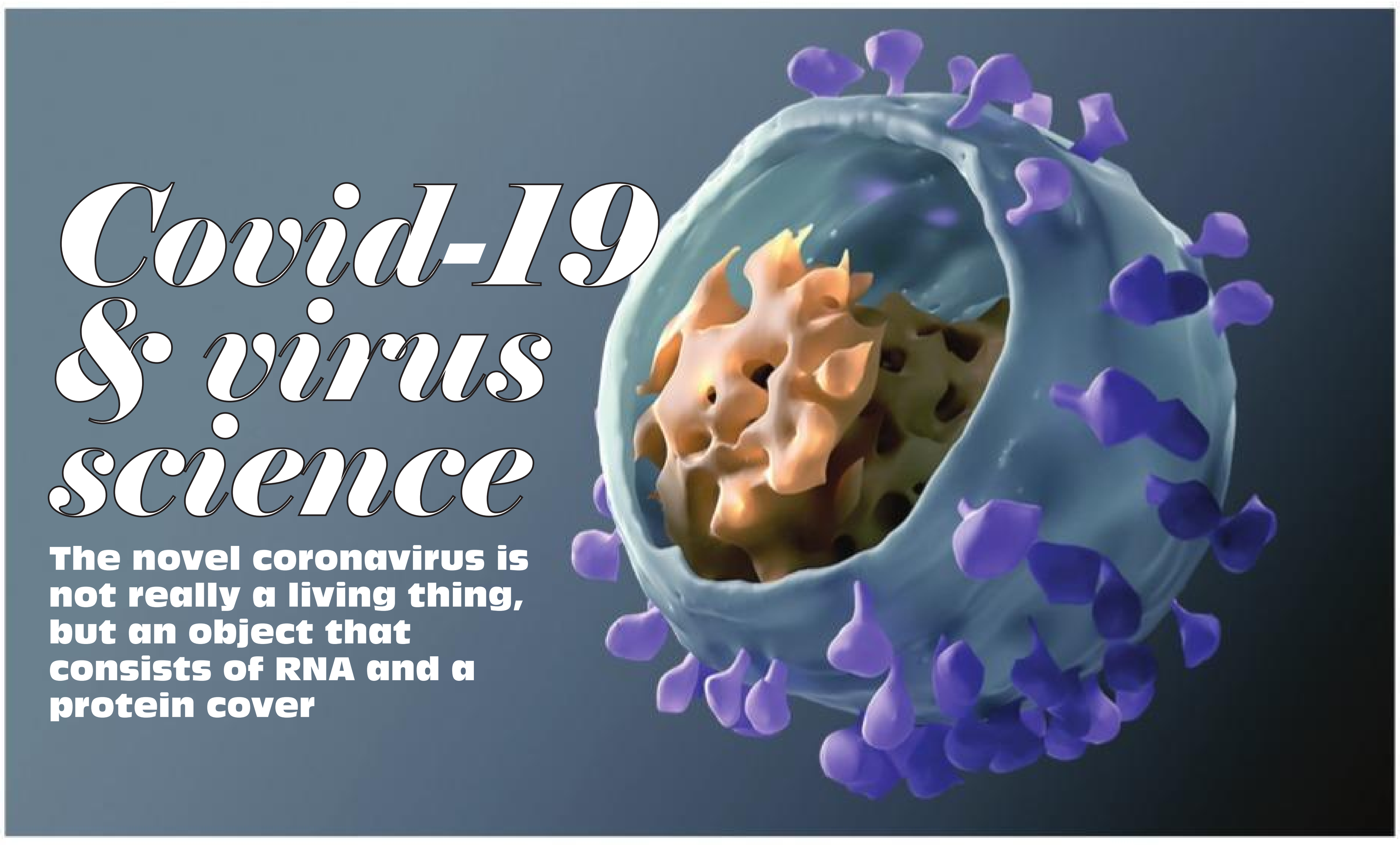


Covid-19 & virus science

The novel coronavirus is not really a living thing, but an object that consists of RNA and a protein cover

S ANANTHANARAYANAN

It has been said that the 21st century would be the age of molecular biology. This is in the sense that it may be natural processes that would help humanity overcome the challenges of waste disposal, energy from sunlight, and even building materials, during this century. The subject, however, has become central during the current crisis of Covid-19.

