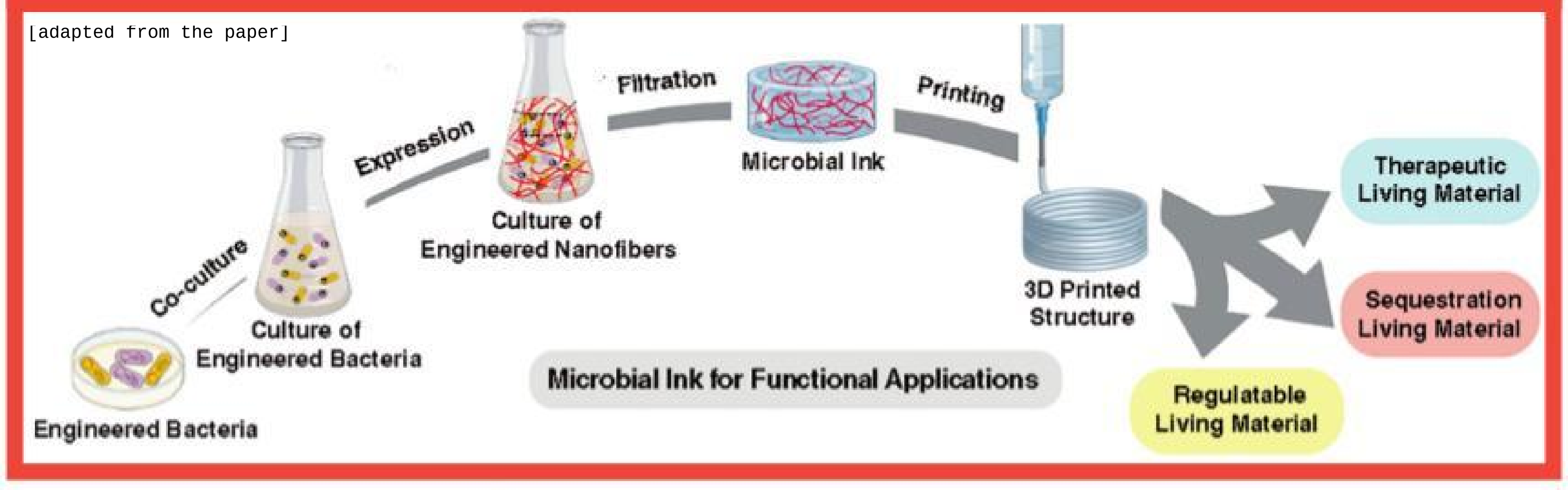
Genetic engineering mixes the mortar

Living tissue as material for intelligent structures



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The cuckoo clock, printing press, steam engine and digital computer are constructs of hard and soft material, ingeniously put together, so that they act like they possess intelligence. Could the functionality of things be built into the very material that objects are made up of?

Architect-artist Haresh Lalwani imagines structures that shape themselves with intelligence, and adapt to the environment, like living things. And on the way to thinking of a "DNA of form", he devises objects and shapes that grow into their function and purpose. But each one stays unique, like individuals of a living species.

Anna M Duraj-Thatte, Avinash Manjula-Basavanna, Jarod Rutledge, Jing Xia, Shabir Hassan, Arjirios Sourlis, Andrés G Rubio, Ami Lesha, Michael Zenkl, Anton Kan, David A Weitz, Yu Shrike Zhang and Neel S Joshi, from Harvard and North-eastern Universities and Brigham and Women's Hospital, Harvard Medical School, report a development that seems to actualise Lalwani's dream. Writing in the journal, *Nature Communications*, the authors describe a technique of building objects with a functional, living material, which can then carry out a purpose and maintain itself.

A development of recent years has been the technique of three-dimensional printing, as a step of progress beyond two-dimensional printing. The older process is nothing but automated placing of dyes on a surface, to create text or images in two dimensions. For creating objects, not just images, we need material in bulk, not just a dye on a surface.

One way of shaping objects, known since long, has been chiselling or carving. In its modern form, this is shaping material on a lathe. And with the computer-controlled lathe we can automate the process, converting just numerical data, a "programme", into a 3-D form.

This process, however, is not "printing" of the object, in the sense that this is a case of "shaving away" and reducing existing material to the desired shape. In two dimensions, this would be like covering a page with ink and then erasing the parts where the text is not to appear.

