Research Newsletter of
the Indian Institute of Science

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KERNEL

Editorial

The Indian Institute of Science (IISc) is India's premier destination for science and engineering. Research at IISc spans six divisions, and is distinctively interdisciplinary in nature.

Five years ago, Kernel was launched as an annual magazine to showcase the Institute's major research contributions. In its new avatar, Kernel will now be published as a monthly digest, providing snapshots of recent research and initiatives. This issue also features efforts to combat the COVID-19 pandemic.

INDIGENOUS VENTILATORS FOR COVID-19

Turbulent Shear Flow Physics and Engineering Lab, IISc

AS THE COUNTRY FACES A LOOMING SHORTAGE OF VENTILATORS FUELED BY THE COVID-19 CRISIS, IISc RESEARCHERS HAVE BEEN RACING AGAINST TIME TO BUILD HOME-GROWN SOLUTIONS

A ventilator can be a life-saver for patients whose lungs are damaged by COVID-19 infection. But India, like all countries grappling with this pandemic, is likely to face a large shortage of ventilators. Manufacturers are unable to procure key components such as sensors and flow controllers from abroad due to the current disruptions in global supply chains.

To address this deficit, two research teams at IISc have been racing against time to build ventilators using locally-available parts. One of them, called Project PRAANA, successfully completed the prototype of a full-fledged ICU-grade ventilator on 29 May 2020. It took the team just 35 days to go from the drawing board to a proof-of-concept

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Photo courtesy: Srinivasan Raghavan

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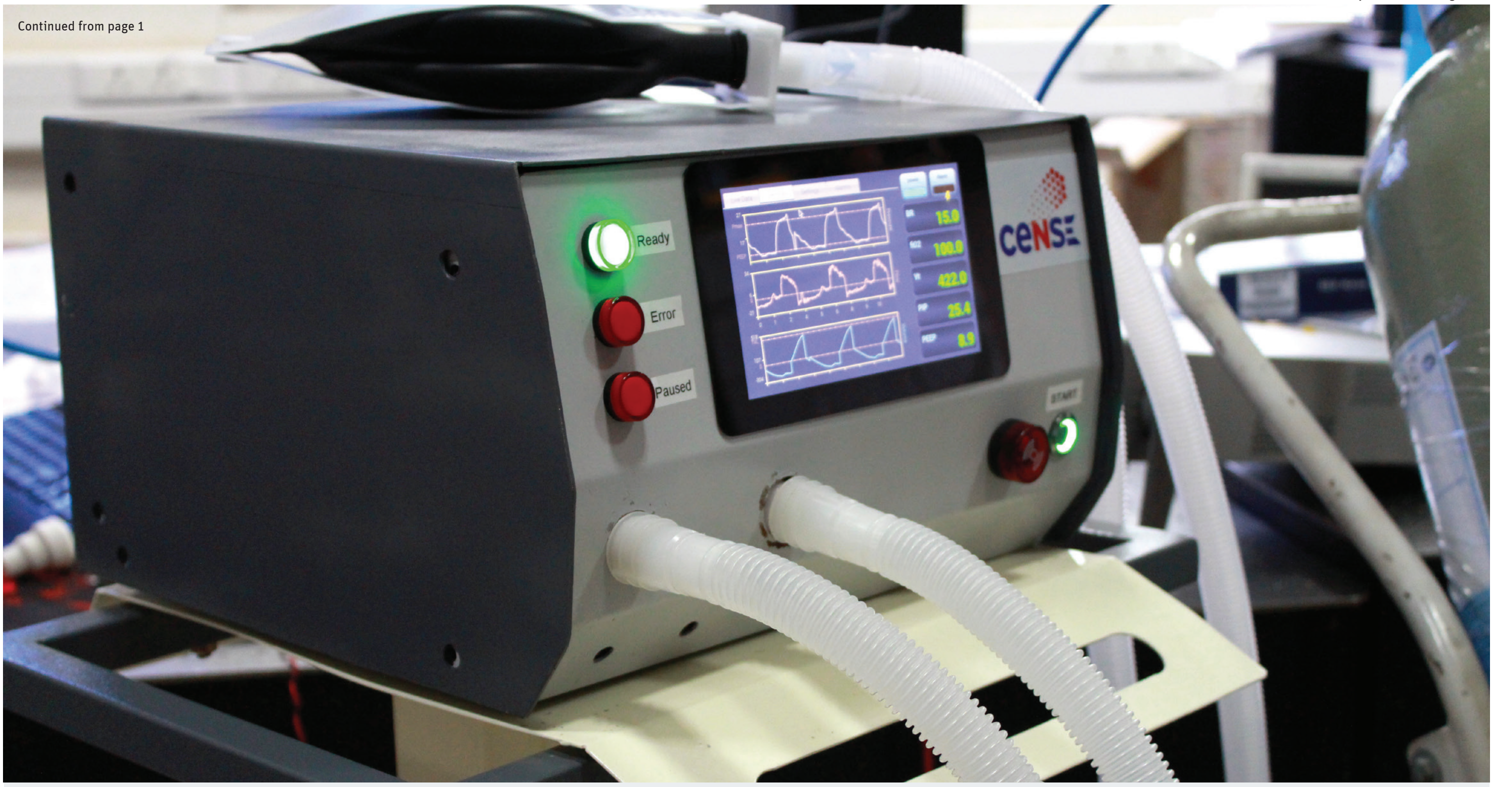


