the allele from the mother is actively expressed while the paternal allele remains silent. For these genes, the organism has only one functional allele. This phenomenon is referred to as genomic imprinting.

Earlier work from my PhD mentor, Prof. Azim Surani at the at the University of Cambridge had demonstrated that it was not enough for an organism to be diploid and have two sets of genomes, but that it was necessary to have a maternally derived and paternally derived genome. In seminal experiments using nuclear reconstitution in the early 80s, Azim Surani showed that androgenetic and gynogenetic embryos - embryros reconstituted to contain two paternal/ sperm-derived nuclei or two maternal/ovum-derived genomes respectively instead of one of each - fail to develop to term. For my PhD in Azim Surani's lab, I investigated what went wrong during the development of such embryos. Specifically, I investigated whether imprinted genes, whose dosage is disrupted in such embryos, govern proliferation and /or differentiation of embryonic lineages. For this, we made chimaeric mouse embryos containing marked androgenetic or gynogenetic cells in addition to wild type (biparental) cells and examined whether the marked cells in each type of chimaera was distributed to embryonic lineages in the same manner as wildtype cells. This allowed us to uncover biases in the allocation of diploid cells with uniparental genomes.

At that time, only a few imprinted genes had been identified. These included H19-a non coding RNA, Igf2 and Igf2R-an insulin like growth factor and its scavenging receptor, and p57 Kip2, a cyclin dependent kinase inhibitor. Their functions suggested that imprinted gene dosage may fine tune the growth and differentiation of tissues. Paternally expressed genes such as Igf2, were seen to enhance the growth of the embryo or the placenta while maternally expressed genes (like p57 Kip2) reduced growth. This led some people to propose "the parental conflict theory" for genomic imprinting that suggests a conflict between maternal and paternal alleles of a gene with respect to optimising the acquisition of maternal resources during the development of the organism. A much larger list of imprinted genes has now been identified, and while newer theories have been put forward to explain why some genes are imprinted, genomic imprinting has provided an excellent model to study the epigenetic regulation of gene expression.

Q2. In an article earlier this year, you mentioned that when you started off as a scientist you were fascinated by how cells in an embryo know where they have to go and how these cells organise themselves into tissues. Based on your extensive studies and research since then, could you please explain to us what triggers the differentiation of cells into specific lineages?

In my PhD, I was looking at whether changes in gene dosage affect what cells could become or differentiate into. This got me interested in understanding how cells, once differentiated know where to go. All life begins as a single cell, and the combination of cell division and differentiation generate large numbers of cells of different types. Differentiation into specific lineages relies on signals that will typically lead to the expression of transcription factors whose target genes govern lineage specification decisions. In the fly embryo for example, gradients originating from the head and tail ends of the embryo set up gene expression patterns that subdivide the embryo along this axis to result in the formation of embryonic segments each with its distinct combinatorial gene expression code. This code dictates where head structures form, where wings form and so on. Likewise a gradient along the perpendicular axis (front-back) results in gene expression patterns that enable the specification of lineages. Both gradients are maternal in origin, that is, they are already present in the oocyte prior to fertilisation. In general, differentiation into specific lineages may rely on signals produced either within the cell (intrinsic signals), or be the result of signals received by it from the surrounding cells. In either case, the signal results in the transcription of specific genes (transcription factors) that specify lineage. It is also necessary for many genes be turned off in each lineage. Typically, differentiation is hierarchical, with commitment increasing progressively. Today, we understand enough about this process to be able to take embryonic stem (ES) cells and differentiate them into the lineage of our choice by giving them the right intracellular and extracellular signals. Lineage specification decisions are stable in the embryo - neurons in the brain stay neurons- but are, in principle, reversible. Differentiated cells can, in case of injury or stress, dedifferentiate to become more stem cell like or transdifferentiate into a different cell type. An approach that has gathered a lot of attention today is the derivation of "induced pluripotent (iPS) cells" from differentiated cells such as a skin cell. This has enormous applications for regeneration and replacement of tissues and organs as well as for gene therapy.

Q3. What inspired you to carry out research on cellular reorganisation? What has your experience, transitioning from genetics to cell biology during your career in research been like?