For 3-D printing, what we need is to deposit material, layer by layer, and build up the desired object from scratch, rather than come down to the object from a larger block of material.

The 3-D printer does just this, using special materials, which can be deposited and would stick, to finally take the shape desired. And the process of deposition is computer controlled. And like automatic lathes are able to shape objects according to computer drawings, the 3-D printer can also take its instructions from designing software.

In its early stages, 3-D printing could create just a look-alike, albeit speedily, and it was known as "rapid prototyping". But the process has evolved and is now used to manufacture complex shapes that are not feasible in the normal way.

A development of 3-D printing is 3-D bioprinting — where what is built up is not just an object with a given shape, but a shape built of living cells. An application of this method is to use cells to generate living tissue, or even organs, which is useful in studying the efficacy of drugs. And another application is in creating scaffolds, which can be implanted to support the natural regeneration of body tissue.

The paper by the Harvard group mentions applications that interconnect a kind of bacteria, which participate in photosynthesis, to create a surface that generates electricity when exposed to light. And others to create devices with materials that respond to the environment or influence other reactions.

These are useful examples, the paper says, but much more is possible if we could work with the properties of the very cells, like the bacteria, of which the material that is used is made. Genetic engineering now allows us to control the features of cells, and hence to plan with precision the properties of resulting materials.

The team hence undertook creating a "bio-ink" that is made entirely of genetically engineered bacteria. It has been possible, the paper says, to ensure that the bio-ink is structurally stable and amenable to being cast in specific shapes. And then, to have the objects created by 3-D printing use active material, with "therapeutic, sequestering and regulatable" capabilities.

The qualities that bio-inks need, the paper says, is that they be free-flowing, so that they can be laid on to create required shapes, yet sufficiently firm to retain a given shape.

Bio-inks are thus such materials, which are compatible with biological material, that can function as a framework to shape the growth of living cells. The team now examined the possibility of constructing this framework itself out of the functional cells that the framework was to support.

In earlier work, the authors say, the team had developed methods to attach bits of proteins to the fibrous exterior of escherichia coli, or e-coli, a common bacterium. To improve the properties of e-coli films, the team turned to components of fibrin — the protein that helps in binding together blood cells to form rigid clots. With the help of genetic engineering, the team created in e-coli a parallel of the "knob and hole" linking mechanism that is found in fibrin. E-coli films then mimicked the binding of fibrin, and could form crosslinks, so that the free-flowing films formed into fibres that were more robust.

Having thus developed a strain of e-coli that could be the material of 3-D printed structures, the team proceeded to enable the e-coli with therapeutic components. First, they programmed e-coli to respond to a specific chemical signal by synthesising and secreting azurin, a biological anti-cancer drug.

Microbial ink made of these cells was now used to print a 2-D pattern, and the pattern was incubated in two separate media — one which contained the signalling agent, and one which did not. In 24 hours, the medium, which had the agent, showed the presence of azurin.

Another trial was by grafting e-coli with a bit of protein that formed a bond with bisphenol-A, a toxic chemical. A pattern that was printed with bio-ink that contained these cells was then incubated in a medium that contained bisphenol-A. The pattern was seen to capture eight per cent of the toxin within 12 hours and 27 per cent in 24 hours, while normal microbial ink did not.

A final trial was to show that e-coli could be programmed to regulate its own rate of growth. E-coli was engineered to produce, when signalled as in the first case, a chemical toxin that arrested cell growth and led to cell death. These cells, in a printed structure, were seen to proliferate in the absence of the signal but shrank by two orders of magnitude when the signal was present.

What has been done is to create, just by genetic engineering, a stable, 3-D printable material, which can form structures that can be induced, by a chemical signal, to produce an anti-cancer drug, to sequester a toxin and then to control its own cell growth.

There is an "ever-growing toolkit of biological parts being developed by synthetic biologists," the paper says, and microbial ink can be customised to serve different functions, in medicine and other spheres. There could be applications in the existing use of living cells in building materials. And this could extend to space travel, where we could need to generate materials on demand, with scarce resources, the paper says.

