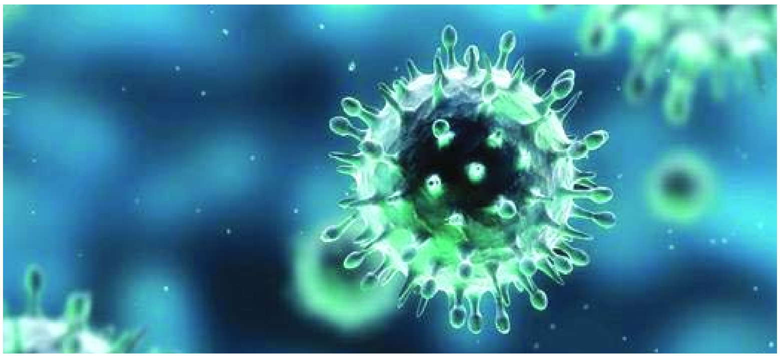
Viral RNA pack themselves

The virus s trick in replication may be its Achilles Heel, says s ananthanarayanan

THE main thing a virus does is to reproduce. It is equipped with the genetic code to make replicates of itself and little else. The virus evolves to have the surface features that allow it to enter a host cell and, once it has entered, it uses the resources of the host to multiply. This prevents the host from doing its usual work and also creates numbers of viruses to infect other cells.

The usual defence against a virus attack has been to block the matching surface feature of the virus, or the host cell, to prevent entry. As the virus is able to evolve and get through anyway, the defence has to be developed afresh for every new "strain" of virus. An alternate strategy has been to prevent the virus from reproducing after it has entered the cell. Alexander Borodavka, Roman Tuma and Peter G Stockley at the University of Leeds, UK, report in the journal, *Proceedings of the National Academy of Sciences*, their work on the reproduction process of the virus, which could show a longer lasting way to stop it.



Researchers Alexander Borodavka (below, from left), Roman Tuma and Peter G Stockley at the University of Leeds have identified a crucial stage in the lifecycle of simple viruses like polio and the common cold that could open a new front in the war on viral disease.

The genetic blueprint of cells is in the DNA, which is a millions-of-units-long molecule that contains the codes for the myriad of proteins that the organism needs to produce. The DNA is in the form of a pair of interlocking segments. At the time of reproduction, the segments decouple and each one recreates its complement from the environment. The new DNA can then move out as a new cell, again to replicate, and so on.

Except that this act of replication is not something that is simply stated. With millions of units, the DNA would normally be many times the size of the cell in which it resides. But it is able to be there, in a small pocket of space, because it is "folded" and wound up into a ball or egg shape and kept in place by an envelope of proteins produced by the cell. For reproduction, the proteins that initiate the process need to "open" specific parts of the envelope and allow segments of DNA to emerge and replicate. The segments then need to "fold" and wind themselves up and then merge to form a new DNA ball.

All this action takes place in the fervent activity of the cell environment, with proteins, bits of DNA, fat, sugars in constant motion, bumping, twisting and bending many times each split second. But the success of replication is important for the virus and the stages of the process are of interest to researchers to find a place where they could step in and block the progress.

Virus genome

The way the DNA acts to create different proteins that define the cell is by sending out portions of the code in the form of segments called RNA (a simplification of DNA). In some cases, the virus does not have DNA or a set of DNA but only a single strand of the simpler RNA. Many of the viruses that cause significant human disease are of this kind.

The usual vaccination strategy is unlikely to control more than a small portion of them. There has been some work on using synthetic, *virus-like particles* that contain a bit of RNA to attack disease-causing organisms, including viruses implicated in cancers, but this approach has been found to have potential pitfalls in case of error in the RNA that are used. Detailed information of what happens at the molecular level when viral RNA replicate is, hence, necessary to develop new ways to control viral infections.

The way the virus RNA coils and bends to get packed and compacted is with the help of specific proteins. These proteins affect specific portions of the RNA by creating electrostatic forces that cause the RNA to bend at those points. The RNA thus "coils" and further action by proteins causes it to *supercoil*, either in the same sense or in the sense opposite the direction of the helix form of the RNA itself. And once the RNA has been condensed, there are other proteins that hold it in that way.