system, and then a working prototype in another two weeks.

Built using a custom-designed pneumatic system controlled by a microprocessor, the ventilator uses specialised algorithms and techniques to blend air and oxygen in the desired ratio. It also has fine-grained control of patient-side respiratory parameters, and supports both invasive and non-invasive ventilation.

Patients with severe COVID-19 infection have inflamed or damaged lungs that struggle to receive sufficient oxygen. When doctors put them on a ventilator, the machine critically assists lung function, feeding the patients a controlled mixture of air and oxygen and buying their body time to fight the infection.

To build their ventilator, the PRAANA team used only components made in India or easily available in the domestic supply chains. Some parts, such as a flow rate sensor that shows how much air is flowing into the patient's lungs, had to be developed from scratch. The team also received inputs from doctors to make the ventilator dashboard user-friendly with preloaded settings, which would make it easy for untrained nurses and technicians to operate it quickly in an emergency. It is expected to be priced in the range of Rs. 1 to 1.5 lakh per unit, which is substantially lower than currently-priced models in the Indian market.

The project was started by faculty members Gaurab Banerjee, Duvvuri Subrahmanyam, TV Prabhakar and Pratikash Panda, Bangalore-based engineer Manas Pradhan, and retired IISc professor HS Jamadagni. Many volunteers and research staff members at IISc also contributed to this initiative. The project received funding from IISc, the office of the Principal Scientific Adviser to the Government of India, Infineon Technologies and SBI Foundation. Narayana Health, Bengaluru, provided medical testing equipment.

"We are now actively exploring options to collaborate with an industry partner to further co-develop the prototype into a field-ready product," says Subrahmanyam.

When full-fledged ventilators are scarce, in an emergency, even low-cost ventilator systems can prove critical. One such solution is being developed by another IISc team with more than 30 members, coordinated by faculty member Srinivasan Raghavan at the Centre for Nano Science and Engineering. They are adapting techniques used regularly in nanotechnology equipment such as Chemical Vapour Deposition and proportional–integral–derivative (PID) controls.