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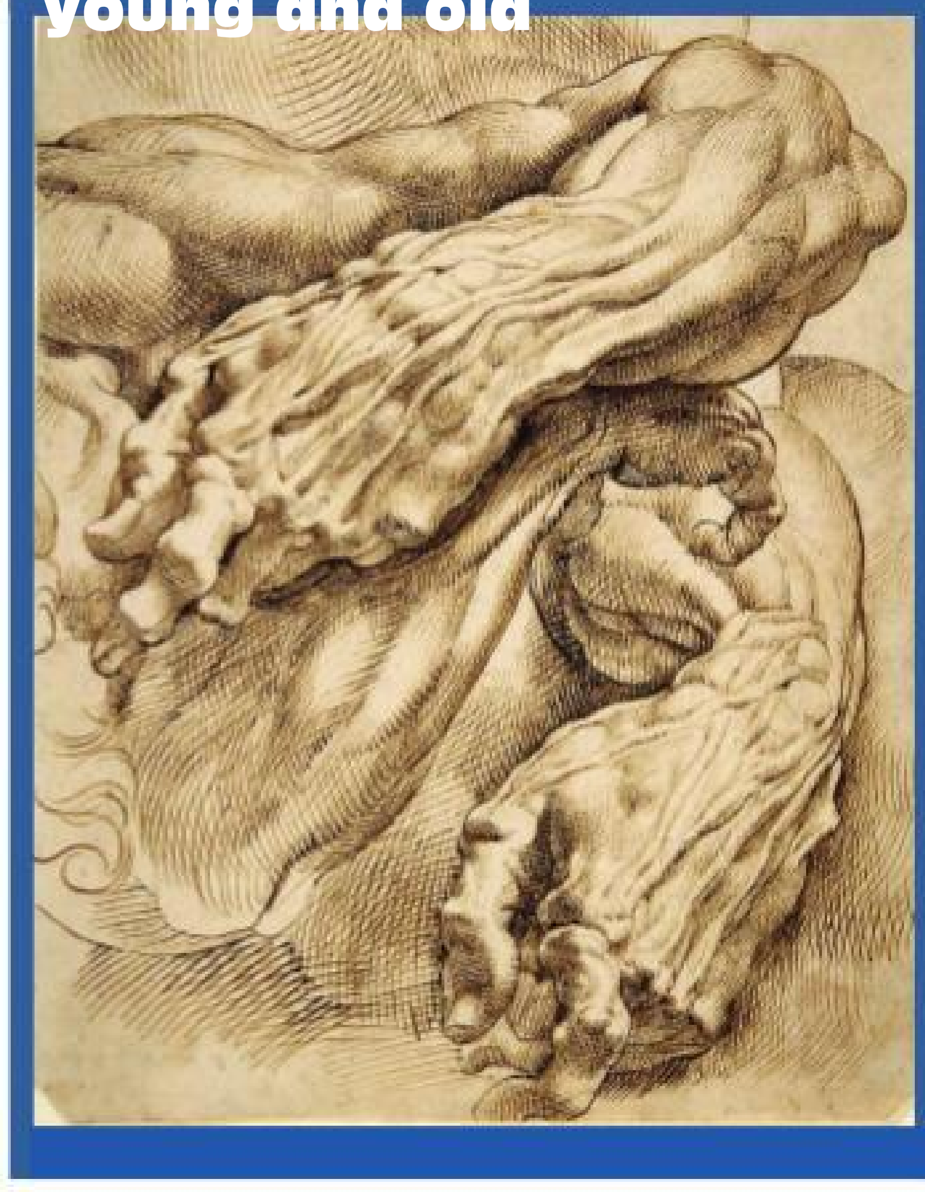
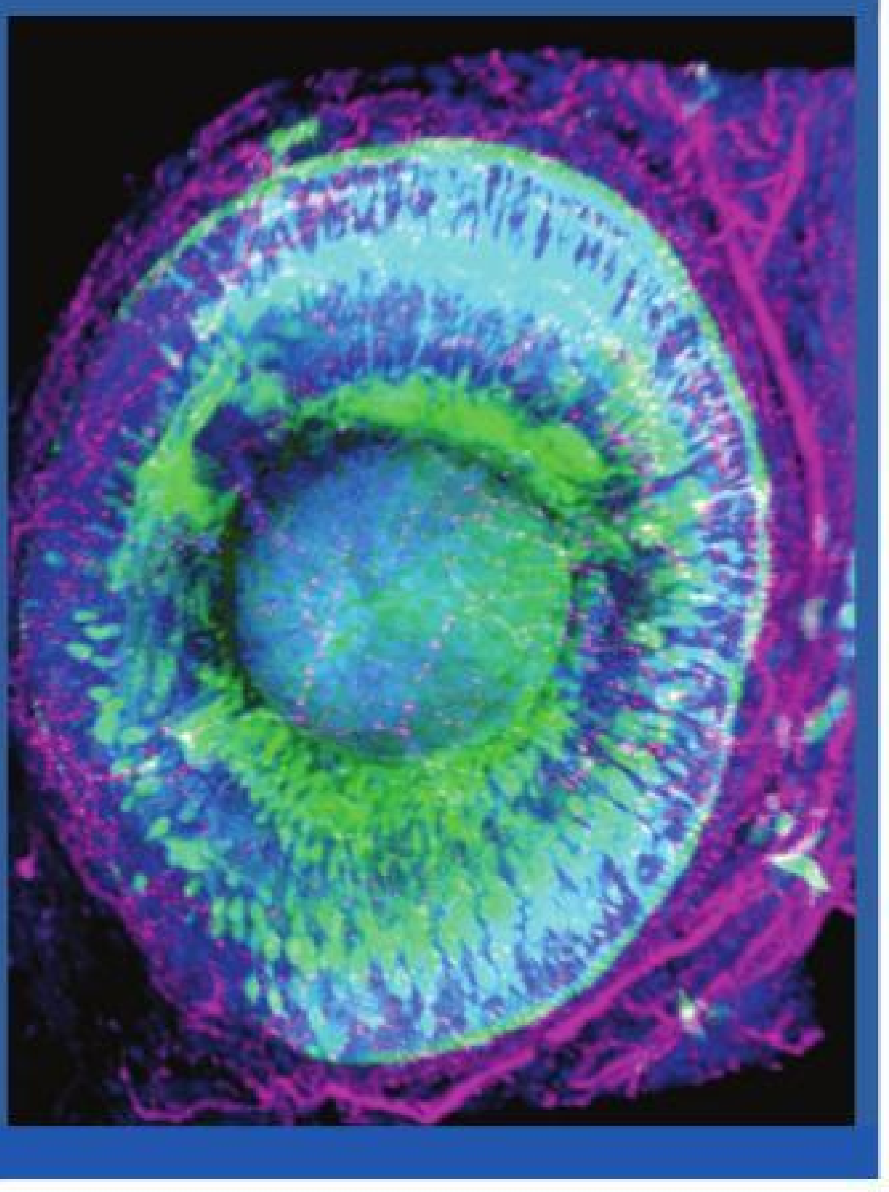
AWE-INDUCING VISUALISATIONS