Till the time comes for the DNA, in the case of cells, to send out portions of code in the form of RNA for creating proteins, or for the RNA in viruses that are replicating to go out and reproduce. At this time, the proteins that maintain the shape of the DNA envelope are modified, which allows portions of DNA to project into the interior of the cell for proteins to form.

In the case of viruses with RNA, the segment that have replicated become well compressed and enveloped by a coat of protein (*coat protein* or *CP*) by a spontaneous process, as the segments are short, unlike DNA strands. The view has been that this takes place as a result of the CP neutralising electrostatic forces that stiffen RNA strands and thus bring about bends and folds.

The Leeds group used a method called single molecule fluorescent correlation spectroscopy (*smFCS*) to catch a glimpse of what happens when a strand of RNA compresses into the CP envelope. The method uses statistical analysis of the flashes that are seen when molecules under observation move in and out of a very small window in the ceaseless motion of tiny particles in solution. Given the concentration of the particles, the number of flashes seen indicates the size and by varying the concentration it is possible to monitor changes in size and the interactions between proteins and RNA at the single molecule level.

The observations revealed an important difference between non-viral RNA and single-strand RNA viruses. On the addition of the coat proteins (CP) that correspond to RNA fragments, the RNA rapidly reduces in volume as the different CP form small envelopes of compressed RNA sections. After this collapse and the formation of sub-units, there is consolidation to form larger units of folded RNA. This process does not take place with fragments of other RNA. In other cases, there is no formation of smaller units and the units formed are not uniform and suited for consolidation, as in the case of viral RNA. This indicates that the process with viral RNA depends on specific RNA-protein interactions. The view so far, based on many CP being able to assemble even without RNA being there, around other kinds of RNA-like strands or even very small particles, has been that it is the proteins that are central to the assembly process. Therapeutic efforts have also been directed at the protein components. But the discovery that viral RNA can be packaged into defined units suggests that there is a mechanism that depends on the RNA structure and sequence. The Leeds team deduced that coat proteins and RNA acted as "mutual chaperones" to enable the protein shell enclosing the folded RNA to grow and complete the replication process with economy and efficiency. This action, of the RNA strand that is being packed influencing the action of the proteins that are the outer cover, has been likened to clothes folding and packing themselves into a suitcase.

"It seems that viral RNAs have evolved a self-folding mechanism that makes closing the 'viral suitcase' very efficient. It's as though 'the suitcase and the clothes' work together to close the lid and protect the content," said team member Roman Tuma.

Lead researcher Professor Peter Stockley said their results overturned accepted thinking about the process and could open a chink in the armour of a wide range of viruses. "If we can target this process, it could lead to a completely new class of anti-virals that would be less likely to create resistant viruses than existing drugs, which tend to target individual proteins."

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Giant reptile that ruled the Jurassic Seas

And it had teeth that would make T-Rex whimper, writes tia ghose

IT'S official, a giant marine reptile that roamed the seas roughly 150 million years ago is a new species, researchers say. The animal, now named *Pliosaurus funkei*, spanned about 40 feet and had a 6.5-foot-long skull with a bite four times as powerful as Tyrannosaurus Rex.

"They were the top predators of the sea," said Patrick Druckenmiller, a paleontologist at the University of Alaska Museum and co-author of the study, published in the 12 October issue of the *Norwegian Journal of Geology*. "They had teeth that would have made a T-rex whimper."

Combined with other fossil finds, the newly discovered behemoth skeletons of *P. funkei* paint a picture of a Jurassic-era ocean filled with giant predators.

In 2006, scientists unearthed two massive pliosaur skeletons in the Svalbard Islands, halfway between the Norwegian mainland and the North Pole. The giant creatures, one of which was dubbed Predator X at the time, looked slightly different from other pliosaurs discovered in England and France over the past century and a half.

Now, after years of painstaking analysis of the jaw, vertebrae and forelimbs, the researchers have determined that Predator X is a new species, and they have officially named it for Bjorn and May-Liss Funke, volunteers who discovered the fossils.

The pliosaurs, marine reptiles that prowled the seas 160 million to 145 million years ago, had short necks, tear-shaped bodies and four large, paddle-shaped limbs that let them "fly through the water", Druckenmiller said.