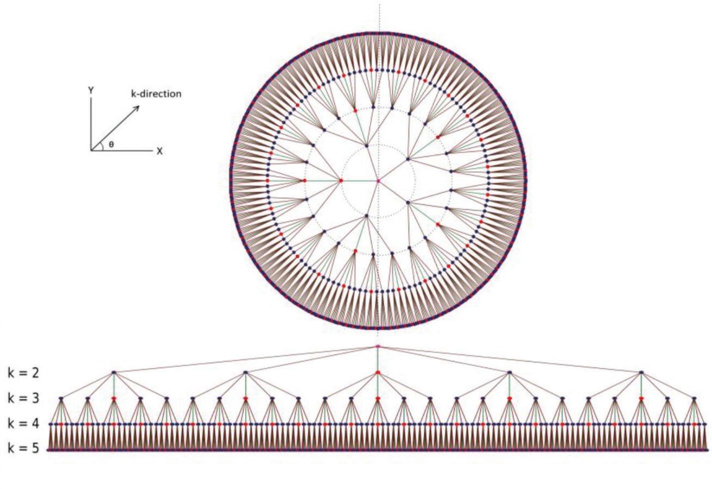
A full-fledged ventilator has sophisticated features to adjust air pressure and volume based on the needs of a patient's respiratory system. It may cost upwards of Rs. 10 lakh and depending on the control it offers, go up to Rs. 25 lakh. As an alternative, this team decided to develop a ventilator or a ventilation mechanism that would use the bare minimum of electronics, and easily interface with existing hospital infrastructure, at a cost of Rs. 50,000 – Rs. 1,00,000.

"After speaking to Dr. Justin Gopaldas, who works in Manipal North Hospital, we realised that while a ventilator is a sophisticated device not to be taken lightly, some patients may not need a full-fledged ventilator," says Raghavan. "One could have cheaper solutions to cater to a large number of people needing some form of forced air or forced breathing."

The team developed four versions, each one more complex than the previous. The basic version was a pneumatics-only variety, while the advanced version with more than 20 alarms offers mandatory and intermittent pressure, volume and pressure-regulated volume control. One of the advanced versions is currently undergoing five-day reliability trials in the lab. The team collaborated with industry partners KAS Technologies for production and Vasmed Health Sciences for biomedical expertise.

- Priti Bangal and Ranjini Raghunath

Image courtesy: Pratik Nandy/Physical Review Letters



DESIGNING EFFICIENT QUANTUM CIRCUITS

RESEARCHERS AT IISc HAVE INVESTIGATED HOW QUANTUM CIRCUITS CAN BE OPTIMISED TO BUILD EFFICIENT QUANTUM COMPUTERS THAT CAN OUTPERFORM CLASSICAL COMPUTERS

Quantum circuits, the building blocks of quantum computers, use quantum mechanical effects to perform tasks. They are much faster and more accurate than the classical circuits that are found in electronic devices today. In reality, however, no quantum circuit is completely error-free. Maximising the efficiency of a quantum circuit is of great interest to scientists from around the world.

Researchers at IISc have now addressed this problem using a mathematical analogue. They devised an algorithm to explicitly count the number of computing resources necessary, and optimised it to obtain maximum efficiency.

"We were able to [theoretically] build the most efficient circuit and bring down the amount of resources needed by a huge factor," says Aninda Sinha, Associate Professor at the Centre for High Energy Physics, and corresponding author of the paper published in *Physical Review Letters.* The researchers also suggest that this is the maximum possible efficiency achievable for a quantum circuit.

Optimising quantum circuit efficiency is useful in various fields, especially quantum computing. Not only will quantum computers give faster and more accurate results than classical computers, they will also be more secure – they cannot be hacked, which makes them useful for protection against digital bank frauds, security breaches and data thefts. They can also be used to tackle complicated tasks such as optimising transportation problems and simulating the financial market.

Classical circuits consist of universal logic gates (such as NAND and NOR gates), each of which performs pre-defined operations on the input to produce an output. "Analogously, there are universal quantum gates for making quantum circuits. In reality, the gates are not 100 percent efficient; there is always an error associated with the output of each gate. And that error cannot be removed; it simply keeps on adding for every gate used in the circuit," says Pratik Nandy, Sinha's PhD student and a co-author of the paper.

The most efficient circuit does not minimise the error in the output; rather it minimises the resources required for obtaining that same output. "So the question boils down to: given a net error tolerance, what is the minimum number of gates needed to build a quantum circuit?" says Nandy.

In 2006, a study led by Michael Nielsen, a former faculty member at the University of Queensland, showed that counting the number of gates to achieve maximum efficiency is equivalent to finding the path with the shortest distance between two points in some mathematical space with volume V. A separate 2016 study argued that this number should vary directly with V.