Making cells of the right type and in the right numbers is in itself not sufficient to pattern a tissue, an embryo or an animal. Tissues and organs have very stereotypical final shapes. It's common to hear someone say, something is "heart shaped" or "finger shaped" or is "tubular" or "stratified". But how did tissues come to be shaped that way? Developmental biology has for long focused on understanding the genetic regulation of tissue specification: that is, how you make cells of a particular type, such as for example neurons, skin, muscle. What we understand much less about is how these cells, often thousands of them, arrange themselves to form complex, dynamic and intricately patterned assemblies that tissues are. We are interested in understanding what guides cells within tissues to adopt the behaviours they exhibit and how these behaviours are ordered in space and time to enable tissues to be sculpted to their final shapes and positioned at their final destinations. How cells coordinate their behaviours to enable tissues, organs and animals to be sculpted to their final form is a question that has fascinated me. This has involved looking at the lives of cells up close and in real time. This has meant that we do a lot of high resolution imaging of cells, and the organelles and molecules within them as tissues are being built in the embryo or as tissues heal themselves upon injury.

Genetics continues to be very important as it allows us to perturb gene function, and through its effects, infer the role that that gene plays in tissue sculpting. We have devised ways by which we can perturb gene function in single cells, in patches of cells, or in all the cells of a tissue. This has allowed us to address whether cells behave autonomously or whether they are influenced by their neighbours. Technology - both with respect to imaging and gene manipulation - is developing very fast and a challenge is to keep abreast with its rapid pace. Confocal and superresolution microscopy, genome editing using CRISPR, and optogenetics which enables the modulation of molecular function by light, have revolutionised cell biology and genetics. Cell morphology and behaviour can also be very quantitatively analysed and this has necessitated the development of computer codes. My younger colleagues - my students - have been very keen to embrace these developments and are putting them to good use in their research projects.

Q4. When you began your research at TIFR, your sub area of interest-cellular organisation into tissues – was an idea not many in India had ventured into as yet. What are some of the obstacles you faced while pioneering research in this discipline of biology in India and how did you deal with them?
The work we do relies very heavily on high resolution imaging, in real time. When I joined TIFR in mid 2006, there were no functioning confocal microscopes in the Department. The first one arrived in early 2008. To get around this, I would travel to NCBS, Bangalore on weekends with my samples to use their microscopes. Today, I am pleased to say that TIFR, Mumbai boasts of an excellent imaging facility including a superresolution microscope and an electron microscope. Over the years, the number of groups whose research has depended on it has also grown.

Q5. What are some of the mechanical and physical factors that influence the organisation of cells into tissues?
Cells and tissues can be influenced by the push and pull exerted by neighbouring cells or tissues and by the stiffness of the substrates (extracellular matrix/ other tissues) on which they sit. The push and pull forces result from the contractile activity of the cytoskeletal filaments, mediated by motor proteins (actin, microtubules and their associated motors), and are transmitted to neighbouring cells or to the substrate through a class of molecules called adhesion molecules (cadherins and integrins). Today, these forces (molecular, cellular and tissue scale) can be measured using tools such as optical and magnetic traps, laser ablation and atomic force microscopy. These forces must be modulated in space and time, and be integrated to allow the right kind of deformation of the tissue. How this regulation and integration occurs is a fascinating problem that we and many others are investigating. The force generating machinery is itself under genetic control. A muscle cell expresses a unique set of contractile proteins compared to an epithelial cell, that are also arranged differently (in sarcomeres). This is under the control of lineage specification genes. How the products of genes influence force production, for example the ability of a muscle cell to generate larger forces, is an interesting question. Equally interesting, if not more so, is how force production influences the function of the products genes encode. Forces generated by the cytoskeleton have been shown to influence gene transcription, protein distribution and protein activity. This mechanochemical feedback ensures that tissues are appropriately patterned.

Q6. What orchestrates the assembly of cells of the same tissue into different layers and once these layers are established what is the kind of interaction that occurs between these layers?
The formation of layers is a conserved theme in the development of many animals. Layers can form in many ways. One way to form a new layer is by invagination. Invagination, analogous to punching an inflated balloon, is achieved by coordinated cell shape changes that cause constriction of the apical end of the cell. This is analogous to how you might build an arch in a building using wedge shaped bricks or stones. Another way of creating layers is by cell sorting- cells with different affinities for each other can "sort out" to form layers, one enveloping the other. Cells with different adhesive affinities thus behave like immiscible liquids. Once separated, layers can interact with each other both chemically (secreted signals produces in one layer can bind receptors in the other layer) and physically (through the extracellular matrix). These interactions are crucial for the behaviours of cells in each layer.