The processes of detection and possible control of the novel coronavirus have become subjects of interest and popular discussion. We have heard of RT-PCR being the test for Covid-19 and the global efforts to find methods to treat the infection, based on the way the virus acts and produces disease. The novel coronavirus is not really a living thing, but an object that consists mainly of something found in all living cells, a scrap of genetic information.

But how do viruses produce disease? They do nothing by themselves -- they do not block a biological process or create a biological nuisance. What they do is enter specific kinds of living cells and then, they simply multiply. When the virus multiplies within the cell, the cell's resources get used up. The cell is hence unable to perform its normal function. And as viral progeny increase, the cell itself is destroyed.

The next step is that the body's immune response is activated. This may control the infection, but in many cases, as in the case of Covid-19, there may be a violent response. This would act against healthy cells too, and the result is organ failure. Certain viruses select and act against the cells that are the very agents of immune response. Such a virus, like HIV, causes no disease, but when immune cells are destroyed, the body is without defence against other pathogens. While this is the way viruses work, the main feature of viruses, unlike bacteria or other parasites, is that they consist of just a bit of genetic matter, which encodes the information for their own reproduction.

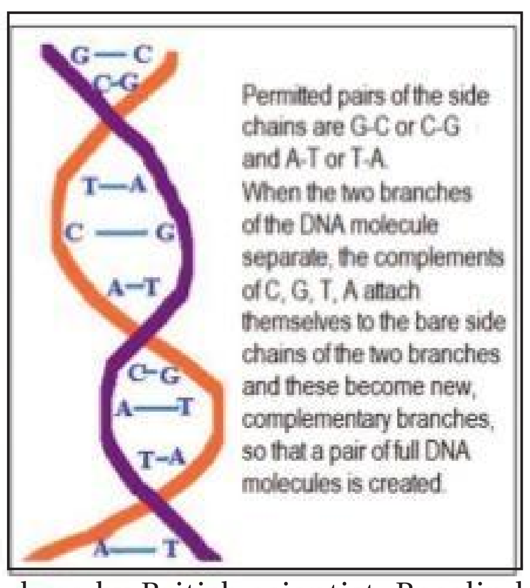
Cell reproduction, and heredity, come about through the agency of the genetic template that every cell carries within its nucleus. Molecular biology can be said to have started with the discovery that thread-like structures in cells, the chromosomes, had something to do with heredity, and then that a substance in cells, called nucleic acid, later DNA, was the medium by which heredity was transferred.

The nature of DNA became clearer in stages, and its full structure was worked out in 1953, by Crick, Watson and Wilkins, with the work of Rosalind Franklin. Crick, Watson and Wilson showed that DNA was a millions-of-units-long chain molecule, and consisted of a code that contained the blueprint for all the proteins that the cells of an organism can produce, and which define the species and the individual features of living things.

The operative feature of DNA, which enables its replication during cell division, is that it consists of a pair of complementary strands, the units on one strand attached to complementary units on the other. During cell division, the two strands separate and the action of *polymerase* enzymes helps the separate units on each strand to generate the complementary units from the environment and rebuild themselves as two full DNA molecules. When the cell divides, each daughter cell gets one of the two DNA molecules and has a full genetic blueprint, to work like the mother cell. Now, within the cell, the DNA molecule takes the help of *transcriptase* enzymes, and copies segments of itself onto structures called RNA. RNA then transfer the information in the unit to other parts of the cell, where proteins are generated. These RNA molecules are very much like DNA, except that they are much shorter, and single stranded.