"We went back to Nielsen's original work and it turns out that his gate counting does not give you a variation with V, rather it varies with V^2," says Sinha. He and his team generalised that study's assumptions and introduced a few modifications to resolve the optimisation problem. "Our calculations revealed that the minimum number of gates indeed varies directly with the volume," he says.

Surprisingly, their results also appear to link the efficiency optimisation problem with string theory, an effort to combine gravity and quantum physics to explain how the universe works. Sinha and his team believe that this link can prove to be instrumental in helping scientists interpret theories that involve gravity. They also aim to develop methods that describe a collection of quantum circuits to calculate experimental quantities that cannot be theoretically simulated using existing methods.

- ***Aniket Majumdar***

Images: Srividya Kumar, Pixabay

USING RAMAN SPECTROSCOPY TO DETECT DISEASE-CAUSING BACTERIA

A NEW DIAGNOSTIC APPROACH TO DETECT PATHOGENIC BACTERIA USES RAMAN SPECTROSCOPY, A TECHNIQUE NORMALLY USED TO PROBE MATERIAL STRUCTURES

The key to treating infectious diseases lies in quickly detecting the pathogen or disease-causing agent, as well as checking for its viability – whether it is alive or dead in patient samples. Determining viability also helps physicians decide the dose of antibiotics to be prescribed, and reduces the possibility of overprescription that can lead to antibiotic resistance.

A research team at IISc has now developed a method to rapidly identify and check whether a disease-causing bacterium in a sample is alive or dead. It employs Raman spectroscopy – a technique that is usually used to identify chemical bonds in materials – to recognise bacteria and test for their viability.

“The uniqueness of this study is the rapidity and sensitivity of the method, and its potential for being modified into a bed-side, table-top device for diagnosis,” says Srividya Kumar, a former PhD student at the Department of Inorganic and Physical Chemistry, and first author of the study published in the journal *Analytical and Bioanalytical Chemistry.*

Infectious bacteria are usually identified by techniques that involve growing them on a nutrient medium in a Petri dish. However, it can take two to three days to track their growth and confirm whether they are dead or alive. In addition, bacteria that are difficult to grow in lab cultures often go undetected. More sophisticated methods such as Polymerase Chain Reaction (PCR) create a genetic profile of the bacterium, but cannot tell whether it is alive or dead.

Raman spectroscopy is used widely in the field of chemistry to probe the structure of molecules. In this study, however, Kumar and her colleagues combined this approach with advanced microscopy to check for the presence of bacteria.

Using a microspectroscope, the researchers bounced a laser beam off the sample and captured the light scattered by it in the form of a spectrum, which varies with the biochemical composition of the bacterium. Each bacterial species generates a unique spectrum with specific values for intensity and wavelength position of the scattered light, depending on the type of chemical bonds present inside the bacterial cell.

The material that is used for mounting the bacteria in this technique, known as the substrate, is also crucial because some substrates can add noise to the biochemical profile. The researchers developed a neutral, aluminium-based thin film substrate which does not generate background signals that may interfere with the spectra.

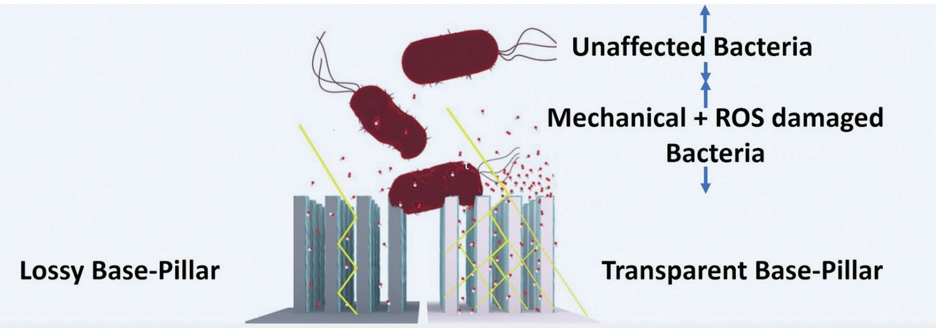
The researchers used this technique to detect whether the tuberculosis bacterium was present in a sample medium that resembles sputum. They also tested the approach on samples containing five other microbes. They were not only able to differentiate between the various bacterial species, but also between living and dead bacterial cells – since the chemical composition of the two differs – within two to three hours after sample collection. The technique was sensitive enough to generate a spectrum even for a single bacterial cell.