Q7. What role does time play in regulating specific cell behaviour?
This is an interesting question. The development of an organism is like a choreographed dance sequence. Time puts constraints on developmental processes: each process has a window of opportunity during which it must be executed. The failure to do so can have a snowballing effect on the processes that follow. The ordered expression of transcription factors dictates fate specification. Likewise, the temporal order of cell behaviour is necessary for shaping tissues. A striking example of this the formation of somites, blocks of mesenchymal tissue that form in sequence with a fixed periodicity. What sets the order and the pace of developmental processes is a fascinating question. Cell fates and behaviours that underlie developmental processes are themselves a product of the molecular processes that drive them. These molecular processes give the cell behaviours their characteristic time scales. However, the same cellular processes may operate at different timescales in different tissues, different contexts or in different organisms. Understanding how different molecular processes might contribute to differences in the speed of a cell behaviour such as cell shape change or cell migration, and whether these differences can account for the differences in the duration of the developmental process are fascinating questions.

Q8. Why did you choose Drosophila melanogaster specifically as the model organism for your studies?
Drosophila is blessed with over a hundred years of genetics: this makes it a very genetically tractable model. Mutants and transgenic lines are easily made. Drosophila also lends itself to very high resolution imaging in real time and this is ideal for cell biological studies. I would argue that Drosophila is the ideal organism to investigate the molecular and mechanical basis of the organisation of cells into tissues in multicellular organisms for two reasons: first, its development encompasses the entire range of processes that include tissue invagination, tissue extension, single and collective cell movement, to name just a few, and second, the molecular and mechanical basis of these processes are conserved across evolution. For me, it is also intellectually very satisfying to work with Drosophila as it allows one to get a deeper understanding of the problem than other model systems will allow.

Q9. Your lab conducts research on different parts of Drosophila- the epidermis, eye, the wing and the embryonic nervous system. What are some of the fundamental differences in the development and organisation of these tissues?
Our rationale for looking at different tissues and sequential developmental processes involving the same tissues, is to allow us to capture the diversity in the modes of cellular organisation within the same organism, and to use that to inform ourselves of the mechanisms that contribute to this diversity. Equally, it should inform us about what mechanisms are conserved at the molecular or cellular levels

Q10. What, according to you, are some aspects of cell biology and developmental biology that students at our stage can focus on now to enable us to understand the complexities of cellular morphogenesis and tissue organisation?
My pet peeve is that students studying cell biology as undergraduates often have a "static" picture of what's going on in cells in our bodies. I did too. It is anything but static: the molecules within the cells are busy moving around, changing locations in response to what they sense (chemically) or feel (physically). So too are the organelles that we are used to drawing: many including the mitochondria divide and fuse and are constantly changing shape. The cells themselves are very dynamic entities: in addition to dividing or dying, they change shape, exchange neighbours within or move out of the tissue they were part of. Appreciating that a cell is a four dimensional entity whose behaviour is governed by the dynamics (in space and time) of its constituent organelles and molecular complexes that are, in turn, sensitive to both chemical and mechanical cues is a good place to start. In addition to excellent text books like Molecular Biology of the Cell by Alberts (which comes with a CD that has some excellent movies), a number of excellent and free online resources are available for those interested in exploring deeper into the topic. These include iBiology (https://www.ibiology.org/research-talks/cell-biology/) and the more recent Xbio (the explorer's guide to biology; https://explorebiology.org/collections/cell-biology) both, the brainchild of Prof. Ron Vale. Nothing however beats the excitement of watching them under a microscope with your own eyes. I still get goosebumps every time I see something new down the microscope. Come and visit us to peer into the dynamics of cells and tissues: we will be happy to share our excitement.

Q11. Is there any message that you would like to give to the current generation of budding scientists?
Doing science is a lot of fun. If you are curious and passionate about how nature works, then doing science is doing what you love. That is a privilege, a luxury. Doing science is also hard: it takes a lot of commitment and requires a lot of resilience. Breakthroughs do not happen everyday but when you are doing research, you are out to find out something about nature that nobody else knows . The possibility that you will find the answer is what keeps scientists going. If you can enjoy the journey with its successes and failures, it is not only rewarding but also the most enjoyable way to spend one's time and earn one's living!

ACHIEVEMENTS

College Toppers and Scholarships

Reanne Fronteiro - MSc topper and awardee of the Shreevrat Goenka Scholarship for a meritorious post graduate student of Life Science.

Spandan Gite- BSc 6U topper and awardee of the The Department of Life Sciences Scholarship for highest in TYBSc (6 units) Life Science.

Judith Fernando – BSc 3U topper and awardee of the Dr. M. P. Sujayakumari and the Department of Life Sciences Scholarship for highest in TYBSc (3 units) Life Science.

