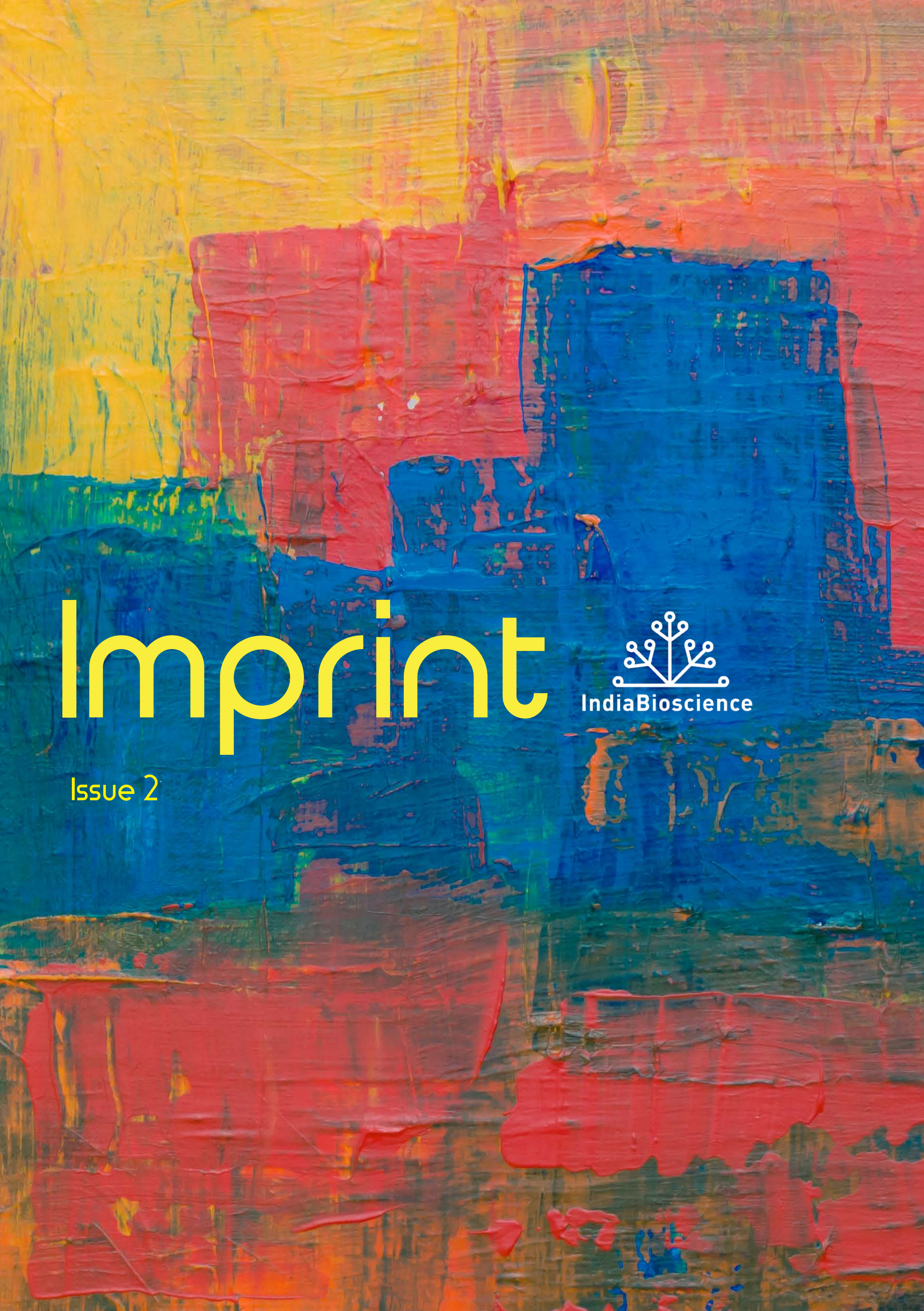

Imprint

Issue 2

IndiaBioscience

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Decoding cholera

How a comma-shaped bacterium creates an epidemic

P Surat

In April 2018, three people in Odisha died from cholera after drinking "pana"- a ritualistic drink that was made from pond water of the village. In India, around eight lakh cholera cases were reported between 2004 to 2008 due to contaminated water.

In a recent study, researchers led by Chandradipa Ghosh from Vidyasagar University, West Bengal, found that Vibrio cholerae, the cholera-causing bacterium, communicates with other bacteria in its vicinity and uses flagella, a whip-like structure, to survive and attach to surfaces in water bodies. This increases its survival potential, leading to the emergence of epidemics.

Vibrio cholerae thrives in aquatic habitats. One of the ways by which it survives is forming biofilms on biotic or abiotic surfaces. Biofilms consist of microbial communities embedded in an extensive matrix of exopolysaccharides (EPS). Cholera bacteria use quorum sensing, a cell-cell communication method where a cell can gauge the density of cells around it, to form biofilms. In this mode of communication, bacteria release a signalling molecule which is then sensed by their neighbours. When the concentration of this signalling molecule is high, the bacteria assume high cell density in their vicinity and secrete EPS, leading to the formation of biofilms.

To determine the role of this communication in the spread of cholera, the researchers mutated the genes

The last two hundred years have seen seven cholera pandemics and multiple regional outbreaks. Now, a new study from researchers at Vidyasagar University, West Bengal, explores how *Vibrio cholerae*, the comma-shaped bacterium which causes cholera, uses flagella and quorum sensing mechanisms to survive and form biofilms, which increase disease spread and enhance the potential for epidemics.

which synthesise autoinducer - the quorum sensing signalling molecule - in the bacterial strain that caused a cholera epidemic in Kolkata in 1992. There are two types of autoinducers in Vibrio autoinducer 1, which is involved in communicating with fellow Vibrio bacteria, and autoinducer 2, which communicates with other bacterial species. The researchers found that bacteria which could not synthesise either or both of these signalling molecules secreted higher EPS matrix, had wrinkled cell surfaces (as opposed to smooth), and produced more biofilms. All of these traits contribute to increasing the cholera bacteria's persistence in variable surroundings.

Vibrio is a highly motile bacterium with a single flagellum on one end. The flagellum not only propels the bacteria, but also doubles as a sensory organ to explore the surfaces around it. The researchers found that removing the flagellum by deleting the gene which creates it also generated similar effects as mutating the quorum sensing signalling molecules - higher EPS matrix expression, wrinkled surface, and greater biofilm production. "This alternate mechanism was observed in a group of *Vibrio cholerae* that are highly toxigenic and virulent," states Ghose.

The researchers found that for these two players in cholera pathogenesis - flagella and quorum sensing - one signalling pathway becomes predominant in the absence of the other. The increase in EPS in the absence of autoinducers is brought about by the flagella, while the increase in EPS in the absence of flagella is dependent on autoinducers.

How does this system work in real life?

When *Vibrio* numbers are low in a local aquatic ecosystem, the concentration of secreted autoinducer molecules in the water is also less. This leads to a flagella-dependent increase in EPS production, wrinkled surface, and biofilm generation, establishing a stable Vibrio population. "EPS signalling provides adaptive features for the pathogen to survive in different environments by inducing rapid biofilm forming ability," says T Ramamurthy, scientist at Translational Health Science and Technology Institute, who was not involved in the study. Interestingly, wrinkled cells with excess EPS also show increased expression of toxins which contribute to the diarrhoea and dehydration associated with cholera.

"This study establishes an alternate biofilm signalling mechanism that comes into action by the interaction of quorum sensing autoinducers with flagellar structure," says Ghosh. The presence of biofilm protects the bacteria from changes in its environment and EPS makes it more potent – potentially triggering a cholera epidemic.

Reference: *Biswas, S., Mukherjee, P., Manna, T. et al. Microb Ecol (2018)*

A deadly frog killer in India

Fathima Athar

Once upon a time, there lived a frog prince. Cursed by a wicked witch, the frog waited for a kiss from a beautiful princess, which would turn him into a handsome prince. One fine day, a lovely princess would find him, but - the frog died of chytridiomycosis caused by a pathogenic fungus, *Batrachochytrium dendrobatidis (Bd)*.

True story, if the frog was a sharp-snouted torrent frog, gastric brooding frog, southern day frog of Australia or one of the stream-breeding toads of Central and South America – all now extinct because of Bd.

Karthikeyan Vasudevan's lab in the Laboratory for the CONservation of Endangered Species (LaCONES), Centre for Cellular and Molecular Biology (CCMB), Hyderabad, recently documented the status of Bd, the frog pathogen that causes the fungal disease chytridiomycosis, in India's biodiversity hotspots. This first-ever nationwide survey reports that Bd does occur in Indian frog populations but with low disease prevalence and high haplotype diversity.

Unlike human skin, frog skin is thin, permeable to water and electrolytes, and helps frogs breathe. Infection with Bd causes the frog's skin to thicken several folds making it impermeable. Frogs become lethargic, adopt abnormal postures with their hind limbs extended and lose their righting reflex when placed upside down. Within a few weeks of the infection, frogs die of osmotic imbalance and cardiac arrest.

Several species of frogs have been pushed to the brink of extinction by Bd worldwide, but very little was known until now about its status in the frog populations of India. "With over 375 different species of frogs, most of which are endemic, the stakes were high for India," said Vasudevan.

Vasudevan and his team tested 1870 frogs from the biodiversity hotspots in India. Each frog was arduously hand-caught and stroked 70 times with a cotton swab to collect the fungal spores on its body. After an examination for clinical symptoms, the frogs were released into the wild, and the swabs brought back to the lab. About 8% of the frogs were positive for Bd suggesting that India is a 'cold spot', a region with a low prevalence of the disease. While this is good news, it is also exciting because cold spots are valuable for understanding the disease and finding solutions for its treatment.

An interesting feature of cold spots is that they harbour multiple endemic haplotypes of the pathogen, which may have evolved due to host-pathogen co-evolution. 80% of the Bd haplotypes identified by Vasudevan's group were endemic or unique to India. Identifying and monitoring different haplotypes with sensitive assays is vital for understanding the dynamics of the disease. However, the researchers found that current assays failed to detect many endemic haplotypes and need to be improved.

Just like lions, wolves and elephants, frogs are an important part of our ecosystem. "The low prevalence of Chytridiomycosis gives us a little respite," said Abhijit Das from the Wildlife Institute of India, Dehradun, who was not associated with this study, "However, with the ongoing climate change, the situation may switch. We need more sampling and monitoring of Bd status, especially in our protected areas".

With a success rate of about one in five, capturing these nocturnal creatures isn't an easy task. Milind Mutnale and Lilly Eluvathingal, two of the researchers who conducted this study, have several exciting stories born out of their fieldwork. "When you are out in the wild, you surprise the animals first," said Lilly. Encountering a wild elephant immediately calls for abandoning plans and quietly backing away from the area. "It's hard, because as a researcher one wants every data from every site. But always, safety first!" said Lilly.