Art illuminates the beauty of science — and could inspire the next generation of scientists, young and old





Scientists have often invited the public to see what they see, using everything from engraved woodblocks to electron microscopes to explore the complexity of the scientific enterprise and the beauty of life. Sharing these visions through illustrations, photography and videos has allowed laypeople to explore a range of discoveries, from new bird species to the inner workings of the human cell.

As a neuroscience and bioscience researcher, I know that scientists are sometimes pigeonholed as white lab coats obsessed with charts and graphs. What that stereotype misses is their passion for science as a mode of discovery. That's why scientists frequently turn to awe-inducing visualisations as a way to explain the unexplainable.

The BioArt Scientific Image and Video Competition, administered by the Federation of American Societies for Experimental Biology, shares images rarely seen outside the laboratory with the public in order to introduce and educate laypeople about the wonder often associated with biological research. BioArt and similar contests reflect the lengthy history of using imagery to elucidate science.

A historical and intellectual moment

The Renaissance, a period in European history between the 14th and 17th centuries, breathed new life into both science and art. It brought together the fledgling discipline of natural history — a field of inquiry observing animals, plants and fungi in their ordinary environments — with artistic illustration. This allowed for wider study and classification of the natural world.

Artists and artistic naturalists were also able to advance approaches to the study of nature by illustrating discoveries of early botanists and anatomists. Flemish artist Peter Paul Rubens, for example, offered remarkable insight into human anatomy in his famous anatomical drawings.

This art-science formula was further democratised in the 17th and 18th centuries as the printing process became more sophisticated and allowed early ornithologists and anatomists to publish and disseminate their elegant drawings. Initial popular entries included John James Audubon's "Birds of America" and Charles Darwin's "The Origin of the Species" — ground-breaking at the time for the clarity of their illustrations.