VIRUSES

Viruses were discovered in the 19th century, as agents, in addition to bacteria, that led to diseases, but were unlike bacteria, which had been understood as the entities that caused disease. The difference was that viruses were much smaller, they could pass through fine filters, and could not multiply in a culture tray – they could multiply only within living cells. Viruses were found to consist of just protein and DNA, but were too small to be seen by optical microscopes. Images were later obtained using the electron microscope and the structure became known with the X-ray work



done by British scientist, Rosalind Franklin. The virus, unlike bacteria, has none of the apparatus of cells, for producing proteins. It has only a bit of DNA or RNA, which, if injected into a living cell, would get the cell to build more viruses. The bit of RNA or DNA has a protein cover, and the external shape helps it penetrate and enter specific living cells.

DETECTION

SARS-CoV2, or the virus that causes Covid-19, is an RNA virus. This means that what it contains is a single strand RNA, not DNA. When a person is infected, a low population of the virus and the RNA can cause disease, but the load in a sample taken from the person is too feeble for detection. The method, known as RT-PCR, which is used to detect viral infection, is a way of multiplying the content in the sample, to enable detection by laboratory methods.

PIONEER

Rosalind Franklin was a gifted researcher in Cambridge, a master of X-ray crystallography, who created the first image of the DNA, in 1951, and laid the ground for its detailed structure to be worked out, in 1953. Franklin then shifted her attention to the three-dimensional structure of viruses and, two years later, she captured X-ray images of the Tobacco mosaic virus. This led to the discovery of how the virus RNA and its protein coat assembled themselves, and then the mechanism of viral action.

Franklin was very much a part of the team that cracked the DNA structure and genetic code. But she died in 1958, before the Nobel Prize was awarded for the discovery, in 1962.

RT-PCR proceeds in two phases – first, conversion of the RNA into a form that can multiply, and then the multiplication. We have spoken earlier of the transcriptase enzymes that open out the DNA to extract portions, for transfer to RNA. When viruses that contain RNA infect living cells, they need to get back into the DNA form, so that the cell machinery can follow instructions to replicate the virus. This is achieved through *reverse transcriptase* enzymes, which act on the RNA to rebuild the segment of DNA from which it came. For detection, what we need is a plentiful supply. Once an RNA is converted into a bit of DNA, this bit can be made to replicate and multiply with the help of *polymerase* enzymes, which enable DNA replication during cell division. Hence, the process is to first use *reverse transcriptase*, or "RT", to build DNA and then cycles of warming and cooling, the *polymerase* chain reaction, or "PCR", to get the DNA to separate and double in numbers, until there is enough DNA for lab procedures to work.

The process is a little complex and time consuming. With increasing infections, another method, looking for antibodies, which the body produces when infections enter, has been pressed in, for faster but less specific detection.

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Understanding animals' magnetic sense

They use the Earth's magnetic field to maintain as well as change direction during migration

SANJUKTA DAS

Magnetic field or magnetism appears in all physics. But there is another side to it as the magnetic field is also associated with the living world.

Ever since the origin of living organisms about 3.5 billion years ago, they have been constantly exposed to the Earth's magnetic field or geomagnetism that is ubiquitous and accessible day or night. Earth's magnetosphere protects the environment from solar wind and cosmic radiation, which is essential for the persistence of life. In the course of evolution of living organisms, natural selection seems to have affected the formation of adaptive features meant for detection of the Earth's magnetic field. Called magnetoreception, it represents a beautiful interplay of physics and biology. Diverse forms of life, from prokaryotes to eukaryotes, utilise this phenotype to carry out different functions for survival. Thus evolutionary biologist Theodius Dobzhansky had aptly remarked that it is "the norm of reaction of the organism to the environment that changes evolution."