Batrachochytrium dendrobatidis (Bd), an aquatic fungus, has been implicated in the decline or extinction of nearly 200 frog species worldwide. Now for the first time, researchers have mapped and assessed the spread of this deadly pathogen in Indian frog populations, performing extensive field studies in locations ranging from the Himalayas to the Western Ghats to the Anadaman and Nicobar islands.

The lab is now interested in monitoring the persistence of Bd throughout a frog's lifespan and studying the influence of frog skin secretions and its resident microbiome on the infection. For anyone interested in checking in on the frog in their backyard, LaCONES offers Bd diagnostic services.

Reference: Mutnale M, Anand S, Eluvathingal L et al. Scientific Reports (2018) 8:10125

Photo: Lilly Eluvathingal

Shambhavi Naik & Megha

The curious case of the missing Indian postdoc

The last decade has seen the Government of India increasing the number of higher education institutions and introducing policies specifically to motivate STEM (Science, Technology, Engineering and Math) students. These interventions are expected to build a pipeline of education to produce large numbers of quality STEM graduates.

How do STEM students view this pipeline? How do they perceive opportunities to pursue STEM careers in India? To address this issue with numbers rather than anecdotal information, we initiated a survey for these students in May 2018. A small vignette (~85 Ph.D. students) from the survey has been used here to discuss one node of the STEM career pipeline: postdocs.

In 2015, India had ~125,000 students enrolled in a Ph.D. program, 62% of whom were in STEM fields. Assuming a fifth graduate in 2018, and with our survey showing 56% of these would pursue a postdoc after their PhD, we arrive at ~12,500 potential postdocs per year.

Despite a large base of applicants, postdocs on Indian campuses are a rarity. India's premier STEM research institute, Indian Institute of Science (IISc), currently hosts just 174 postdocs. To understand how low this number is, we examined the Faculty:Postdoc ratio. In IISc it is 2.8:1, while for Stanford University it is 1:1. Correspondingly, Faculty:Ph.D. student ratio is 1:5.6 for IISc, as compared to 1:1 at Stanford. This minor analysis suggests that we are under-utilizing the trained Ph.D. students we are investing in.

Moreover, absence of a strong postdoctoral culture negatively impacts our research output. Consider one parameter: publications. In 2018, the Nature Index pegged India at 13, behind countries including USA, UK, Switzerland, South Korea, Spain and Italy. Postdocs would be an ideal workforce to contribute to our publication numbers because unlike faculty, they don't have teaching or administrative duties and unlike Ph.D. students, they have no course-work commitments.

Here, we identify reasons behind our poor postdoc numbers and propose strategies to develop this cohort of scientific research personnel.

Many identifiable factors contribute to low postdoc numbers: economic, social and scientific.

Postdocs are poorly paid in India and sometimes, even less than Ph.D. students. The Prime Minister's Research Fellowship Scheme awards INR 70,000/

“Absence of a strong postdoctoral culture negatively impacts our research output”

month for outstanding Ph.D. students, while a similarly competitive National Postdoctoral Fellowship pays only INR 55,000/month. Although poor pay for postdocs is a global issue, when considered in terms of purchasing power parity, Indian PhDs prefer poor pay overseas to poor pay in India. Delay in release of salaries and grant money further compounds the poor economics of doing a postdoc in India.

The social perception of an India-trained postdoc is low. Students are strongly advised by their Ph.D. mentors to pursue a postdoc overseas. This advice is substantiated by the widespread habit of prominent research and educational institutes of hiring mostly, if not exclusively, foreign-trained postdocs. The net result: ~70% of surveyed students felt a need to train overseas for a job in Indian academia. There is of course, nothing wrong in students seeking work experience outside India; but, isn't there something remiss in our system if students feel compelled to do so?

Scientifically, India-trained postdocs have less glamorous publication records compared to their overseas counterparts, an inherent challenge of doing science in India. This issue is not acknowledged by the Indian scientific community.

“In the current system, we train a large number of Ph.D. students only to encourage them to go overseas, of which a fraction return”

Opaque hiring processes further fuel the perception that a bias exists against hiring India-trained postdocs.

These factors combined lead to a subpar postdoctoral population, both in quantity and quality, as well as programs that are not attractive to either domestic or foreign postdocs. Increased funding is an obvious solution for improving postdoc numbers, but more money without institutional and structural changes will be ineffective. We suggest below some broad interventions that may be considered at a policy level.

Include a long-term (>1 year) overseas training component to Indian postdoc fellowships

Our survey suggests 60% of those wanting to go abroad will remain in India if such a fellowship is available. Overseas training would expose students to experiential learning from international laboratories. Structuring the Fellowship so that the last 1-2 years are spent in an Indian laboratory would help to utilize the Fellow’s foreign training in an Indian context.

Encourage foreign postdocs

We have dedicated schemes to attract overseas researchers at the faculty level, but perhaps these would be more valuable when applied to postdocs. Increasing foreign participation on our campuses will enable India to break into the Top 100 global university rankings, an aspiration which now has political momentum. At MIT for example, more than 60% of postdocs are international. Given the contractual nature of postdoctoral work, these India-trained foreign postdocs can serve as ambassadors of our research institutions. However, to promote harmony and preclude prejudice, it would be important that these postdocs are treated on par with domestic postdocs in terms of pay and opportunities.

Create mechanisms for structured postdoctoral and research student training

We currently fund Junior Research Fellows (JRFs) with the intention of developing them as PhD students. However, JRFs are provided no help or counselling to help them navigate through the research environment. Thus, many end up training in subjects and working on projects which may be vastly different from their education and ambitions. To structure JRF training, we envision a national program that asks postdocs to compete to employ JRFs (with the support of their lab head) for specific projects. Postdocs would have to write a 1-2yr proposal, outlining the science and the skills the JRF would learn in the training. Both pools of research personnel, JRFs and postdocs will benefit from this scheme: the JRF is guaranteed individual attention and a co-owned project, while the postdoc can improve their productivity and develop management skills.

Recognize postdocs as valuable trained research personnel for academic and non-academic careers

In our current set-up, an academic job is seen as the best outcome of Ph.D. and postdoc training. This needs to change. Even in the US and UK, just 8% of postdocs get an academic job. We, therefore, need to initiate non-academic training opportunities. Unfortunately, most postdocs are unaware that their training can be valuable in other professions such as research administration, consulting, policy making, journalism, curriculum development, teacher training, entrepreneurship and facility management. It does not help that these careers carry a social stigma by being labelled as “alternate”.

Structured programs for professional development and paid internships during the postdoc training period would be helpful (for e.g., not one law school in India has an IP course that is run on a research campus). Institutions should also be allowed to create a slew of positions that allow them to utilize and acknowledge postdoctoral training for broader application in the research ecosystem. For e.g., imagine the usefulness of an India-trained postdoc as a lab manager to a newly appointed faculty.

In the current system, we train a large number of Ph.D. students only to encourage them to go overseas, of which a fraction return. Perhaps it is time we stop being complacent about losing our best-trained people.

Digital imaging ethics

Where does India Stand?

P Surat

Between January 2018 and May 2018, 12 papers published by two researchers from the Indian Institute of Technology (Indian School of Mines), Dhanbad were retracted because of image duplication and manipulation.

On April 19th 2018, a PhD student from Calcutta University wrote a public post about the data manipulation in her lab where her guide and a senior research scholar drew "molecular weight markers with pencil on a blot and 'rescanned' the blot to convince the reviewers and the editorial board of the journal".

In recent times, India has been in the limelight for several cases of fraudulent imaging practices. In a study published in 2016, researchers from Stanford University, Johns Hopkins School of Medicine and Washington School of Medicine analysed the prevalence of image duplication across different countries. To do this, they looked at 348 papers with image duplications published between 2013 and 2014 in Plos One and mapped their country of origin. The papers with duplicated images most frequently originated in India, followed by China and Taiwan.

Honest mistakes or fabrications?

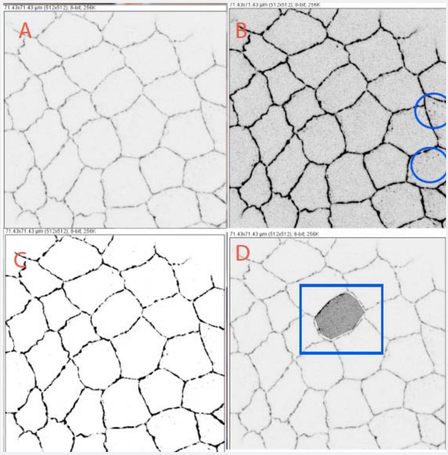
Before we can discuss strategies to combat this trend, we need to understand the origin of this behaviour. Is it possible to determine if these cases arise from honest mistakes during image processing, data compilation or figure preparation – or are they outright acts of misconduct?

In a recent study available in pre-print format in BioRxiv, researchers visually analysed 960 papers published in Molecular and Cell Biology between 2009 and 2016 for inappropriate image duplication. Out of these, 59 papers (6.1%) contained inappropriate image manipulations. Interestingly, most authors who made formal corrections reported that the error arose during image assembly. For example, sometimes they accidentally included the same image twice, selected the wrong image, or assembled panels with incorrectly placed images.

This study is reassuring in the fact that most such errors could be resolved by improving the imaging and compiling practices of the authors. However, these results may not represent a general trend for papers from different countries, and we do not know how many of those 960 papers were from India.

The line between 'adjustment' and 'manipulation' can be blurry

The images to the right show a view of few cells from a tissue during development in Drosophila. The first image (A) is unadjusted. The second (B) is adjusted, but there is no loss of information. The third image (C), though cleanest in appearance, has been adjusted such that certain information is now lost from the image—you can no longer see the small dots in some cells in the bottom right (blue circles, B). The last panel (D, blue rectangle) shows a view where the intensity of one cell has been selectively increased. Out of these cases, the second modification (B) may be acceptable, but the third and fourth (C and D) undeniably count as 'manipulation'.



First point about making these changes – it is easy! If someone wanted to make such changes a decade ago, they would have had to put in real effort. Today, one can create a panel within minutes showing that one cell selectively shows increased levels of x protein.

Second, even if the error arose due to an erratic mouse click, it still counts as 'manipulation'. Below is a list of some 'honest errors' which still count as manipulation:

- If you splice two gel images from different experiments into one without specifying.
- If you duplicate a lane in a western blot into another panel.
- If you specifically modify certain parts of an image in contrast to the whole image.
- If you combine images from different regions/time into one without specifying or showing the borders.
- If you do not possess unaltered original images/blots for each of your panels.
- If you label your images/panels incorrectly.
- If you use Photoshop to remove certain signals to make your image look 'nice and clean'.
- If you crop certain parts of an image without mentioning.

"If you desperately want to see a particular result, you can probably find it in some corner of your image – despite the fact that the major part of the data says a different story", quips Sudipto Maiti, Professor at the Tata Institute of Fundamental Research (TIFR), Mumbai and a regular instructor at the Bangalore Microscopy Course at the National Center for Biological Sciences (NCBS), Bangalore, one of the few courses in India

> "If you desperately want to see a particular result, you can probably find it in some corner of your image – despite the fact that the major part of the data says a different story"

which imparts training in microscopy and image processing.