Annabelle Jose and **Misbah Shaikh** - Dr. M.A. Eswaran Scholarship for a deserving student pursuing the Master's programme in LifeScience.

Riyansha Arora (SYBSc) - Meenal Dinkar Rao Mugve Scholarship for highest in chemistry at the FYBSc examination and continuing with Chemistry in SYBSc and the Fr Sierp, Prof SK Chhapgar Scholarship for highest in chemistry at the FYBSc examination and continuing with Chemistry in SYBSc.

Scholarships

Ira Trivedi (SYBSc) was selected for the JNCASR Summer Research Fellowship Programme 2019 in the area of Life Sciences. She worked at the Jawaharlal Nehru Centre for Advanced Scientific Research between April - July 2019.

Arjun Udupa (FYBSc) and **Bivas Nag(FYBSc)** were selected for the 'National Initiative on Undergraduate Science' (NIUS) Camp of the Homi Bhabha Centre for Science Education (HBCSE) in collaboration with TIFR and BARC, held in Mumbai. Arjun worked with Dr Swati Patankar at IIT-Bombay and Bivas with Dr Sasikumar Menon at Ruia College, Mumbai.

Awards

The following awards were won at the research convention on "Nurturing UG and PG Research in Biological Sciences" organised by the National Education Society's Ratnam College of Art, Science and Commerce, Mumbai under the DBT-Star College Scheme:

1st Prize, oral research paper presentation:**Alicia Anand Dias (MSc-I)**

2nd Prize, oral research paper presentation:**Merlin Johns (MSc-I)**

Consolation Prize,oral research paper presentation:**Aradhya Kapoor (MSc- I)**

3rd Prize in the UG poster presentation: **Kennith Castelino (TYBSc)** and **Upasana Shah (TYBSc)**

The follwing awards were won at the Biochemistry Festival held by the KJ Somaiya College, Mumbai:
3rd Prize in the poster presentation event: **Sanskriti Agarwal (FYBSc)** and **Bivas Nag (SYBSc)**
3rd Prize, debate competition:**Sanskriti Agarwal** and **Yash Bhandare (FYBSc)**
3rd Prize, 'Ad-mad Show: **Bivas Nag, Sanskriti Agarwal, Kevin Abraham, Yash Bhandare and Khyatee Shah(FYBSc)**
2nd Prize, treasure hunt: **Bivas Nag** and **Kevin Abraham (FYBSc)**
3rd Prize, treasure hunt: **Sanskriti Agarwal** and **Yash Bhandare**

Kareena Gala (FYBSc) and **Pooja Mehta (FYBSc)** won the 3rd prize at Awareness and Action research for Youth Awakening (AARYA) Intercollegiate Interdisciplinary Undergraduate Research Competition organized by College of Home Science, Nirmala Niketan, Mumbai.

Alicia Dias (TYBSc) and **Zubia Shaikh (TYBSc)** won the 2nd prize in the event 'Let's Research' a survey and report writing competition at 'Youth for Green Fest –Climate change, the intercollegiate festival conducted by Wilson College, Mumbai.

Assumpta Fernandes (TYBSc) won the 2nd prize for her poster presentaion at the International Science Conference 'From Health to Well-Being - An Interdisciplinary Approach', held at St. Xavier's College (Autonomous) Mumbai in collaboration with Creighton University, Omaha, USA

Arjun Udupa and **Bivas Nag (FYBSc)** were awarded the DD Kosambi Young Scientist Award 2019 by Collaborative Undergraduate Biology Education (CUBE).

Extra Curricular Achievements

Dr. Sangeeta Shetty, Dr. Manasi Kanuga, Dr. Maya Murdeshwar, Dr. Seema Das and **Dr. Bhaskar Saha** won a teaching staff event at the annual sports day.

Mr.Sudhakar Kolge, Mr. Kishore Sinawane, Mr. Sandeep Pawar and **Mr. Avinash Agre** were part of the college cricket team that stood first at the intercollegiate cricket tournament hosted by MD Shah Mahila College, Malad.

Neele Ujrekar, FYBSc: (Overall) Senior Boys Individual Champion, gold medal in 100m, 200m and Long jump, silver medal in 400m and bronze medal in 800m at the annual sports day.

Mr. Sudhakar Kolge stood first in a non teaching staff event at the annual sports day

NOT ALL GREY !

Ms. Zubia Shaikh and **Ms. Karishma Katpitia**, TYBSc (2018-19) won the mentorship program jointly held by US Consulate General, Mumbai and Ekonnect foundation. Their project titled "Recycled Greywater after treatment by Electrocoaugulation won 4500 US dollars for implementation. Given below is a brief description of their work.