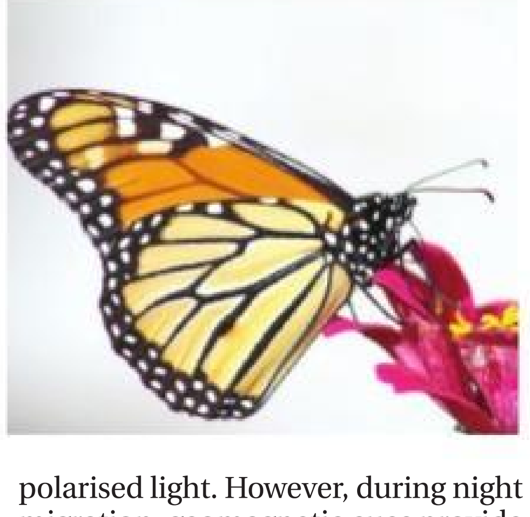
The origin of the concept of magnetoreception in animals can be traced back to late 1700s when a German doctor named Franz Anton Mesmer articulated the healing system as animal magnetism, which is also popularly known as "mesmerism". According to him, magnetism is central to human health. All living beings contain magnetic fluid and a diseased state emanates from its imbalance.

In the animal kingdom, different taxa comprising both invertebrates and vertebrates, notable examples being bees, birds, salamander, fishes and sea turtles detect and respond to magnetic field as they do to other stimuli of their natural environment such as sight, taste and smell to determine direction, altitude and location. They take clues from geographic variations in strength and inclination of the Earth's magnetic field to determine their position.

Animals derive two kinds of information from magnetic field – one is compass information and the other, map information. The first helps in maintaining direction along the path of movement and the second gives the positional information to change direction during migration or navigation.

Fishes, elasmobranchs and teleosts use magnetic field for orientation and navigation. Elasmobranchs detect magnetic field by electric sensor, a structure called Ampullae of Lorenzini located in their snout. The very noteworthy long journey in migrant fishes such as the European eel, which spans a distance from the Sargasso Sea in the North Atlantic Ocean to European rivers and streams, uses magnetic sense to determine direction of their migration. According to Michael Muller, an eel biologist in Nihon University, Japan, "Magnetic sense may be an important component of fishes that make long migrations in the ocean".

Like fishes, birds show migratory behaviour and about half of the world's bird species migrate. Thanks to magnetoreception, small song birds like garden warblers, pied flycatchers and bobolines, with "eye brains" weighing only a few grams, fly long distances in order to avoid the winter blues. Day migrants use celestial cues including the Sun, stars and



polarised light. However, during night migration, geomagnetic cues provide useful information, which birds use to determine direction of their path and approximate position.

In a similar way, among reptiles, sea turtles have caught much attention. Despite having a small brain in proportion to body size, they have got a remarkable navigational ability. They navigate vast expanses of water without any topological clue for an ideal place for nesting and mating.

Magnetic field sensitivity has been reported in eusocial insects like honey bees, ants and termites. Insect groups like isoptera (termites), diptera (flies), coleopteran (beetles), hymenoptera (ants and bees) and lepidoptera (moths and butterflies) appear to use magnetic sense for both orientation and navigation. Like birds, but with a simpler brain, insects have got remarkable navigational ability. For instance, the Monarch butterfly covers a distance of 3,000 km while migrating from the US and Canada to Mexico during autumns. Besides orientation and navigation, it is generally considered that insects show magnetic sensitivity in the absence of visual cues due to lack of light when the sky is cloudy.

Research has shown that these butterflies use changes in the magnetic field to orient themselves. According to neurobiologist Steven Reppertas, "The dominant compass system in monarch butterflies is the sun compass. But the magnetic field is a good back up system when visual cues are lacking as when sky remains cloudy". Perception of magnetic field in case of honeybees has been demonstrated while building combs in darkness and termites build mounds for alignment of their structure.

The magnetic sense in mammals has not been underscored much. However, research conducted by Tali Kimchi in Tel Aviv University, Israel has shown that the blind mole rat, having a subterranean life, makes long journeys in search of food and in the process takes the help of Earth's magnetic field for direction.

The mechanism by which organisms perceive magnetic field has been fascinating as well as elusive. It is a million dollar question whether there is a physical basis to magnetoreception in animals. Since biological tissues are transparent to magnetic field, any localised structure on the surface is unlikely.