The changing landscape of image submissions to journals

Journals are now adapting to the increased threat of image manipulations, and most journals require that images be minimally processed and that all unprocessed data and metafiles be submitted at the time of review. All image acquisition tools, image processing software, and processing manipulations to improve the image should be mentioned.

Journals are also training their editors to detect 'tell-tale' signs that an image is manipulated. Some journals perform 'spot check' where all images of a randomly selected paper in each issue are visually checked for image manipulations. Recently, researchers developed a software which could check image manipulation in papers. In time, the use of such software, similar to software that check plagiarism, could become prevalent in journals. Maiti has another suggestion along these lines. "It may not be too much work to get the image processing software providers to make their software so that it always embeds the raw image inside the processed image," he says, "This will enable anyone to say do a left click on the image and check what the raw data looked like. This embedded raw image should be non-manipulable and traceable to the original machine. The journals should insist on having the image in this format, so that at least on the online format, the raw data is always available".

What can the scientific community do to counter image manipulations in India?

Increasing awareness

"Training in advanced microscopy and imaging is indeed lagging behind," states Rahul Roy, Assistant Professor at the Indian Institute of Science (IISc), Bangalore and also an instructor at the Bangalore Microscopy Course. "There have been several efforts to impart such training through workshops and courses but they are still limited. Therefore, 'imaging literacy' is poor and access to new technology without proper training and support is already an impediment to doing good science", he says.

Shifting from qualitative to quantitative reporting of images

Roy stresses that "the focus should be shifted from qualitative research reporting (like images) to quantitative reporting with statistical analysis from raw images that accompany the images". This can be useful in cases where a single image is displayed which may not be representative of the actual data.

National and institutional legal policies

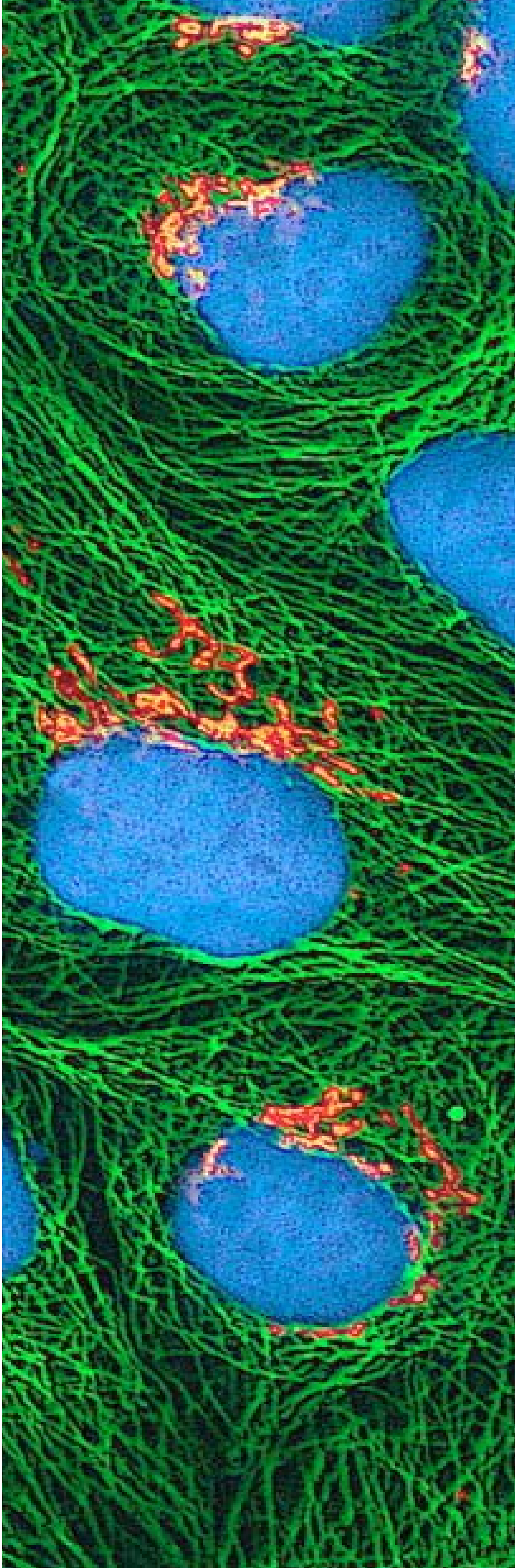
Two recent studies assessed various risk factors for scientific misconduct. Interestingly, the most common factor which is usually attributed to this behaviour – the pressure to 'publish or perish' – was not found to be a significant risk factor. Instead, the likelihood of retraction was lower for countries where policies against scientific misconduct were legally defined either at the level of the nation or the institution. Thus, establishing legal infrastructure in Indian institutes and government against all categories of scientific misconduct could be a potential deterrent against deliberate malpractice.

Peer control and cultural factors

Open communication and mutual criticism are two of the pillars of science. A scientific culture where peers or collaborators are discouraged or scared to criticize their peers' work breeds an environment ripe for fraudulent practices. As a scientific community, we should encourage an environment where student and colleagues can provide honest and unbiased peer control both locally (as lab members and intra-institute members) and globally.

Misconduct does not affect one person or a lab; it shapes the view of science in our country and is a reflection of us as a scientific community. Thus, sincere and urgent efforts are required from both the scientific community and the government to improve the pursuit of science in India.

[Photo: Imaged by P Surat, courtesy Maithreyi Narsimha lab, TIFR, Mumbai]



Proof in the Poop

Priyanka Runwal

Rodents and hare are regular staples in Red Fox diets. In the wild, these comprise the natural prey base. But, increasingly, human-derived foods are becoming more popular among these opportunistic canids.

By examining the contents in Red Fox poop, a new study finds that these animals consume less wild prey when easily-procurable, human-subsidised alternatives are available in plenty. Not only that, in areas where such alternatives form a larger proportion of the diet, foxes were relatively more abundant. But one big hurdle to accessing these food resources is the presence of more dominant animals – feral dogs.

A team of scientists from the Wildlife Institute of India (WII) and Stanford University, California, walked nearly 470 kilometres across the Trans-Himalayan region of India and bagged 1264 Red Fox scats. Fortunately for them, in these regions of low temperatures and rainfall, scats as old as six to seven months remain undeteriorated.

The researchers wanted to assess how

A team of scientists walked nearly 470 kilometres across the Trans-Himalayan region collecting Red Fox poop to understand how its dietary habits are changing with growing human proximity.

human settlements and activities like agriculture, animal husbandry and their by-products i.e. unmanaged garbage and free-ranging dogs impact Red Fox diet and their abundance. This was of particular interest as cold deserts are typically characterised by low availability of natural food resources.

Traces of undigested food in the poop gave the team clues to what foxes dined on. These included hair and bones of wild and domestic animals, feathers of wild birds and poultry, even plant material like apricots and cereal. Sadly plastic and rags too.

But by looking at a strand of hair in the Red Fox poop, how can one tell if it belongs to a wild animal or say, livestock? "Every species has its own medullary hair pattern. When observed under a microscope, the medulla, or the innermost layer of hair, in goats, for example, shows fewer vacuoles and different disc like structures as compared to that of a blue sheep," says Hussain Reshamwala, a PhD student at WII and lead author of the study.

The scats revealed that rodents and hare continued to remain the main food item across the study region. Interestingly, however, local religious and cultural practices indirectly dictated what foxes could access near settlements and their numbers.

Chiktan, a site found to be most favourable for foxes, was dominated by Muslims, and saw a lot of discarded poultry and livestock, ideal to scavenge on. For religious reasons, these communities keep dogs away. "Here, the fox numbers have shot up indiscriminately," observed Hussain. Spiti, on the other hand, is a site of low human activity, and dominated by Buddhists, who are tolerant of all kinds of creatures. With dogs present, human-provided foods are less or not at all accessible to foxes, due to competition. "The foxes here don't stand a chance. Dogs chase or even kill them," said Hussain.

"This study reiterates the fact that garbage management is important, not only to keep human commensals such as the domestic dog in check, but also for wildlife, that can become dependent on such handouts," said Abi Tamim Vanak, an expert in dog ecology and small carnivore biology at the Ashoka Trust for Research in Ecology and the Environment.

So what if foxes are on the rise and scavenging on human food? Increasing populations may drastically bring down numbers of wild prey, and continue to remain insulated despite this decline, due to the supplementary food provisioning. With disruption of natural prey-predator cycles, there is little scope for recovery of species of the lower trophic levels, possibly leading to local extinctions in the Trans-Himalayan landscape.

Reference: Reshamwala H, Shrotriya S, Bora B et al, Journal of Arid Environments (2018)150 :15-20

Discrimination via Drugs

The dark side of India's indigenous preparations

Navodita Jain

While pharmaceutical formulations are regulated for their chemically defined compounds, traditional medicines circulate on the foundation of faith and desire. The use of these uninvestigated indigenous preparations (IPs) forms an integral part of an alternative health care system that targets a vulnerable chunk of the population. These preparations are often put to unethical use and serve a big blow to our long fight against social evils. A striking example is the consumption of IPs in the form of sex-selection drugs by expectant mothers in the hope of a male child. Though the Pre-Conception and Pre-Natal Diagnostic Techniques Act has been in place for almost 24 years, the country still grapples with prenatal sex selection and female foeticide, posing a risk to the health of newborns and mothers.

Sutapa Bandopdhyay Neogi, Indian Institute of Public Health - Delhi, Public Health Foundation of India, and her team have been studying the causes of congenital malformation in the state of Haryana for several years. The researchers had earlier found that consumption of sex-selection drugs by women during pregnancy was associated with 25% of children being born with structural abnormalities.

"We were quite convinced of the harmful effects of the IP," says Neogi, "While we initiated animal model studies, we also thought it would be fruitful to start investigating the chemical components contributing to the effects". The group found alarming quantities of lead and mercury in three traditional drugs containing Shivalingi (*Bryonia laciniosa*), Majuphal (*Qtuercus infectoria*) or Nagkesar (*Mesua ferrea*) as their major components. Quite infamously, Haryana suffers from a severely skewed female to male ratio of 832:1000 (compared to the national average of 898:1000).

Exposure to heavy metals is a cause of major concern for pregnant women. In the aforementioned indigenous preparations, lead quantity was roughly tenfold higher while mercury was four hundred-fold higher than the recommended FDA levels. Such high maternal loads of heavy metals can cross the placental barrier and damage the developing fetus, especially in the first trimester, when these drugs are usually consumed.

The presence of heavy metals is not the only concerning factor. An earlier study by the same authors reported the presence of phytoestrogens in these formulations, which are chemicals that mimic natural hormones and can cause hormonal imbalances in pregnant women, potentially even leading to sterility. A few samples even contained testosterone, a hormone strongly contraindicated during pregnancy.