The advancement of human civilisation in the Anthropocene epoch has profoundly altered many processes on Earth. We are beginning to bear the brunt of our pervasive activities. The symptoms of rising temperatures, depleting ozone, acidifying oceans, recurring floods/drought have been aggravated by the increased disease proliferation and uncompoundable economic-ecological loss. We Mumbaikars witnessed erratic heavy rains till November, the Chennai-ites have just recovered from the impacts of flood and simultaneously the interiors of the country are facing severe drought. Several such instances are testimony that urge us to steer sustainable journeys rooted in efficient management of our resources.

The NITI Aayog Report(2018) cautions us that nearly 600 million Indians face “high to extreme water stress". About 75% households do not have drinking water on their premises and around 2 lakh people die every year due to inadequate access to safe water. Moreover the country’s demand for water is likely to double by 2030.

The team from St. Xavier’s College,(Autonomous), under guidance of Dr. Binoj Kutty had proposed a technology solution for water management at ‘Youth Leadership for Environment Conservation’ organised by the U. S. Consulate and Ekonnect Knowledge foundation. The project titled-‘Recycling Grey water after treatment by Electrocoagulation’ got selected among the top 5 projects. The students underwent three capacity building workshops spread over a period of six months from December 2018 to June 2019. The workshops helped us transition from the project idea to the concrete concept. At the final pitch workshop, the team was awarded a grant of $4500 for implementation of the Eco-Entrepreneurial Model.

The pilot project has been implemented at the Hostel Building, St. Xavier’s College. The grey water from the hostel building is being treated by the Electrocoagulation treatment pilot plant to supply recycled water to flush tanks at the ground floor washrooms. This shall help offset significant amount of fresh water and thus contribute to savings from fresh water purchase, otherwise. It was a meaningful contribution back to the college. This was the journey of an endeavour to responsibly manage water and contribute towards a sustainable living.

Karishma Katpitia and Zubia Shaikh in front of the electrocoagulation treatment plant.

Dr. Binoj Kutty with the electrocoagulation treatment plant.

GLIMPSE OF CHAOS

-By Neha Kumari, MSc(II),Biotechnology

Deep within everyone,
These ordered things revolve
Which make our cognition stronger and bold.
How will you appreciate it?
Unless you have seen a glimpse of chaos.

Researchers work day after day,
Distorting the sorted hope of ray.
Is it really the right way?
To understand the complicated survival array.

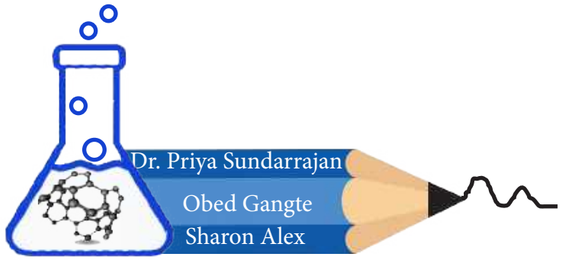
Universe is working hard,
To fight the unpredictable event class.
To untangle the mess?
To outlast the regulated process.

Disordered set contains heaps of energy,
Looking for an orientation.
To uphold its potency?
To be one of the conventional legacy.

Which one is the end,
Which one is the start.
Is it really important?
Or both are just,
On a journey within themselves to embark.

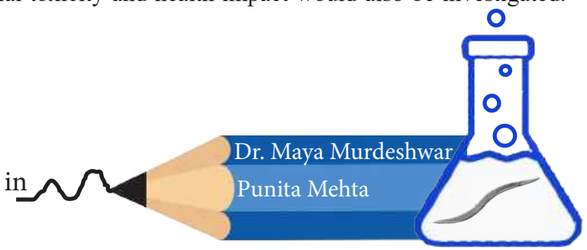
Backgrond Illustration: Khyatee Shah

CURRENT RESEARCH



Green Synthesis of Silver Nanoparticles and its Applications

Nanotechnology has made a revolutionary advancement in therapeutics including drug designing and delivery due to its various unique properties such as enhanced surface area, chemical and thermal stability, antimicrobial, anti-inflammatory, optical and magnetic properties. Silver nanoparticles due to their inertness, cost effectiveness, less toxicity, ease of synthesis and stability have been used in medical, electronic and aerospace industries. The antimicrobial properties of silver nanoparticles has been especially used in designing air sanitizer sprays, cosmetics, food packaging, disinfectants and coating of medical devices and as therapeutic agents. Nanoparticles synthesized via classical procedures like chemical method of synthesis has been observed to have toxic effects. Green synthesis using biological sources has been widely explored as an alternative approach. The present study aims at synthesis of silver nanoparticles (AgNPs) by using various plant extracts, characterize and use them for various applications. The antimicrobial properties of AgNPs are studied by screening using E.coli and S.aureus. The project also aims to develop a colorimetric detection assay kit using enzyme-nanoparticle conjugate system for the detection of various pathogenic organisms. The inhibitory effects of AgNPs on advanced glycation end-products (AGEs) would also be studied. The interactions of the AgNPs in vitro using *S. cerevisiae* as model system to study its potential toxicity and health impact would also be investigated.