Publishers soon followed with well-received field guides and encyclopaedias detailing observations of what were seen through early microscopes. For example, a Scottish encyclopaedia published in 1859, "Chambers's Encyclopaedia: A Dictionary of Universal Knowledge for the People," sought to broadly explain the natural world through woodblock illustrations of mammals, microorganisms, birds and reptiles.

These publications responded to the public's demand for more news and views of the natural world. People formed amateur naturalist societies, hunted for fossils, and enjoyed trips to local zoos or menageries. By the 19th century, natural history museums were being constructed around the world to share scientific knowledge through illustrations, models and real-life examples. Exhibits ranged from taxidermied animals to human organs preserved in liquid.

What began as hand drawings has morphed over the past 150 years with the help of new technologies. The advent of sophisticated imaging techniques such as X-rays in 1895, electron microscopes in 1931, 3D modelling in the 1960s and magnetic resonance imaging, or MRI in 1973 made it easier for scientists to share what they were seeing in the lab. In fact, Wilhelm Roentgen, a physics professor who first discovered the X-ray, made the first human X-ray image with his wife's hand.

Today, scientific publications including *Nature* and *The Scientist* have taken to sharing their favourites with readers. Visualisations, whether through photography or video, are one more method for scientists to document, test and affirm their research.

Science, art and K-12 education

These science visualisations have found their way into classrooms, as K-12 schools add scientific photographs and videos to lesson plans. Art museums, for example, have developed science curricula based on art to give students a glimpse of what science looks like. This can help promote scientific literacy, increasing both their understanding of basic scientific principles and their critical thinking skills.

Scientific literacy is especially important now. During a pandemic in which misinformation about Covid-19 and vaccines has been rampant, a better understanding of natural phenomena could help students learn how to make informed decisions about disease risk and transmission. Teaching scientific literacy gives students the skills to evaluate the claims of both scientists and public figures, whether they're about Covid-19, the common cold or climate change.

Science knowledge, however, appears to be stagnating. The 2019 National Assessment of Education Progress measured the science knowledge and scientific inquiry capabilities of United States public school students in grades four, eight and 12 from a scale of zero to 300. Scores stagnated for all grades from 2009 to 2019, hovering between 150 to 154.

A survey of K-12 teachers shows that 77 per cent of elementary teachers spend under four hours a week on science. And the 2018 National Survey of Science and Mathematics Education found that K-3 students receive an average of only 18 minutes of science instruction every day, compared to 57 minutes in math.

Making science more visual may make learning science at an early age easier. It could also help students both understand scientific models and develop skills like teamwork and how to communicate complex concepts.

Deepening scientific knowledge

The BioArt Scientific Image and Video Competition was established 10 years ago to both give scientists an outlet to share their latest research and allow a wider audience to view bioscience from the researcher's point of view.

What's unique about the BioArt competition is the diversity of submissions over the last decade. After all, bioscience encompasses the wide range of disciplines within the life sciences. The 2021 BioArt contest winners range from a zebrafish embryo's developing eye to the shell of a species of 96 million-year-old helochelydrid fossil turtle.

I have served as a judge for the BioArt competition over the last five years. My appreciation for the science behind the images is often exceeded by my enjoyment of their beauty and technical skill. For instance, photography using polarised light, which filters light waves so they oscillate in one direction instead of many directions, allows scientists to reveal what the otherwise hidden insides of samples look like.

Whether today or in the past, science elucidates the foundation of our world, both in miniature and at scale. It's my hope that visually illuminating scientific processes and concepts can advance scientific literacy and give both students and the general public access to a deeper understanding of the natural world that they need to be informed citizens. That those images and videos are often beautiful is an added benefit.

The writer is professor and director, neuroscience programme, Northern Kentucky University, United States. This article first appeared on www.theconversation.com