Neogi's team previously explored the demographics of consumption of such sex-selection drugs in a population-based study. Approximately 40% of the mothers who consumed these drugs had received primary education while most fathers were manual labourers. The paper reported that the risk of having a child with congenital malformations was increased threefold among mothers who had a history of IP intake. Moreover, the statistics from the study suggest that the risk of malfunction is stronger for a family with a prior girl child.

The claims of these alternative drugs are brazened and can be misleading. Even a quick internet search leads to websites like this which propound the use of Shivalingi seeds as "putr jeevak" (male birther). Shivalingi is also touted as a sexual prowess enhancer. While published experiments using male rats indicate that Shivalingi can increase testosterone levels, this may have unintended consequences. "With the overload of steroidal hormones, the drugs can potentially influence the reproductive fertility in adults. However, they are detrimental to the development of reproductive organs of the fetus," says Neogi. "More research is needed to scrutinize and verify the biological effect of individual components. To investigate at a molecular level, we need funding and are actively looking for collaborations,"

she adds.

It is imperative to state here that sex of the developing fetus cannot be altered by any drug. The chromosomal combination that determines the sex of the fetus is sealed at the time of fertilization. An informational video about this process, created as part of a project supported by the Department of Science and Technology can be found at this address - https://bit.ly/2GUKoLl

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1. Ganguli, A., Rai, P., Balachandran, S. et al. Biol Trace Elem Res (2018)
2. Neogi, S.B., Negandhi, P.H., Sandhu, N. et al. Drug Saf (2015)

The Dark side of light

Lessons from a crow

Divya Khatter

Remember the crow that taught us 'Where there's a will, there's a way?' It went on to build a promising research career studying circadian rhythms with a part-time job preaching life's little lessons. Decades later, it is back with a new story and a new moral on how to get a good night's sleep.

A team of researchers led by Vinod Kumar at the IndoUS Center for Biological Timing, University of Delhi recently discovered that exposure to artificial light during night disrupts the biological clock ticking inside us. This, in turn, adversely impacts the brain region involved in cognition and mood, resulting in reduced sleep and increased risk for mood disorders.

The human brain is programmed to be active during the day and to rest during the dark hours. This 24-hour internal biological clock, also called the circadian rhythm, determines our sleep/wake cycle. When it is dark at night, the brain receives a signal to release melatonin. This makes our body feel tired and coaxes it into sleep. Artificial light at night disrupts the circadian rhythm by altering melatonin levels, thereby influencing sound sleep, and consequently our mental and physical well-being.

To understand behavioural alterations caused by artificial illumination at night, the researchers used adult Indian crows as a model system. These birds have remarkable cognitive abilities at par with mammals and are diurnal creatures that rely on visual and auditory cues, much like humans. The scientists exposed the crows to dim light at night and found that it significantly reduced the daily rest period of the crows. This seemed to affect the crows' mood as well, as they reduced their food intake and spent less time grooming themselves. Interestingly, this behaviour was reversible. When dark nights were restored, the crows resumed normal eating and self-grooming behaviours.

"Working with a non-model wild species was challenging," says Taufique. "It demanded a standardisation of all behavioural patterns and measures to study the effects on sleep behaviour and mood," adds Abhilash Prabhat, an author on the study.

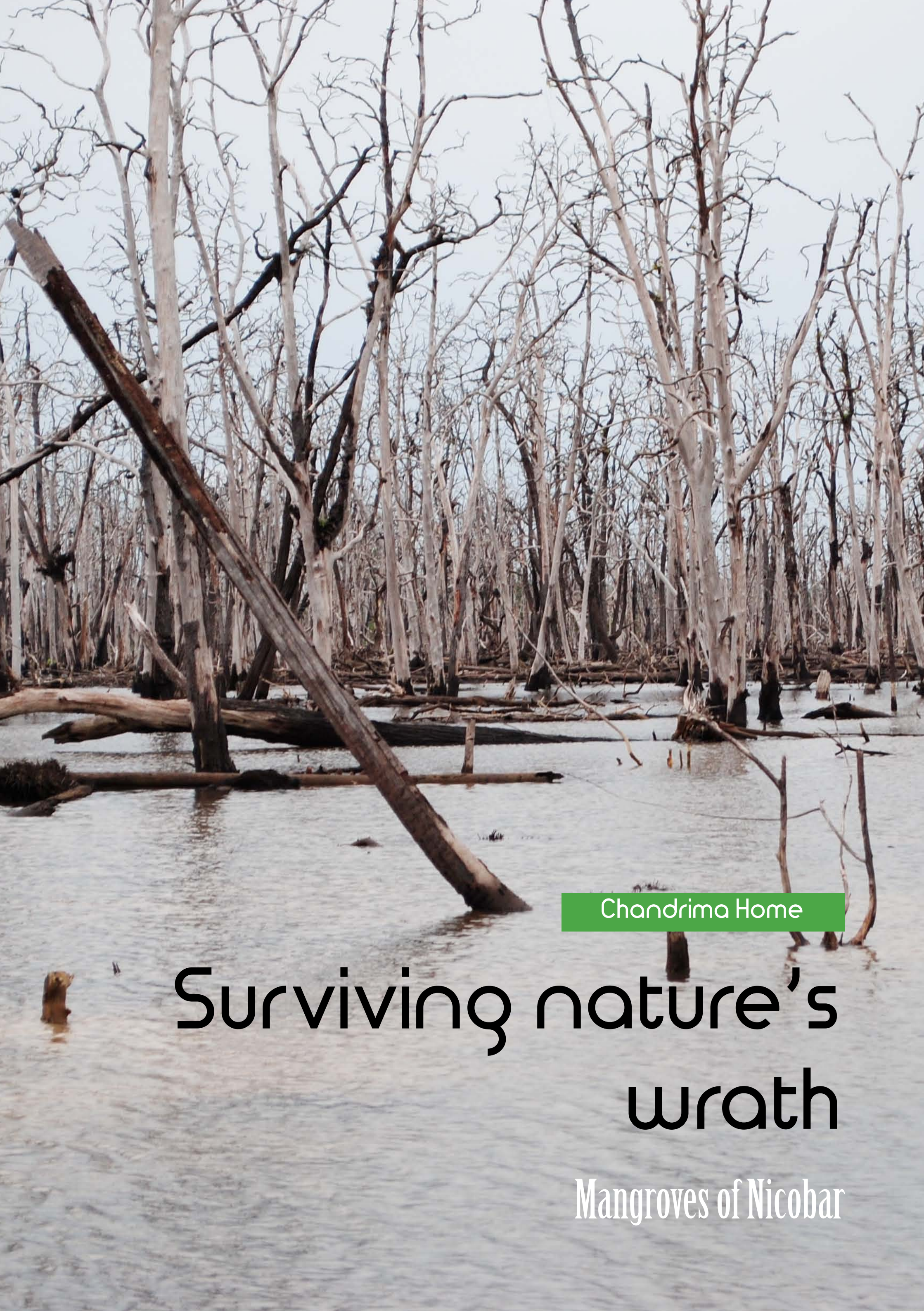
When the team investigated the plasma melatonin levels of the crows that experienced illumination at night, they found that melatonin levels at night had dropped down to near daytime levels. At the cellular level, they found that exposure to light at night suppressed new neuron formation and compromised neuronal health in the hippocampus, the brain region involved in learning and mood. The genes associated with depressive-like responses were also observed to be negatively influenced. In addition, the researchers found transcriptional and epigenetic changes that may underlie the night-time illumination-induced negative effects in crows.

Artificial light at night has rapidly transformed the 24-hour day-night cycle. While the sight of a beautifully lit up city at night may be aesthetically pleasing, the associated health consequences are far from being so. Reports have linked excessive and repeated night time light exposure with sleep disorders, obesity, diabetes, depression, bipolar disorder, and cancer.

"The value of this study lies in significant behavioural dysregulation noted in crows, a species with which humans share urban ecosystems," says Aurnab Ghose, Associate Professor, Indian Institute of Science Education and Research (IISER), Pune, who was not associated with this study.

It is important to understand how biological clocks work and keep time. Light in particular is an important synchroniser for these clocks, and has been shown to be effective in the treatment of circadian rhythm disorders. Our very own crow has spent many sleepless nights to uncover the risks to diurnal animals and humans living in an overly lighted urban ecosystem. "Studies like this, therefore, become important at the level of understanding animal physiology and awareness of ecological consequences of human activities and choices. The richness and diversity of such studies is something that makes possibilities of interventions more plausible," says Ghose.

Reference: Taufique SKT, Prabhat A, Kumar V. Eur J Neurosci. 2018;48:3005–3018



Chandrima Home

Surviving nature's wrath

Mangroves of Nicobar

The 2004 Tsunami wreaked havoc on the rich mangroves of the Nicobar islands. In a new study, scientists from the Salim Ali Centre for Ornithology and Natural History, Wildlife Institute of India and Leibniz Center for Tropical Marine Research (Germany) investigate the current recovery status of these crucial ecological niches.

In the wake of a natural disaster, there is an increased recognition of the role that "natural barriers" such as coral reefs, mangroves and sand dunes play in protecting coastlines across the world. Mangroves are unique ecological communities found along tropical and sub-tropical shorelines or estuaries that help in safeguarding the resilience of coastal areas to the threats posed by tropical storms and tsunamis. While anthropogenic disturbances have been regarded as one of the principal causes of mangrove loss, natural disasters can be equally fatal.

The 2004 tsunami affected large parts of south-east Asia, including the Indian coastline and the Andaman and Nicobar Islands, and was accompanied by a tectonic subsidence, a large-scale sinking of the land surface. In a recent study, scientists led by Nehru Prabakaran from Salim Ali Centre for Ornithology and Natural History, Wildlife Institute of India and Leibniz Center for Tropical Marine Research (Germany) examined the diversity and composition of mangrove species in the Nicobar archipelago post the 2004 tsunami and tectonic subsidence and demonstrated significant impacts of this large scale disturbance on the coastal vegetation.

The scientists sampled 34 locations across the Nicobar Islands to assess the diversity of mangrove species and compared it with the diversity reported in the past. Of the 34 locations, 22 were sampled for species abundance and composition. The researchers also sampled new inter-tidal habitats that are formed on the erstwhile terrestrial forests after the sinking of the land to understand the natural colonization of mangroves.

While the study did report the presence of new successional habitats for mangroves, the estimated loss of mangrove areas was an astounding 97%, a loss much higher than reported in previous studies. The researchers found only three sites with surviving patches of pre-subsidence mangroves for the entire group of islands.

"The studies that used satellite data less than six months from the tsunami probably considered the dead standing trees as a mangrove vegetation. This is evident from the fact that most of the survived mangrove patches indicated by the earlier studies were actually habitats with vast stretches of dead trees," said Prabakaran.