As each bacterial species gives rise to a unique spectrum, it might be possible to eventually build a database of pathogens that can be used in clinical diagnosis.

“Though we have validated the method for tuberculosis, the methodology can be extended to any type of bacterial infection,” says Deepak Saini, Associate Professor in the Department of Molecular Reproduction, Development and Genetics, and one of the senior authors of the study.

- Priti Bangal

Image courtesy: Jagriti Singh et al./ACS Applied Materials and Interfaces

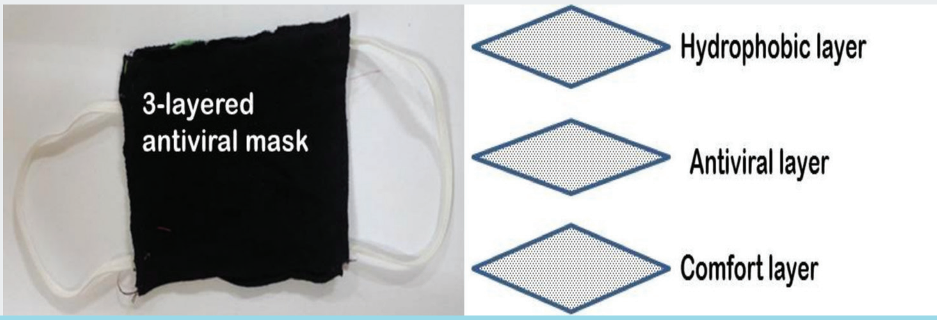


WHAT SHOULD ANTIBACTERIAL SURFACES BE MADE OF?

Drug-resistant bacteria often spread through surfaces such as doorknobs, public seats and medical equipment like stethoscopes. Previous attempts to develop antibacterial surfaces, by coating them with chemicals, have led to bacteria becoming drug-resistant. Another approach involves surfaces using photocatalysts such as titanium dioxide (TiO_2) which on exposure to UV light generate chemically reactive molecules called Reactive Oxygen Species (ROS) that kill bacteria by disrupting their membranes. But these surfaces typically absorb light poorly and produce few ROS.

To counter this, researchers at the Centre for Nano Science and Engineering have devised a comprehensive design principle for such surfaces. Through simulations and experiments, they maximised ROS production using TiO_2-coated, non-absorbing nanostructures of a particular height, and found that the best underlying material for these nanostructures is a transparent non-photoreactive material such as Black Silica. These design rules can be used to build highly efficient antibacterial surfaces in hospitals, airports, public transport, and other areas.

- Anoushka Dasgupta



THREE-LAYER ANTIVIRAL MASK FOR COVID-19 PROTECTION

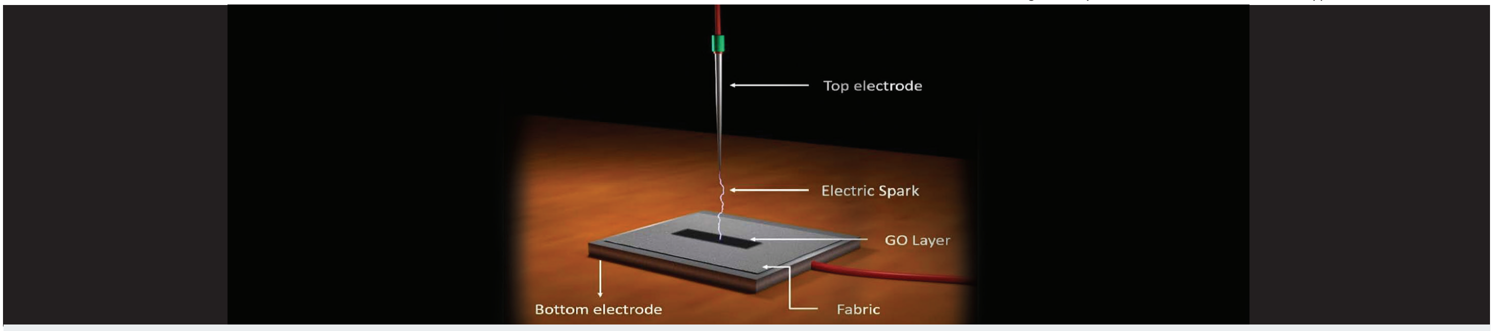
An IISc team has developed a cost-effective, three-layer antiviral and antibacterial mask that could prove helpful for healthcare workers and high-risk groups in the context of COVID-19. Currently available antiviral masks are either expensive or inefficient in reducing viral transmission. There is a need to rapidly manufacture affordable multi-layered masks. For maximum protection, the fabrics used in masks and other Personal Protective Equipment (PPE) should be virucidal.