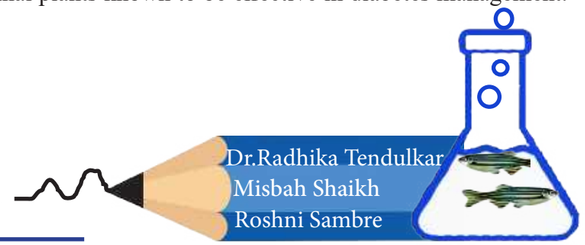
Building the Zinc Toxicity Interactome in *C. elegans*

Zinc (Zn) is an essential trace element required in cellular functioning. Abnormal homeostasis of Zn can lead to deficiency or toxicity effects, leading to growth retardation, immunodeficiency, hypogonadism, neuronal and sensory dysfunctions, largely affecting neurons. Zn toxicity in humans is rare but can happen by acute-intoxication and long-term, high-dose supplementation. In this study, Caenorhabditis elegans is chosen as the model organism as 83% of its proteome is seen to have human homologues. The study aims to use an in silico approach to draw parallels between C. elegans and human genes that are regulated by Zn, with specific reference to Zn toxicity in the nervous system. Important pathways and the molecules involved will be identified, conserved domains and protein functions will be studied, and protein-protein interaction maps will be generated using bioinformatics tools like Cytoscape, MyProteinNet and Integrated Interactome System (IIS).

Development of a System for Rapid Screening of the Anti-Maltase Activity of Plants

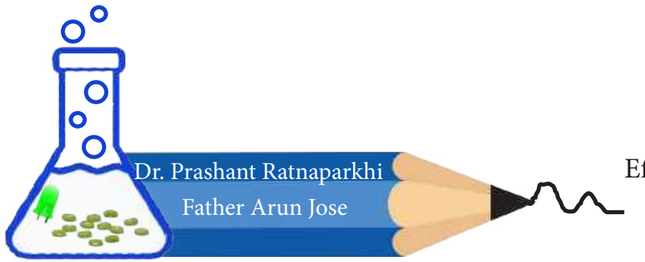
Diabetes is the most common metabolic disease, characterized by high blood glucose levels due to dietary and lifestyle changes. The body either doesn't make enough insulin or can't effectively use the insulin it makes. Despite improved diagnosis and advanced treatments for diabetics, there are significant and unavoidable side effects. Hence a suitable treatment with lesser complications is required. Decreasing postprandial hyper-glycaemia is an effective strategy in the management of diabetes, which can be done by retarding glucose absorption in the body by inhibiting the key enzymes involved in carbohydrate metabolism. Alpha-glucosidase (Maltase) an enzyme in the epithelium of intestine, cleaves complex carbohydrates to monosaccharides (glucose).

Plant species that can inhibit mammalian glucosidase to the same extent as commercial alpha glucosidase inhibitors with fewer side effects and low toxicity would be a better option to produce a phyto-formulation in the fight against diabetes mellitus. This study is focused on developing an easy and laboratory friendly detection system for screening plants that serve as potential alpha-glucosidase inhibitors. This standardized method will help in the screening of a variety of medicinal plants known to be effective in diabetes management.



Effect Of Estradiol On Regeneration Using Zebrafish As A Vertebrate Model

Regenerative medicines are an upcoming biomedical approach having the potential to replace damaged tissues of the body (in vivo) through the mechanism of cell proliferation. In addition, they also aid in growing tissues and organs under lab conditions which has proven to be a boon for organ transplantation and has bypassed the need of searching for a compatible donor. 17β-estradiol (E2), a natural steroid hormone, apart from its conventional role in development of female reproductive system and bone has also been known to enhance cell proliferation. Upsurge in estrogen levels in females with increasing use of contraceptives has been documented to be a leading cause of breast cancer. Hence, it desirable to determine the effect of estradiol on regeneration that would aid in understanding its applications in optimizing regenerative medicines. Danio rerio, a teleost fish, sharing 70% of the genome with humans, is known for the "epimorphic regeneration" of multiple organs. Of these, caudal fin of zebrafish larvae is the most easily accessible, simple in structure and completes regeneration within 3 days. Ergo, was chosen as the organ for testing the effects of estradiol on its regenerative capacity. The effects of estradiol on zebrafish were assessed by morphometry, protein profiling and dual staining of bone and cartilage.