The authors reported 20 surviving mangrove species in the Nicobar Islands, with the highest diversity in the Central Islands. Four species recorded pre-disturbance were not reported in the current study indicating local extinctions. However, some species were recorded in areas where they were never reported earlier. Successional habitats showed a dominance of two mangrove species (mainly *Rhizophora mucronata* and *Bruguiera gymnorhiza*) which contributed to the bulk of their abundance.

Considering the fact that there has been a large-scale loss of mangrove habitats, the study has important implications

Trees devastated by the tsunami and land subsidence

for mangrove restoration. “Restoration activities must initially focus on facilitating the growth of well-adapted species so as to ensure a functioning mangrove cover,” said Prabakaran, asserting that the zone preferences of mangrove species should be kept in mind during these restoration activities. “Further, some of the areas can be left alone from human interventions to understand the natural recovery process, providing a comparative evidence to the effectiveness of the restoration activities in restoring such habitats,” he suggested.

“There are very few studies that document mangrove succession post natural disturbances. Species such as Nypa fruticans once common in southern Nicobar pre-tsunami, has been stripped away by the tsunami from almost every creek and inter-tidal zone where it used to occur,” said Vardhan Patankar, scientist at Centre for Wildlife Studies, and National Centre for Biological Sciences, with several years of research experience in the Nicobar Islands. “Traditional housing on Little and Great Nicobar Islands used these leaves as thatch, thereby stressing the importance of Nypa rejuvenation as a management intervention,” said Patankar.

Mangrove forests are a crucial part of the coastal ecosystems and form the first line of defense for any natural disturbances. The loss of such habitats by both anthropogenic and natural causes has significant impacts on the stability and functionality of these systems.

Reference: Prabakaran N, Balasubramanian P, Forest Ecology and Management, 427 (2018); 70-77

Photos: Nehru Prabakaran

Shreya Ghosh

Are we reaching the 'public' with our public outreach programs?

Dipyaman Ganguly is an immunologist and currently a senior scientist at the Indian Institute of Chemical Biology (IICB), Kolkata. In this interview with IndiaBioscience, he talks about how public science outreach efforts in India need to expand beyond already engaged audiences in big cities and towns and make forays into remote geographical locations to reach children and adults who lack previous scientific exposure.

Science outreach efforts currently reach a very limited section of the public in our country, i.e. there are a large number of citizens whom we are not reaching. Why do you feel this is happening?

The existing public outreach programs of science in India are inherently bound to the availability of science educators, who are usually taken from a pool of science enthusiasts with required communication skills. So what they end up doing in most of these public outreach sessions is reaching out to similar science enthusiasts. Now, there are immense amounts of efforts being put in, but they are directed towards people who are already enthusiastic about science. We are not reaching the right people - people who are hitherto disengaged in science. Unless we engage the disengaged, there is no progress. Here, geographical location plays a big role. We arrange all our public outreach programs in and around cities and towns where the population is already exposed to science. But we are not reaching out to people where they don't have that kind of exposure. It is not that no one is doing it, but we are not reaching the perimeter that we want to reach.

You have written about how our current methods of outreach encourage appreciation of the human achievements in science, but do not encourage rational thought. Can you elaborate a little on this?

Definitely that is a contentious issue, but here is my personal understanding. As an example, talking about the fact that the Mars rover is roaming around on Mars is nothing but factual scientific knowledge being given. Instead, we should incorporate in our public outreach programs how this can be achieved and what are the parameters that scientists have to keep in mind to make it happen. Unless you talk about that, real appreciation doesn't come. And while you cannot really explain to a general mass in detail how the Mars rover works, I think you can explain to people how optical magnification works. So, when you try to engage people into basic scientific methods, that's how you gain real scientific temper and real appreciation about science. But, my understanding is that most public outreach programs don't incorporate that.

Moving forward from here, how do you propose we change this? For example, you have written about the importance of reaching young minds. How do you think we can achieve this?

What would have been ideal would have been a curricular rejuvenation, wherein schools impart some understanding of scientific methods rather than scientific information. But it is easier said than done. So, that's why perhaps we should have supplemental centres or resource centres for kids all around the country. In this way, kids can have their regular school and curricular commitments, but whenever they have some questions, they can go to this resource centre and find out what is behind this phenomenon or what is behind those mechanisms. And you don't really need a lot of things to do that. If a fifth-standard student can be given access to very simple, scientifically motivated instruments or models, he/she can actually understand quite a lot by himself/herself. This idea has been around for so long and a lot of district science centres have cropped up in many parts of the country, but the problem is that in making such a district science centre, you actually take into consideration a lot of things that are not necessary, for example, how it should look. But we can actually serve the same purpose by having a science centre in a mud hut in a rural location. It doesn't need all those peripheral things that drive the cost high and which are not necessary for rural science outreach. For science outreach, you just need a few models and very simple instruments and simply giving access to these kids and that can be done anywhere.

A large portion of the public – the voting and tax-paying public - are adults who are already set into their own dogmas and biases. So, do you have any ideas on how to reach such people with science outreach efforts?

So, that is the most difficult part - adult, disengaged people. Mainly because the sources of information in their day to day life, for example, newspapers (and these days, internet), are very difficult to change and have no gradation of reliability. I think, if geographical spread is incorporated into public outreach programs, you will start reaching out to these people. Even in a location where 50 families live, out of which one family is scientifically engaged and the rest are disengaged, if you have a program there, some of the members of those disengaged families can come forward, and that's how you reach them. Even one member per family is a good start. But if you keep on doing science outreach only among science enthusiasts, people who have religiously attended your popular science lectures for the past 10 years, you are not achieving that. You have to put in extra effort to do it in a place where there is no history of past public outreach programs, no history of popular lectures being given, and then you will definitely get some of the people who never got exposed to science gaining that exposure.

In the last few years or decades, have there been any outreach efforts that you admire, which you think can be used as an example for others to emulate, going forward?

So, I definitely admire Arvind Gupta. He has a very different take on public outreach, doing it in a very different way. He's not someone standing on a podium and talking about achievements, but instead he is someone who has people making models themselves, finding out how scientific principles and natural laws work. I think that is definitely difficult - you will have thousands of popular lecturers, but it's very difficult to get a thousand Arvind Guptas. So, when you get at least one Arvind Gupta, you should capitalize on that and make him mentor similar people. Secondly, I am actually very fond of the amateur astronomy programs, which are present all over the country now. You are given a telescope, you are taught how to use that telescope, you are given some idea about what to look at, and then you go out on your own and try to record. I think that's the best example of placing the scientific method in the hands of people who are not scientists - citizen science programs. In fact, there are many avenues where you can actually engage citizens, for example, conservation biology. People have been doing it all over the world. We should come up with these kinds of ideas. When you give a ninth-standard student the job of counting sparrows in his locality, and he finds after one year that indeed the number of sparrows is going down, he will try to find out why. This kind of awareness is different.

So, you are hopeful for the future?

Yes, definitely. We should have a positive outlook on this.

Interdisciplinarity

How to make it work for you

Gautam I Menon & Sandhya P Koushika

Before a priest, I am a physician;
Before a physician, a reverend priest.
When neither is present, I am both;
When both are present, I am neither

These lines are from a letter written by the poet Mirza Ghalib in 1858, quoting a Persian verse. The sense of imposter syndrome that they evoke affects, sooner or later, all scientists whose work crosses disciplines.

Here, we describe what drove a theoretical physicist and a *C. elegans* neurobiologist to collaborate and what they each gained from it. On both sides, this was the first attempt to bridge such a stark disciplinary divide. Each story of a successful interdisciplinary interaction is different. There are no easy guides to making things work. However, what we say here may be more generally useful to others interested in starting interdisciplinary work, perhaps even with a specific collaborator already in mind. Our own example shows that the benefits of interdisciplinary approaches can be transformative, even if initially accompanied by feelings of imposter-hood.

Our work together began at an interdisciplinary meeting on traffic, organised about a decade ago at the Indian Institute of Technology (IIT) Kanpur. The term “traffic” covers a surprising number of contexts, from vehicular traffic to the traffic of vesicle-encapsulated cargo by molecular machines within cells. These machines are molecular motors, driven by ATP hydrolysis.

Sandhya Koushika (left) and Gautam Menon (right)

Theoretical physicists have devised a number of models for such motor-driven cargo transport. Almost all such models avoid the complications of experimental systems, elevating elegance and simplicity over the messiness of the real world. But complexity in biological experiments, given inherent variability and experimental caprice, is the norm, unlike physical measurements where error bars can often be so small as to not be worth even displaying.

The question that seeded our work together was the following: in experiments which tracked cargo motion within specific nerve cells in live *C. elegans* worms, such cargo inevitably wound up entering regions where other cargo had stalled. Once moving cargo came up against a stationary cargo cluster, it was unclear what happened to them. Sometimes, such clusters appeared to emit more cargo than the numbers that came in. At other times, they seemed to be able to accumulate more than they released.

We now believe that we understand this observation (*Sood et al, Traffic, 2018*). Our conclusions have been tested in detail in simulations. But to achieve this understanding, theory and experiment first had to play off against each other, with the model suggesting specific measurements and analysis. The experiments acted as a brake, discouraging unanchored theoretical speculation. Theory both drove, and in turn was driven by, the experimental observations. Several other observations and predictions from the simulations led to questions that continue to intrigue us today.

For the physicist, the experience of dealing with the messiness of real biological data coupled with the clumsiness of biological tools (as in, "You mean we can't just find out what it's doing in a cluster by looking at it?") was new. So was experiencing the intuition of the biologist for the many processes that could explain the observations as well as the careful enumeration of different tests that one could do to eliminate or confirm each of them. For the biologist, the idea that one could and should step back to look for over-arching principles that might be general (or even, as physicists like to say, "universal") outside of a narrow context was novel.

With this background, our first piece of advice: Finding the right scientific collaborator is key to any successful collaboration. Identifying the right problem is equally important. The interaction must also work both ways: A collaboration that is one-sided, in commitment or in intensity, will simply not survive in the long term. Having a shared sense of adventure and the ability to take risks, helps.

Most collaborations across disciplines start in plug-and-play mode, as in "experimental data with specific method meets new way of analysis or alternative method". They are good routes to easy papers. However, they may never transition into problems with a longer horizon because neither partner needs to step out of their zone of comfort. We will reserve the term "interdisciplinary" largely for those situations where both collaborators accept the need to deviate from established disciplinary paths as well as to deal with the intellectual disruption that results from such a change.

Our second lesson: It takes time, energy and hard work to be interdisciplinary. The best and worthiest problems rarely come pre-packaged; if they did, practical problem solving would be the larger part of the interaction.

The interactions that led to our first paper took years. Much of this time was spent in discussion and arguments, as well as in learning each other's language. We spent time with each other's students, post-docs and project assistants. This had positive consequences. The biology students learnt new ways of thinking about data. Students with a physics or a computational background understood the complexities of an actual experiment and the crucial role of experimental skill and perseverance. The collaboration has significantly transformed students in the Koushika lab, who have learnt to pay far more attention to numbers, as opposed to qualitative behaviour, than they did earlier. The more courageous among them have even attempted simple simulations, realising their value in developing the right intuition.