The mask developed by the IISc team from the Department of Materials Engineering consists of modified polyester, with a nanofibrous polymer membrane deposited that renders the first layer highly hydrophobic, restricting the entry of liquid droplets that may contain the virus. The middle layer is also coated with a nanofibrous membrane loaded with antiviral agents, to inactivate microbes that may have escaped the first layer. The innermost layer is a cotton fabric for the user's comfort.

This nanofibrous membrane can also be deposited on the surface of other PPE such as gloves and lab coats.

- Suryasarathi Bose and Kaushik Chatterjee

Image courtesy: Vaishakh Kedambaimoole et al./ACS Applied Materials and Interfaces



INSTANTANEOUS SPARK REDUCTION FOR WEARABLE SENSORS

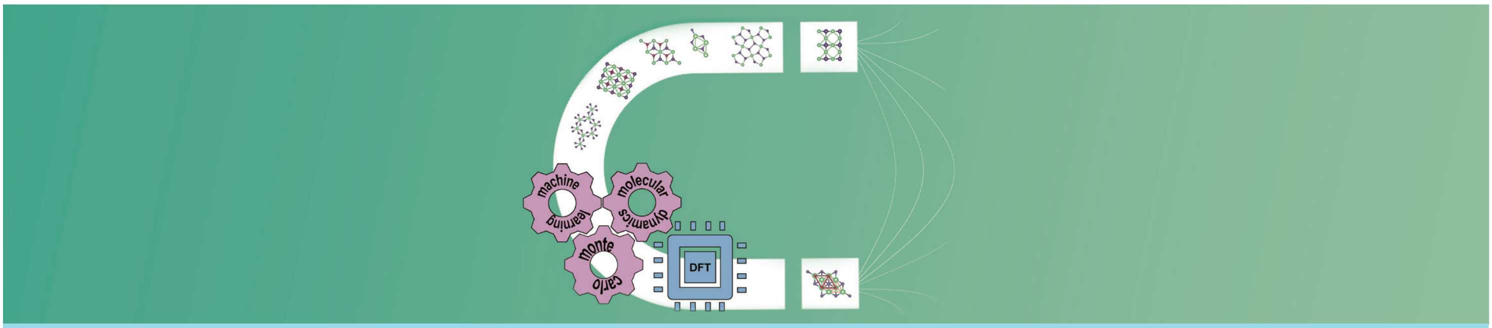
Wearable electronic devices are currently in great demand. 2D nanomaterials such as graphene, with their exceptional electrical and mechanical properties, play a key role in fabricating these devices. Graphene oxide (GO) is a scalable and low-cost alternative to pristine graphene. However, GO is an insulator and needs to be reduced to an electrically conducting form called reduced Graphene Oxide (rGO) to make it useful for sensors.

A group of IISc researchers in the Department of Instrumentation and Applied Physics has now devised a novel method to instantaneously reduce graphene oxide using an electric spark.

This method is efficient and cost-effective, which would allow easy industrial scale-up. It is also more environment-friendly compared to existing methods as it does not generate chemical residues. Sensors developed using this method can have applications in gesture control, in biomedical rehabilitation to detect the degree and intensity of body movements, and in the field of robotics.