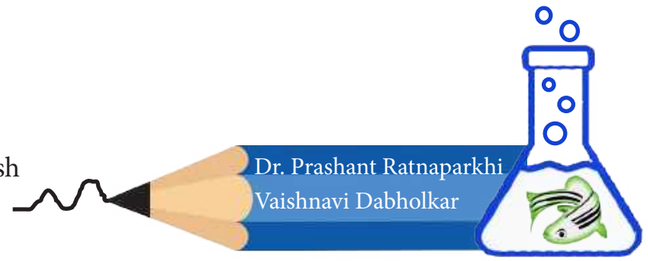


Effect of ELF-EMF on Plant Growth (Mung Bean)

Magnetic field is one of the inescapable natural and environmental factors on earth and is called geomagnetic field (GMF). This GMF has effect on living system ass it influences certain biological processes. The geomagnetic field at earth's surface ranges from 30μT – 70μT but normally speaking GMF strength of earth is 60μT.

At the level of an atom, the electron spin generates two types of distinct fields: electric and magnetic fields. They are referred to as EMF- electromagnetic field. Extremely low frequency electromagnetic field (ELF-EMF) has intensities from 100nT-0.5mT.

Test samples (Mung Bean- *Vigna radiata*) would be exposed to different low frequency magnetic fields (ELF-EMF) generated in lab set up (using Helmholtz coil) for varied time period and control samples without exposing to ELF-EMF. The test and control would be grown in cotton bed in petri dishes. After a period of 96 hours, parameters like time taken for seed germination, percentage of seed germination, total fresh shoot weight and shoot length would be recorded. The control and test samples would be observed and compared to assess the effect of ELF-EMF.



Effect of ELF-EMF on Zebrafish (*Danio rerio*) Development

Extremely low frequency (ELF) electric and magnetic field (EMF) is known to cause health concerns above 100 microTesla (μT), such as nerve and muscle stimulation and changes in nerve cell excitability in the central nervous system. These are short term effects. Long-term risks from ELF magnetic field exposure has focused on childhood leukaemia. ELF EMF is produced by both natural and artificial sources.

The use of Zebrafish (*Danio rerio*), a model organism for the project stems from the observation that zebrafish genome is similar to a large number of human genes.,

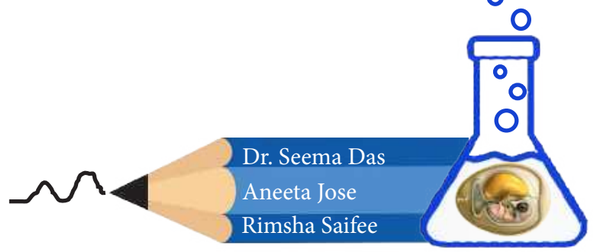
Zebrafish has fast fertility, embryonic development outside the parent fish is faster, transparent embryo allows for easier cell development examination. It is also used for clinical research. To experiment is designed to determine the effect of ELF EMF on zebrafish embryo, Embryos of the experimental group, belonging to different stages of growth, measured as hours post fertilization (hpf) would be continuously exposed to 50-Hz sinusoidal EMF with low intensities for a period of 24 hrs and 48 hrs. The effect of ELF-MF exposure will be studied using developmental landmarks like hatching of the embryo, heart rate at the early developmental stages, body length, yolk sac utilization and eye area.

Bioethanol Production Uisng Cellulolytic Extremophiles

Energy consumption has increased steadily over the last century as the world population has grown and more countries have become industrialized. Crude oil has been majorly used to meet the growing energy demand. However, the major disadvantage of crude oil is that it is a non-renewable energy source, which is getting depleted at a very high rate. Unlike fossil fuels, ethanol is a renewable energy source which can be produced via fermentation of sugars.

This study aims to use lignocellulose biomass as a substrate to enzymatically produce bioethanol using extremophilic cellulolytic bacteria. A wide variety of lignocellulosic raw materials can be used to produce bioethanol, eg. fruit and vegetable waste, forestry waste, agro-residues etc. These substrates are rich in polymers such as lignin, cellulose and hemicellulose. Therefore their degradation requires a conconction of enzymes and cellulases being one of them.