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PLUS POINTS

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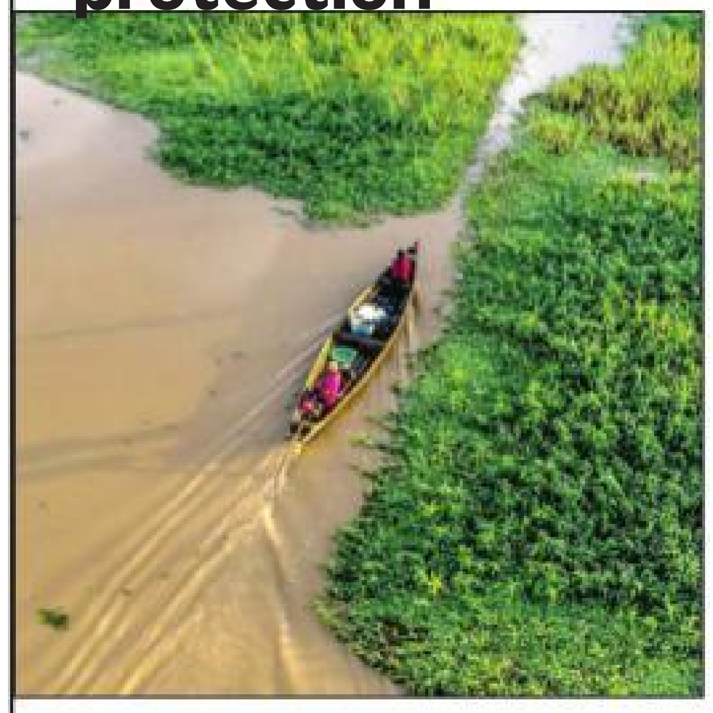
Indigenous protection

Indigenous protection



A team of researchers, led by the University of Sheffield in the United Kingdom, has discovered that rates of deforestation and degradation in tropical forests are lower in indigenous lands compared to other areas.

The findings, published in *Nature Sustainability*, show that across the tropics, indigenous lands had a fifth less deforestation on average compared to non-protected areas, and in Africa, indigenous lands reduce deforestation more effectively than protected areas. In Asia, deforestation rates in protected areas and indigenous lands were similar, with both having reduced deforestation by roughly 20 per cent compared to non-protected areas.

Jocelyne Sze, a PhD student from the University of Sheffield's Grantham Centre for Sustainable Futures and lead author of the paper, used maps of protected areas and indigenous peoples' lands to identify what areas are protected formally under state regulations, are managed or owned by Indigenous peoples, are covered by a combination of both, or are not protected at all. She used recent satellite data to calculate their levels of deforestation and degradation.

Sze said, "Indigenous peoples have been saying for decades that they are the best guardians of their homelands, and our results affirm this point. With upcoming international policy discussions on safeguarding biodiversity and climate, this is a particularly opportune moment to recognise and support indigenous peoples in their efforts both legally and financially."

Surprisingly, however, it was discovered that in the Americas, deforestation was higher in indigenous lands compared to protected areas by about 15 per cent. Previous studies have largely found that deforestation was lower in indigenous territories in Latin America compared to protected areas. Sze believes this may have started changing in the last decade as a result of government policies that weaken environmental regulation, such as those in Brazil, which are making it harder for indigenous peoples to protect their forests.

Professor David Edwards, senior author of the research from the School of Biosciences at the University of Sheffield, said, "We must support indigenous communities in our shared goal to deliver on the lofty ambitions of the Glasgow Declaration on Forests to halt deforestation by 2030. Failure to do so will edge us closer towards breaching the 1.5oC in global temperature rise."

Coating for masks

Coating for masks

Researchers from the Indian Institute of Technology-Guwahati have developed a "nanometre thick superhydrophobic coating" material to modify ordinary cloth or silk masks that will maintain comfort but offer better protection against aerosol-driven infections such as Covid-19.

According to World Health Organisation guidelines, N95 masks or double masking protects people to a great extent from the novel coronavirus. But the drawback is that people feel suffocation after wearing them for a long time. Besides, N95 masks are costly and thus unaffordable to large sections of the population. Instead, people resort to cheaper and readily available cloth and silk masks.

To address these challenges and to bring in a safer, economical and comfortable alternative, the researchers of IIT-Guwahati have developed a coating material to modify the easily available cloth mask into a hydrophobic mask to repel virus-laden droplets and avoid breathing difficulties even when worn for a longer period of time. Another advantage is that these masks are versatile and can be used with other additives such as antibacterial nanomaterial for additional protection against viruses.

The research was led by professor Arun Chattopadhyay, department of chemistry and Centre for Nanotechnology, IIT-Guwahati and Partho S G Pattader, department of chemical engineering, School of Health Science and Technology, and Centre for Nanotechnology, IIT-Guwahati. It has recently been published in the journal *ACS Applied Bio Materials*.