- ***Anoushka Dasgupta***

Image courtesy: Santanu Mahapatra



MACHINE LEARNING FOR DISCOVERING 2D MAGNETS

2D materials are atomically thin, single-layered films arranged in a crystal structure, with potential applications in next-generation electronics. Ferromagnetism in such materials – the mechanism by which they act as magnets – was considered implausible until recently.

As the temperature increases, the magnetic order in these materials gets disturbed. The temperature at which they lose their ferromagnetic properties is known as the Curie point. Curie point is therefore a critical property of these materials for practical applications, but determining it involves very complex calculations.

A research team from the Department of Electronic Systems Engineering, IISc, has now developed an open source computer code to estimate Curie temperatures from the crystal structures of materials. They were able to identify 26 high-temperature 2D ferromagnetic materials from large open source databases, which could be ideal for use in high-temperature devices. The team has also developed a machine learning model to predict the Curie temperature of such materials.

- ***Priti Bangal***

COVID-19
RESEARCH AT IISc

Hospital Assistive Devices
- PRAANA: Indigenous electro-mechanical ventilator
- 3D printed valves for split ventilator use
- Cyclone separator for compressor cleanup
- Low-cost ventilator using inexpensive electronics
- Aerosol shield for intubation and anaesthesia
- Oxygen concentrator
- Medical oxygen generator

Modeling, Simulation and Analysis
- Automatic phase analysis
- Infection rate estimation
- Simulation of cough/sneeze flows
- Studying testing strategies
- Medical inventory short-term projection
- Modeling epidemic spread in cities
- PDE-based infection modelling
- Rapid suppression in small world communities

Vaccines, Drugs and Biological Studies
- Protein-based recombinant subunit vaccine
- Drug repurposing targeting SARS-CoV-2 main protease
- Functional genomics of Indian SARS-CoV-2 strains
- Modeling SARS-CoV-2 and immune system interplay
- Role of flu and BCG vaccination in lowering mortality
- Targeting host proteases to prevent virus entry

Diagnostics and Surveillance
- Coswara: Sound-based diagnostics
- Mobile diagnostic testing labs
- Rapid point-of-care test for public transit systems
- CovidWATCH: WhatsApp-based monitoring
- GoCoronaGo: Contact tracing app
- Antibody testing kit
- Paper-based diagnostic test

Sanitisation and Disinfection
- Drones for disinfection
- N95 mask renewal and testing
- Plasma sterilisation and disinfection
- UV-based disinfecting device
- Virucidal composite fabric for PPE

covid19.iisc.ac.in

Photo courtesy: Amit Singh lab, CIDR

IISc SETS UP A TEST CENTRE FOR COVID-19

In the fight against COVID-19, increased testing is a crucial requirement in addition to physical distancing and lockdown measures. Towards the end of March 2020, a test centre for COVID-19 became functional at the Centre for Infectious Diseases Research (CIDR) at IISc. It was set up within a short span of two to three weeks with support from the Institute and the Government of Karnataka.

As of 30 June 2020, the centre has tested 9,000 samples for the novel coronavirus, SARS-CoV-2.

IISc already has a Bio Safety Level-3 (BSL-3) facility with labs where there is active research ongoing on infectious diseases such as TB and HIV. These facilities are required for handling infectious agents that can be transmitted through the respiratory route.

Personnel who work at the COVID-19 test centre undergo training for two weeks in the Standard Operating Procedures (SOPs) specific to working with SARS-CoV-2 samples. The tests use RT-PCR kits developed by different companies that have been approved by the Indian Council for Medical Research.

Faculty members Shashank Tripathi (CIDR), Amit Singh (Microbiology and Cell Biology) and Deepak Saini (Molecular Reproduction, Development and Genetics) are involved in managing the test centre along with several dedicated research staff members.

- *Samira Agnihotri*

Office of Communications
Indian Institute of Science (IISc)
Bengaluru - 560012
news@iisc.ac.in | office.apc@iisc.ac.in

EDITORIAL TEAM
Deepika S
Karthik Ramaswamy
Nithyanand Rao
Ranjini Raghunath
Samira Agnihotri

DESIGN
TheFool.in