Those on different sides of a collaboration must also realise that there are aspects to the other field that will seem simply incomprehensible on a first encounter. For example, to a theoretical physicist, the idea that very similar proteins with virtually identical functions can have entirely different names in different model systems can be a source of discomfort. To realise that they will have to make some effort to learn these names is disturbing. To the biologist, the physicist's constant desire to side-step the details and look at the "larger picture" can be a source of frustration as well as not infrequent irritation.

Our third piece of advice: Be open to new experiences. The act of an interdisciplinary collaboration involves painful personal exposure, the repeated feeling of understanding nothing in a new field and wondering if the journey will

Members of Sandhya Kaushika's lab at TIFR hard at work at data analysis (left) and science outreach (right). Parul Sood (pictured in both images) took the collaborative study on cargo trafficking in neurons to completion.

be useful at all. The Nobel prize-winning physicist P.G. de Gennes, a pioneer of cross-disciplinary science, puts it beautifully : ".. every time one switches to a new field, one has to catch up with the rest of the class, to learn all over again from scratch … To change research fields is as traumatic as moving to another country." The only real way to deal with this trauma is to embrace it head-on.

At a practical level, this might mean forcing yourself to go to scientific meetings where your collaborator might be the only person you know, certainly at the outset, and where most of the proceedings could be entirely opaque to you. Another way to do this is to participate actively in the writing of manuscripts from beginning to end, rather than confining yourself to just those sections which include your contributions.

Some of our most enjoyable moments spent discussing science happened during the writing of our joint papers. We spent time parsing each line, clarifying where a physicist's wording would simply irritate a reviewer for a biology journal, or where the results of a long and difficult computation, a source of some pride, would have to be pithily summarised in half a line. One of our students said of this writing process: "You both argue about every sentence and inference and nearly everything leads to revisiting the data with a new analysis."

In difficult times, it is good to remember that the true value of a good collaborator is that they help you find your way around complex literature, sort out elementary confusions, and inject the right note of positivity into your interactions.

Fourth: Be confident that you have

something new to contribute. It is easy to feel that a collaborator has sufficient momentum to carry on on their own, and that they would be less encumbered by a bumbling coauthor to weigh them down. This is where one's confidence in what one brings to the table is crucial. Only then can a scientific interaction attain its natural state of flow.

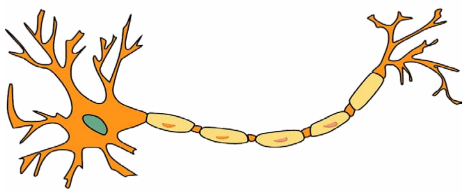
We were lucky that neither of us felt that this was particularly a problem. Both of us had other things to work on as well, so our own scientific advancement was not tied solely to whether we would achieve something publishable in the short term. Working in the Indian context also meant that we could look beyond the grant cycles that factor into the practice of science in much of the first world. This certainly made our collaboration easier, since we could afford to be open-minded in identifying questions of interest.

Fifth: Communicate your joy and excitement at working together. Realise that your collaborator needs, as much as you do, a feeling of validation and excitement. Again for us, as a consequence of the long periods of discussion that preceded our even understanding what the core problems were that we wanted to address, this came naturally. But for others, in different situations, a more systematic approach to keeping the excitement alive might help your collaborator as much as you.

Sixth and finally: The best interdisciplinary interactions are those where the problem matters, not so much the method. A set of tools and our own way of thinking define us, certainly for experimentalists but also for the theoretically inclined. When we encounter a new problem, we fall back upon what we know, translating what we must learn and understand into familiar terms. This is a reasonable starting strategy, but one that is sometimes not optimal for long-term success. A tool sharpened and adapted for one problem may simply be too blunt for another. The need for flexibility and adaptation lies at the core of making interdisciplinarity work for you.

What should we expect to gain from interdisciplinary interactions? From de Gennes again, "I cannot emphasise enough the importance of … transposition of methods between two apparently unrelated fields of science. What has been learnt in one field can at times help completely solve different problems". At a subtler level, it is also the value of attempting to answer the sorts of questions that children or total novices could put to you about your field, except that it is your collaborator who might be asking them and perhaps with a specific purpose in mind. As every scientist knows, these are the questions that are often the most difficult to answer, but that also wind up teaching you the most.

For both of us, looking back on close to a decade of interactions, much of which was spent in adjusting to the philosophy, language and practice of another, very different field, we can agree that this was time well-spent.



Leslee Lazar

Monkeys evolve a new way to communicate with humans

If you have ever lived in a place with monkey menace, you would know that monkeys are highly intelligent and have impressive ability to use tools. They can open latches, screw cap bottles and door handles and are very efficient in getting food even in urban settings.

Monkeys can also communicate with other monkeys using gestures and vocal calls, for example they have separate calls for when they are in danger and for food availability. However, could their communication be considered as a language system or is it just reflexive gesturing or calls?

One of the main features of language is intentionality, which means that the animal can understand the mental state of the animal it is communicating to. This intentionality can manifest in different ways. Two communicating humans can understand each other's intentions, mental states and goals and intentions. This ability is called 'theory of mind'. David Premack in his classic 1978 paper- *"Does the chimpanzee have a theory of mind?"*- showed that chimpanzees can also understand the intention of a human actor. However, intentionality can also occur without theory of mind, like in captive monkeys, where studies have shown intentional communication between monkeys and human caregivers.

When it comes to wild monkeys, the issue is contentious. Anindya Sinha and his group from National Institute of Advanced Studies, Bangalore, who study communication behaviour of troupes of wild bonnet macaques (*Macaca radiata*) in the Bandipur area in Karnataka, have shown that wild bonnet macaques show intentionality while signalling among conspecific members within a troupe. In a new study published in Scientific Reports they have showed that wild macaque monkeys make intentional novel communication with humans using vocal calls and gestures to ask for food. When the human had food, the monkeys made a hand extension gesture with an open palm towards the human. This is new behaviour, which is different from other food reaching or handling behaviour seen in the wild. These monkeys also orient their head towards the human, monitoring their reaction and adjusting their posture to get the attention of the human. The monkeys persist until the food reward is obtained and made a specific coo-call during this interaction.

The authors say that this is the first documented evidence of such behaviour in monkeys in the wild. To prove intentionality of this gesture, the authors say that it passes the criteria for intentionality established by previous research in other monkey species. Adwait Deshpande who is the first author in the paper says "We showed that monkeys use hand extension gesture depending on the attentional state of human receiver. They perform this gesture only when humans are directly looking at them. This is an evidence for underlying intentionality."

This shows that the monkeys have the mental capability to communicate flexibly with humans. They were able to figure out if the human is paying attention. If the human is not paying attention, they change their posture to make their presence felt. Finally, they persist in the communicative gesture until food is delivered. They gestured only when they encountered a human with food and stopped when they got the food.

This study shows for the first time, wild untrained monkeys communicating intentionally with unfamiliar humans using a novel communicative gesture. Intentionality is an important concept in understanding consciousness. Daniel Dennett, the philosopher coined the phrase 'intentional stance' to indicate the highest level of analysis by an organism, which is to understand other's mental state and predict their behaviour. Intentionality is also the cornerstone of evolution of language in humans. This study shows that the building blocks needed for the evolution of language is present in the monkeys.

Reference: *Deshpande A, Gupta S, Sinha A, Scientific Reports (2018)8:5147*

When profits damn ethics

What ails clinical research in India?

Urvashi Bhattacharyya

It took a controversy, as it usually does, for the Indian public to learn about the adverse side effects associated with ASR (Articular Surface Replacement), a hip replacement implant manufactured by Johnson and Johnson (J&J). The J&J fiasco, among many others, could perhaps be avoided if India had a strong pharmacovigilance system in place. Defined by WHO, pharmacovigilance is "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem".

We spoke to Anant Bhan, Adjunct Professor, Yenepoya (deemed to be University), Mangaluru, about key questions surrounding pharmacovigilance and conduct of clinical trials in India. Bhan is a researcher in the area of bioethics and global health & policy.

According to a report filed by an Indian NGO, 3458 deaths occurred and more than 14300 people reported side effects in clinical trials between 2005 and 2013. Yet in only 89 cases was any compensation given. Why the huge gap and what needs to be done to ensure that patients are duly compensated?

We have had a large number of reported deaths linked with clinical trials—this might be an understatement or less likely, an over-statement. More importantly, we need to have knowledge on and clear processes to establish causation. The process currently can be quite onerous and requires ethics committees to play an active role when it's unclear if they have the training/resources for judgment in this matter. An ideal mechanism might be to move to a true no-fault compensation model. At the very least, we need strict and prompt mechanisms for deciding on compensation with due process built in so that compensation is paid out on time to those eligible.

Does the issue of clinical trial malpractice differ in rural vs. urban settings?

I won't say there is a huge difference between the two; it is also incorrect to say cities have no issues of clinical trial related malpractices. Overall though, there is a higher availability of trained staff in urban settings and they typically have larger and more well-resourced centres.

In rural or tier II/III cities, availability of staff and resources such as space or beds is low. Staff training may happen through an initial exposure only rather than for a sustained duration. They may also be more likely to cut corners. Some of the recent clinical trial controversies emerged from such cities (e.g. Indore) where medical practitioners engaged in clinical trials were earning a lot of money, but not conducting the trials properly. Large cities also often have greater and stricter oversight, with state drug controller offices often being located there, and (more) frequent site monitoring.

What is the percentage of blame in these cases on the system, the government, the doctors, or is it still a historical baggage we carry?

It is a mix of everything. There was a huge growth phase a few years back and a large number of stakeholders benefited from the boom. Supportive industries such as clinical research organisations and clinical training courses emerged during the time, but their quality control measures were not in place. There was flow of money, but clear guidelines and regulations to address malpractices were lacking. Ethics committees were not exemplary and many of them didn't understand their responsibilities. Some of them were functioning as independent committees where ethics review was a business. Institutional oversight was lacking and patient awareness was low. Lately, the situation has improved on all of these counts.

How can we ensure quality control and ethical conduct in clinical research organizations (CRO)?

Most good CROs would have existing internal and external systems to oversee or conduct quality research in their institution. Internal systems would include data audits, regular checks and timely filing of data to regulatory authorities. External oversight would include regular checks by sponsors and ethics committees including conducting surprise monitoring visits. There are other mechanisms, like Data Safety Monitoring Boards (DSMB), that look at data in a non-partisan, collective manner in large clinical trials. There are also dedicated firms who perform independent monitoring and audits.

The idea is not to police clinical research all the time, but to pick up deficiencies in the system while they are happening, rather than on a post-hoc basis when the system has defaulted, and controversy has broken out. For all of this to happen, the leadership should be equally committed to preventing malpractices and should assign resources and build mechanisms for making ethical research a priority.

Despite so many controversies, we still see new drug-related issues cropping up frequently. Does this raise questions about the implementation of pharmacovigilance in our country?