In this study cellulases from alkalophilic bacteria *Paenibacillus spp*. isolate 50-01, and *Cupriavidus spp.* M141 will be used to hydrolyse the cellulose in pretreated lignocellulosic biomass. The sugars obtained as a result of hydrolysis will then be fermented using *S. cerevisiae* to produce ethanol.



Lead-induced Oxidative Stress On Developing Chick Embryo And Recovery Using Antioxidants

Lead is a ubiquitous heavy metal that has been shown to have deleterious effects on living organisms. Human exposure to lead occurs primarily through drinking water, airborne lead-containing particulates, and lead-based paints. Recent studies have shown that lead mediates its toxic effects via the generation of reactive oxygen species (ROS) like superoxide radicals, peroxynitrites besides others thereby simulating oxidative stress in the system. Under normal conditions, ROS are generated in the cell for maintenance of cellular functions, clearance of which is done by the antioxidant defense system present in the cell. This system comprises three main enzymes- CAT (Catalase), SOD (Super oxide dismutase) and Gpx (glutathione peroxidase). Imbalance between the ROS generated and the levels of cellular antioxidants creates oxidative stress in the cells, implications of which can be seen primarily on DNA, lipids and proteins. The exact mechanism of how lead causes the damage via ROS generation is still being researched. Natural and synthetic antioxidants exist, that seem to have similar effects as that of in vivo antioxidant systems.

This project aims to study the variation in the concentrations of the aforementioned enzymes with varying concentrations of lead using chick embryo as the model system and subsequent recovery using green tea extract and Ascorbic acid as natural and synthetic antioxidants respectively. The effect on DNA would be analysed using the Comet assay. All the above parameters would be assessed in-vitro on cultured fibroblast cell lines.

Studies on the Survival of Microorganisms Exposed to Visible Light from a LED Source.

There has been a steady increase in the use of Light emitting diodes (LEDs) worldwide, for both indoor and outdoor lighting needs. LEDs are semiconductor-based devices that emits high intensity light over a wide range of spectrum in the visible light region depending on the elements used in its chip. The fact that exposure of humans and our surroundings to artificial lighting especially LEDs has increased, and that not much data on the effects of LED illumination on organisms exists, it would be interesting to study the biological effects upon LED light exposure. Both natural and artificial visible light (in the range of 400 to 800 nm) have been shown to affect biological systems, even in those with no photoreceptors. Published studies indicate that LED illumination (especially blue light- 405 nm) have an antibacterial effect due to the phenomenon of photodynamic inactivation via excitation of light sensitive compounds like porphyrin in the visible range (400- 800nm), leading to the reactive oxygen species (ROS) production. ROS can damage important cellular components and ultimately lead to cell death. Commercial use of this property has led to introduction of 'Anti-Bac' LED, which claim to reduce 85% of microbial load by giving white light with an increased amount of the blue component. Our project aims to verify this claim by following the viability of microbial cells (*Escherichia coli, Staphylococcus aureus* and *Saccharomyces cerevisiae*) after LED light exposure from 'Anti-Bac' bulbs. We would be interested in further evaluating the effect of LED light on the action of antimicrobials. If LED light exposure do reduce viability it can be used a disinfectant to control microorganism numbers especially in hospital setting.

Study of the Role of Zinc Toxicity on Non-associative Memory and Neuroblastoma Cells

Zinc is an essential micronutrient that is involved in various functions involving structural and functional roles in numerous proteins, regulation of gene transcription and signal transduction processes. Although zinc, in trace amounts, is found to be neuroprotective, elevated levels of zinc leads to neurodegeneration. It is known to induce cytotoxicity leading to disruption of normal neuronal signaling and synaptogenesis. Zinc at elevated levels has a toxic effect on the glutamatergic neurons, which are involved in the memory process. Hence, we want to study the toxic effects of zinc on the memory process using *Caenorhabditis elegans* as a model system. Our focus is on both short-term- and long-term memory. In-vivo analysis involves setting up behavioral assays targeting different memory paradigms and to observe the effect of zinc toxicity on these paradigms. Furthermore, we also want to analyze the differential toxic effect of zinc on neurons and glia. Previously our group has worked on glioma cells line, and therefore, we will focus on the neuroblastoma cell line N2A for in-vitro studies. Our in-vivo study will help us understand how zinc toxicity affects memory processes and in-vitro study will help understand whether a particular subset of neural cells can be specifically used for drug targeting with respect to their comparative vulnerability towards zinc toxicity.

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