However, independent discovery of magnetosomes in bacteria, specifically called magnetotactic bacteria and in some animal species such as honey bees, birds, salmon, and sea turtles, suggests the possible role of these structures in magnetoreception. Magnetosomes are intracellular membrane-bound ferromagnetic crystals, which are nanosized magnetite, maghemite or greigite particles. These magnetite crystals are made through the process of biomineralisation – by extraction of minerals from the environment and converting them to usable forms. It has been shown that bacteria having these internal magnets are capable of orienting themselves with respect to magnetic field and move to regions suitable for their growth.

This discovery in bacteria raised a lot of curiosity regarding the presence of a similar kind of structure in animals. The first structural candidate for magnetite-based magnetoreceptor has been identified in the olfactory neuroepithelium of the rainbow trout.

Besides ferromagnetic crystals, there are certain blue-sensitive photoreceptor proteins called cryptochromes, which are attractive candidates for magnetoreceptors as are found in the eyes of magnetoreceptive birds during migration.

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PLUS POINTS

Turmeric drugs

Researchers from the Indian Institute of Technology-Mandi and Indian Association for the Cultivation of Science, Kolkata, have developed a new route by which curcumin, the medicinal chemical present in turmeric, can be incorporated into drug nanoformulations.

Their work has recently been published in *Crystal Growth & Design*, a peer-reviewed scientific journal from the American Chemical Society. The research team consists of Prem Felix Siril, principal investigator of the research and associate professor, School of Basic Sciences, IIT-Mandi, and his research scholar Kajal Sharma, along with Bidisha Das from the IACS, Kolkata.

Turmeric has been used as a food item in India for centuries, not merely as a condiment but also as a medicinal material. Curcumin, a low molecular weight compound present in turmeric, has been reported to be the active medicinal principle because of its antioxidant, anti-inflammatory, antiproliferative (tending to inhibit cell growth) and antiangiogenic (a substance that reduces the growth of new blood vessels needed by tumours) properties. Thus, curcumin is considered a potential drug for a variety of illnesses including cancer, cardiovascular problems and neurodegenerative disorders.

Despite promise and the extensive use of turmeric in alternative and lifestyle therapies, the development of mainstream drugs based on curcumin has been hindered by a few problems. Curcumin, in its natural form, is insoluble in water, which makes it less bioavailable and hence difficult for the drug to reach the tissues and cells in which they are needed. Furthermore, free curcumin is unstable; it is susceptible to fragmentation with time, especially in a neutral medium. This leads to loss of efficacy of the drug. Thus, the incorporation of curcumin in drugs depends on increasing the water solubility of the compound and enhancing its stability and bioavailability.

The researchers used Indomethacin, a well-known nonsteroidal anti-inflammatory drug to precipitate along with curcumin in order to stabilise it in amorphous form. The combination is expected to have the therapeutic benefits of both curcumin as well as Indomethacin.

Additionally, they coated each nanoparticle of co-amorphous curcumin and indomethacin with a natural polymer called chitosan, which is extracted from shells of shrimps and other crustaceans. The chitosan generates a hydrophobic (water repellent) covering around curcumin nanoparticles and prevents it from sticking to each other and forming crystals.

Hope for Mars

Scientists have found "dense" communities of creatures living deep beneath the sea, in a discovery that gives hope that similar life could be found on Mars.

Volcanic rock more than 100 metres underneath the sea floor was discovered to be "teeming" with creatures, according to the new report. The discovery suggests that other, similar environments – such as that of the red planet – could also be havens for life. It has recently been published in *Communication Biology*. The tiny cracks in ancient rocks have a community of bacteria that is roughly as dense as the human gut, the researchers say. At about 10 billion bacterial cells per cubic centimetre, they are vastly more populated than the average mud sediment on the sea floor, which is estimated to be about 100 cells per cubic centimetre.

The single-celled creatures were discovered by researchers who took a decade of trial and error to try and examine the rocks deep beneath the sea. When they did manage to study them, they found that the cracks were actually a "very friendly" place for life, teeming with creatures.

The creatures found in the cracks are aerobic bacteria, which make energy through a similar process to that of humans, using oxygen and organic nutrients. But they are living in an environment that scientists expect to be similar to that inside rocks on Mars.

The independent