Pharmacovigilance gives a better sense of the long-term benefits and risks of drugs & devices. The clinical trial environment is a strictly controlled one, with a smaller number of participants. When large-scale marketing occurs and the number of people taking a drug/device increases, one starts picking up issues that might not have been registered in the controlled setting.

Usually, mechanisms in (industry) sponsor-driven trials and follow-up for pharmacovigilance purposes are often robust, as they have to submit data to regulatory authorities on a regular basis and face swift penalties in case of data manipulation. At the same time, they also have the interest of making their product look beneficial in clinical studies and in long-term follow-up, having invested heavily in it. Obviously, relying on them alone for submitting information is not prudent, and one must have external oversight.

So how do we tackle malpractices in the pharmaceutical sector, specifically for pharmacovigilance?

The solution requires a larger nationally available pharmacovigilance framework where regulatory bodies acquire clinical data independent of company sources. We now have a national program in place, but it is still a work in progress. Our doctors need to get in the habit of reporting issues on a regular basis and we require larger resources and trained staff for effective investigation of any adverse reactions. They must have an awareness of what needs to be reported, having established causality of adverse reaction due to a given drug or device. It is also important that while a company might get to protect its Intellectual Property (IP), data should be available for public scrutiny to the extent possible for ensuring transparency.

Why do we not see more whistleblowers coming out?

In case of whistleblowers, the whole system often turns on you with zero protections, possibility of threats, with those brave enough to come forward being sidelined, victimized and thrown out of their jobs. Many of the cases where a whistleblower did come out have not seen the expose come to fruition. Unlike Ranbaxy where Dinesh Thakur could bring about a certain level of change, partly due to existing mechanisms within the US regulatory system, India lacks a system with in-built protective mechanisms for people to share information without facing major repercussions. Some of these issues would also be picked up and addressed anyway if we have more transparency available through independent watchdogs.

What international efforts are being put in place to regulate clinical research, especially in low- and middle-income countries, and how do we improve India's status as a hub of global clinical trials?

Reforms in international guidelines (Helsinki 2013, CIOMS 2016) have tried to address some vexing issues. Today, there is a realization that collaboration is the way to go in a globalized world. Funding agencies are moving towards ensuring accountability and zero tolerance to research malpractice. There is an increasing concerted global focus to ensure that lax regulations in low- and middle-income countries are not taken advantage of and that there is oversight both from the sponsor country and local country where research is happening to prevent any kind of exploitative research.

India is a large market; it's also an important R&D hub for a variety of reasons. So while there was a dip in clinical trials post-2013, there should be recovery happening now. The key question is - are we rebuilding an ecosystem which is now ethical, resilient & top quality in nature? This is necessary to avoid further pitfalls, and to make sure we engage our patient participants in a respectful manner. We need to move towards a model where India takes its rightful share as a major R&D producer and destination not because how cheap costs are, but because of the quality, reliability, and ethical conduct of science.

Using bio-entrepreneurship to solve indigenous problems

Sujoy Deb

Priyangshu Manab Sarma, an academician turned entrepreneur, shares his journey from being a Professor at The Energy and Resources Institute (TERI) to heading a company, Innotech Interventions, which is growing mushroom that can supplement vitamin D. Innotech is also involved in projects dealing with bioremediation, waste water management and clean energy, and aims to work towards a better and sustainable future.

How did you decide to leave a full-time academic position at The Energy and Resources Institute (TERI)and start your own company, Innotech Interventions?

In the beginning, while I was working on academic projects, guiding PhD students, publishing papers etc. at TERI, I was very fortunate to be associated with three projects that were subsequently commercialised and became a major revenue earning source for TERI. In the process, apart from designing experiments, I learnt facets of tech transfer, technology licensing, forming of joint ventures etc. This made me realise that there are immense opportunities and research leads available in Indian Labs that need to be tapped. With this objective in 2015 I started a joint venture with my co-founder, Hamendra Das, that would facilitate in translating and commercialising laboratory innovations – Innotech Interventions.

What were the initial challenges you faced after you transitioned from academia to industry?

The initial challenge was to convince myself that I don't belong to pure academia anymore. When we try to commercialise innovations, there are a different set of challenges that needs to be considered. I have also realised that academia is well-funded but the scope of getting funding to set up a company is far less. At TERI, I had the backing of a huge institution, but it is difficult to establish credibility when you are a small 4-5-member organisation. Fortunately, the start-up initiative kicked in and there were some good opportunities that we would avail.

You are involved in the production of a mushroom fortified with vitamin D. How did you arrive at the idea? How does this project aim to improve agricultural economy?

Over 70% of India's adult population is suffering from Vitamin D deficiency. We have conceptualised and developed a simple yet scalable technology for producing organic mushrooms fortified with Vitamin D. Our intervention for vitamin D supplementation targets a natural property of mushrooms and can enhance vitamin D by over 200%. This agro-venture will not only counter the nutritional deficiency of the masses, but also enhance the profitability of mushroom growers. We will attempt to promote mushroom cultivation in an altogether different platform, wherein it serves as a potential business venture for generation of skill-sets, wealth creation, nutrient supplementation and subsequent application in nutraceutical companies. We have planned a marketing strategy to enhance the product value, ensuring a higher rate of return to the farmers. This model can encourage entrepreneurs to take up this venture for enhancing profitability upon implementing different agri-business strategies.

Can you elaborate on your bioremediation/clean-energy project and share some of its benefits?

Exploration and extraction operations of conventional fossil-based energy resources like petroleum and natural gas, as well

The Innotech team (Photo: Priyangshu Sarma)

as the newer non-conventional resources like coal bed methane, shale gas and gas hydrates, generate significant amount of waste water. This huge volume of water brought from the subsurface along with the fossil resources is also known as produced water (PW). Conventional treatment processes fail not only in handling the volumes of PW, but also in meeting the regulatory standards of the effluents due to its unique composition.

The concept developed by Innotech is focused on the very same properties of PW that renders conventional systems unfit for its treatment. The low organic content and high salinity that makes PW unfit for most conventional systems, turns out to be ideal for the prototype developed by Innotech. Our technology integrates an electrochemical process with controlled microbial conversion of sulphate to sulphides. Apart from generating water that is fit to meet the regulatory standards, caustic soda will be generated as second value-added product during this process.

How did you get your funding at different stages? Did you face any struggles in the process?

Funding was never easy. We initiated the process by bootstrapping and investing some of our own money. The first major break was received from IKP Knowledge Park, Hyderabad. The data generated at IKP helped us pitch the concept and its applicability for a much larger start-up fund from Oil India Limited. Our concept also won the Indo-Israel Innovation Challenge, jointly organised by the Indian and Israeli governments. This gave us necessary credibility. In 2018 we got the Water Digest Award in the Best Research Innovation category in Waste Water Treatment. This generated immense interest among the investors.
The story is similar for our Vitamin D fortification project on Mushrooms. It started with our personal money. There

were more rejections for this project. At one point we thought it may not be a feasible idea but we went on with the initial experimentation with help of a friend and a cousin who spared some land and resources to start the production. I had sent in applications and given presentations to over 30 different funds and organisations, but all in vain. Finally, I encouraged my colleague to apply again in Biotechnology Ignition Grant (BIG) for the same project. We cleared the BIG hurdle and received a 50 lakh seed fund from them, a major breakthrough. Later we were winners of the Economic Times Power of Ideas competition, and received another seed grant of 5 Lakhs from the Centre for Innovation, Incubation and Entrepreneurship at Indian Institute of Management, Ahmedabad.

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How important is the role of incubators and start-up grants for setting up a company?

Incubators are extremely important to set up the experiments to either establish the proof of your concept or to scale up the concept. It provides not only the lab place but an ecosystem with like-minded people. Start-up grants are equally important in the early stage. They are the best bet after the bootstrapping phase, as they normally do not seek equity. Investors at early stages may take a significant amount of equity in your venture and this may become an issue at later stages of funding.

What would your message be to a young scientist who wants to become an entrepreneur?

This is the right time. When we completed our PhD (2004), we use to hear about start-ups and spin-offs only during our visits abroad. However, with the start-up ecosystem growing rapidly in the country, this is just the right time to dive in. Personally, I think most of us are afraid because of the financial insecurity and risks involved. Therefore, I would urge the youth to become financially literate as soon as possible, which is not usually the case in our country. One more point I would like to make is that help and assistance are available, one just has to ask and seek. Most importantly, if you have the passion and a good idea, it will be noticed and appreciated. Passion is the best way to get other people involved in your dream. I believe the rest falls in place automatically.

What is the one lesson you have learnt from your journey so far that you would like to share with everybody?

A good team that can take care of all the aspects of the business and pure passion of the founders would be the key to start as well as sustain a venture.

YIM at 10 years

And thoughts on why India's research program should follow a different path from the USA

Ron Vale

The first Young Investigator Meeting in Trivandrum in 2009 was inspired by a dinner that I had with three junior faculty in 2008 while I was on sabbatical at NCBS. The dinner conversation was centered around their questions and concerns regarding establishing their own independent laboratory. When I returned home from dinner, the evening's discussion raced through my mind and loomed larger in its importance. These young scientists' aspirations and insecurities in their transition struck me as similar to India's predicament as a whole. How can India make the transition to becoming a leader in scientific research?

As I pondered this larger question, India's scientific future seemed to be inextricably linked with the futures of these three junior faculty. They, and their peers throughout India, had to succeed if India was to succeed as a whole. However, the need for more mentoring by these three junior faculty revealed a gap in the Indian system as a whole. Something needed to happen at a bigger scale than just one dinner conversation. Furthermore, a spotlight needed to be placed on the careers of young scientists that was bright enough to draw the attention of senior scientists, institute directors, and government leaders. The Young Investigator Meeting became that spotlight as well as the nation-wide extension of the mentoring conversation that happened over dinner in Bangalore.

Many of the topics that I had discussed with the junior faculty over dinner are similar to those covered at YIM. What are the skills needed to run a successful lab? How does one succeed within the opportunities and constraints of India? How does one guide students? How does get research funds, get papers published, and nucleate collaborations? How can one get great young Indian scientists who have trained abroad to come back to India? What are inspiring stories of people who have succeeded scientifically in India? What more can be done to help women scientists succeed, allow for the success of scientists in universities and colleges, and create research programs in the diverse regions of India? Now in its 10th year, the YIM has served as a forum for these discussions as well as a wonderful opportunity to learn about outstanding science being done by young and senior scientists in all areas of biology.

Perhaps even more important than the scientific discussions and mentoring of young scientists is the strong sense of community that has developed around each YIM. Collaborations and friendships have grown out of YIM. Young scientists have received inspiration from other peers and learned that they are not alone in their frustrations. Most importantly, most leave feeling more optimistic about their future. YIM is a shared experience that connects young scientists from different scientific fields, different parts of the country, different stages of the academic ladder, and even across different YIMs. "Which YIM did you go to? I went to the one in…." YIM creates a sense of being part of something bigger that unifies young scientists throughout India and across time. This sense of connectivity is important for the success of Indian science, as I will discuss later.

"YIM is a shared experience that connects young scientists from different scientific fields, different parts of the country, different stages of the academic ladder."

The 10th anniversary of the YIM presents an opportunity to "take the pulse" of the biological sciences in India and explore where it might be headed. The meeting will engage young scientists in thinking through issues that are relevant to their future, and we hope that several white papers will emerge. In this blog, I will highlight perspectives that will discuss in my opening talk at this year's YIM. I will make the case that India should not blindly follow the path taken by the US in some areas and rather be willing to adopt new ideas and Indian-specific solutions. In closing, I also will reflect on what 10 years of YIM may have offered to India as a whole.

Propelling unique research programs in India

Academic scientists in India have considerable freedom in choosing their research topic. However, often, the seeds of those choices are planted in the US or Europe and not in India. Indians typically go to the US or Europe for postdoctoral training. Those that return to India as junior faculty often continue to work in the same area as their postdoctoral training. Familiarity and inertia are part of the reason. However, the reward system also favours the continuation of past projects, grant review committees often require preliminary results and evidence of competency in the field. In addition, the time to tenure for junior faculty is short and papers must be

> "India could benefit from more actively nurturing research that is pertinent to its needs and environment."

produced for promotion committees. Young scientists understandably feel these pressures to be productive and continuing past work often seems like the safest route.

The problem with this model is that one's postdoctoral work may not be well-suited to circumstances in India. In a large US university, the postdoc may have been aided collaborations, or critical resources from cores and/or neighbouring labs. However, as a junior faculty in a smaller Indian institute or university department, the resources may be limiting and perhaps there may be few, if any colleagues, in their specific area of research. In addition, if the field is moving fast, it might be difficult to compete with US labs given the longer time needed to train students and establish a well-functioning lab in India.

India also could benefit from not just importing research programs from the US but more actively nurturing research that is pertinent to its needs and environment. Such areas include microbial biology, infectious diseases, plant sciences, ecology, among others. Many research topics are less studied and supported in the US. In addition, India contains unique biological resources that merit study, including its enormous biological diversity and the genomes of its human population that contain insights into human biology and disease.

India is expanding research efforts along the lines described above. The recent effort by the DBT to establish a marine biological research station in Goa is an example of a program devoted to understudied biology and India's natural resources. However, many other ideas and efforts should be encouraged. It also important to consider initiatives that would re-train Indian scientists, but do not require building brick-and-mortar institutes. Let's imagine a young or mid-career faculty member who is interested in transitioning part of his/her laboratory from, let's say, Drosophila development, to studying the cell biology of malaria. Transitional grant mechanism (or "schemes" in the Indian parlance) that facilitate such work could be helpful. Such funding could include travel funds for short visits to labs abroad or in India to learn new techniques and forge collaborations. Establishing (and perhaps providing some funding) for "collaborative networks" within India also could help in welcoming and lowering the barrier for entry of newcomers to a field. Participation a "collaborative network" (e.g. in malaria) could involve data and reagent sharing, student exchanges, annual or semi-annual meetings, and training workshops. These networks also could help to connect a critical mass of investigators to tackle a problem within India.

Developing National Solutions for Cutting-Edge Technologies

Access to cutting-edge technologies is becoming increasingly important in modern biological research. The latest cryo-electron microscopes, super-resolution microscopes, DNA sequencers and mass spectrometers are just some of the instruments deemed to be essential. Thus, American universities are in continual "arms race" to acquire the latest instruments to retain their stature as a top university. Naturally, this requires that universities raise funds for instruments with ever-ballooning price tags. And blunders are not uncommon. In the eagerness to be at the leading edge, sometimes instruments are bought that are rarely used or show up without personnel in place, who know how to run them properly.

> "Indian institutes and universities need to pay attention to their recent expansion of postdocs and decide how they want to treat these young scientists."

The instrumentation "arms race" in the US, China and Europe could leave India at a disadvantage. Because of the high cost, it is simply not possible for large numbers of Indian institutes and universities to follow the US model of being entirely self-sufficient in their suite of technologies. India must be more strategic to reach the same goals.

One strategy would to be to create more emphasis on national or regional centers of technology. Building facilities whose intention is to serve multiple institutions would facilitate broader and more democratic access to technologies. Importantly, by limiting the numbers of such facilities, focus could be placed on their excellence. Some facilities might require considerable resources and highly skilled individuals as directors and might operate at a national-scale. An example is the national cryo-EM facility (with its new Krios electron microscope), which has recently begun operations at NCBS/InStem and could expand in the future. Others facilities with broader use might be regional (e.g. mass spec and sequencing). A team of faculty (potentially from multiple institutions) could oversee such facilities. Because instrumentation is becoming increasingly automated, samples can be shipped from labs to these facilities (easy for sequencing but also possible for crystallography and cryo-EM). However, it is also important for investigators to come in person, which will require short-term housing Other associated challenges are to organise fair access and structure usage fees for such facilities.

Instruments are only as good as the people who run them. However, US institutions rarely have career tracks for individuals involved in technology development and support. Unlike the US, India could consider creating more technology support/development career track positions, ideally with a similar stature to academic faculty.
If this happens, India would be more competitive in hiring such such individuals than the US. Technology development faculty also could develop courses for students and postdocs, which will have great value to India as a whole. The Bangalore Microscopy Course is an example of an outstanding course open to students throughout India and the world, and is now organised primarily by core facility managers at NCBS.

Building a sustainable pipeline of graduate and postdoc training

Between the first and the 10th YIM, the postdoctoral work force in India has grown considerably. While perhaps an outlier, the number of postdocs at NCBS has grown 10-fold during this period time (now numbering ~100), while its faculty has only doubled in size. Postdocs are no doubt valuable additions to a laboratory and the research workforce overall. Good postdocs also are great mentors for younger students.
However, increasing the number of postdoctoral fellows has led to certain undesirable outcomes in the USA. A few decades ago, postdoctoral training typically was brief (e.g. 2 years). Now, a five year postdoc period is the norm; some stay longer. The postdoc period is becoming less about receiving training and more about obtaining the right type of scientific papers to get a job. PIs in the US also have become "addicted" to the highly skilled and relatively inexpensive postdoc workforce to fuel their research. Because of the long period of postdoc training and uncertainty of a job, many postdocs in the US have become disillusioned.

What can India learn from the problems that the US faces? First, Indian institutes and universities need to pay attention to their recent expansion of postdocs and decide how they want to treat these young scientists. Indian postdocs need to receive quality training, including in skills needed to obtain jobs, and be treated as trainees not just as labourers. Young scientists in some areas in India have self-organised to form Postdoc

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Associations, which is a positive step forward. However, senior leadership also should take responsibility for well-being and careers of the postdocs at their institutions. Furthermore, institutions (and perhaps India as a whole) should collect data on the length of time of postdoc training and their job outcomes. The US has failed to collect such data, and as a result, postdocs have become an invisible workforce. Since the postdoc expansion is so recent in India, now is the time to do things properly right.

India also must be attentive to its own attitudes and biases when it comes to hiring its own postdocs. Indian institutes and universities generally hire faculty who have gone abroad for postdoctoral training, recognising the valuable experience of being in a US or European laboratory. However, now India faces a dilemma. If India wants to have excellent postdocs working in their own country, rather than going abroad, then it needs to find jobs for them. Doing a postdoc in India must have value. Thus, Indian postdocs should be given a fair opportunity in the Indian academic job market, and indeed Indian postdocs are watching the situation to see what will happen. Even if a few Indian postdocs are hired to India's top institutes, then this will send a clear message to young scientists that an Indian postdoc is not a dead-end for high career aspirations. Establishing more staff scientists positions (similar to Europe) also might provide new job routes for postdocs in India and be a good investment for Indian science overall.

One difficulty in evaluating Indian postdocs is recognising that they may not have papers in "fancy" journals like their some of their counterparts that went to labs in the US. Sadly, papers have turned into a quick and easy solutions for hiring committees to make decision. However, more important than papers is judging the character and scientific potential of an individual, which is the core of long-term success. India should invest the time to evaluate individuals, locally and abroad, using multiple means including recommendations and interviews (in person or via Skype).

Rigorous evaluation of individuals, and not their CVs, also may allow India to become more competitive in its hiring practices versus the US. For example, India might take some chances in hiring younger scientists to faculty positions, which would be a welcome change to the current trend of increasing time to independence. Many of the great discoveries in science were made by individuals in their twenties or early thirties. Offering a future faculty position to a brilliant Indian scientist who has just finished his PhD or after 1-2 years of postdoc might only be done in unusual circumstances of excellence (not politics). However, India would then reach these talented individuals before they receive more lucrative offers in the US. These individuals also could be allowed to train for a year or two abroad before starting their job in India.

Concluding remarks

After 10 years of YIM, where are we? Has it made a difference? About 800 junior faculty and postdocs have attended the first 9 YIMs. My sense is that it has done them some good. YIM has not solved the issues facing young scientists in India. But it has drawn significant national attention to their careers and mentoring. Many institute directors came to YIM skeptical at first, but left understanding what YIM seeks to accomplish for of young scientists. >50 international senior scientists also have attended YIM, many for the first time, and left inspired and more willing to engage with Indian science. YIM also has given Indian postdocs abroad a chance to see what returning to India might be like, not with glossary brochures but with frank discussions that expose the messy realities, opportunities, and warmth that are altogether characteristic of India. YIM also has served as a national forum where issues of Indian science could be discussed freely between junior and senior faculty and government leaders. Indeed, the 10th anniversary YIM is structured primarily to address key national issues and produce white papers.

Many young scientists came to YIM seeking jobs, mentoring, collaborations, and perhaps inspiration. While these are all important, my greatest hope was that YIM might instill a sense of leadership and community-mindedness in young scientists. More than new buildings and equipment, India needs new leaders. I heard a senior scientist bemoan that Indian science is like a bucket full of crabs; when one crab manages to get to the top and escape, it is pulled down by the others. Such perceptions need to change. The future of Indian science cannot be dictated by those who complain but rather should be handed to those who have the energy and inspiration to build. As a Chinese proverb says, "The person who says, 'It can't be done' should not interrupt the person who is doing it."

New Indian leaders must rise from the ranks of this generation of YIM attendees. Young and mid-career scientists need to roll-up their sleeves and become the change that they want to see in India. Driven by passion and duty, these new leaders can do many things, big and small. The jobs include eventually becoming heads of institutes or departments, developing better graduate programs, working with government in the implementation of their programs, developing better institutional recruitment practices, helping with running instrument cores, volunteering in local schools, communicating science to the public, and the list can go on for pages. YIM has tried to plant this seed of public duty and community spirit. If this seed might be remembered by its attendees and germinate in the future, then YIM indeed will have been a great success.

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ENGAGING COMMUNITIES, ENABLING CHANGE

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We thank the Department of Biotechnology (DBT) for funding and support.

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