P.funkei probably ate plesiosaurs, a related species of long-necked, small-headed reptiles.

The new analysis showed that *P. funkei* had proportionally longer front paddles than other pliosaurs as well as a slightly different vertebrae shape and different spacing of teeth within the jaw, Druckenmiller said.

In 2008, scientists estimated that Predator X might have been up to 50 feet long. The current study suggested the creature was smaller than that but still about 10 feet bigger than the largest living apex predator — predators with no predators of their own — the killer whale, Druckenmiller said.

The *Pliosaurus funkei* fossils were just two of nearly 40 specimens discovered at the Svalbard site. The authors also describe two new ichthyosaurs, or dolphin-like reptiles, the longest-necked Jurassic-era plesiosaur on record, and several invertebrates. Together, the fossils suggest an ancient Arctic sea teeming with fearsome predators and invertebrate fauna, study co-author Jorn Hurum of the University of Oslo said in an e-mail.

"It's not just that we found a new species – we've been discovering a whole ecosystem," Druckenmiller said.

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The Independent

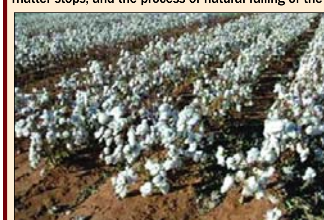
Keeping it simple

tapan kumar maitra **explains the roles played by defoliants, dessicants and retardants in the agricultural process**

DEFOLIANTS are substances that cause the leaves of plants to fall while desiccants are substances that accelerate the drying of plants or their parts. Both find the greatest use in cotton growing because the machine harvesting of cotton is possible only after defoliation and desiccation.

As a result of chemical defoliation, the leaves fall in four to 15 days after treatment. This is attended by a speeding up of the ripening and opening of the bolls, ripening of the seeds, an increase in the yield of the highest grades of raw cotton by four-five per cent, and harvesting of up to 90 per cent of the cotton before frost sets in. The quality of the fibres and the biological and sowing properties of the seeds are not impaired by defoliation.

Such action of defoliants is explained by the fact that at the end of the vegetation of cotton, the use of chemicals in the stage of ripening and opening of the bolls does not conflict with the biology of the plants. In this period, the formation of seed elements stops in plants, the growth of the stem retards, virtually no nutrient substances are used, the accumulation of dry matter stops, and the process of natural falling of the leaves begins.



Defoliants appreciably accelerate this process because they stimulate the formation of an abscission layer in the leaf stalks. Defoliation commences when one or two bolls open on most plants, while in more southern regions the largescale opening of two to four bolls occurs.

Desiccation (the preharvest drying of standing plants) is recommended, in addition to cotton, on grass planted for seeds, on plantations of sugar beets, sunflowers, castor-beans, lupine, rice, hemp, etc. Desiccation accelerates the ripening of seeds and fruits and reduces their moisture content. This allows the harvesting and processing of the seeds to be mechanised and prevents their spoilage in storage. Desiccation is especially helpful in conditions of unfavourable autumn weather, upon prolonged rainfall, and also when large amounts of fertilisers have been used and with irrigation, when the vegetation periods may become extended. Desiccation is used as a way of drying standing plants after the formation of the crop, when it can have no negative influence on the magnitude and quality of the yield. A variety of substances can be used as desiccants, but most often magnesium chlorate, calcium chlorate-chloride, butylcaptax and diquat are recommended.

In the Northern Caucasus, the desiccation of castor-beans is practised because this plant vegetates for a long time (the repeated growth of shoots and leaves occurs), which hampers machine harvesting.

The defoliation and desiccation of cotton are interrelated procedures when preparing the crop for machine harvesting. They substantially speed up the rates of ripening and opening of the bolls, which occurs not only because of the positive influence of the defoliants and desiccants but also because of the change in the micro-climate of the shrubs, their thinning and, as a result, the diminishing of the humidity of the air and the moisture content of the soil, and elevation of the temperature in the air layer adjoining the soil surface.

The combination of cotton defoliation and desiccation makes it possible to harvest the crop earlier and advance fall ploughing accordingly, which is essential for obtaining a high yield the next year. Defoliants and desiccants have an insecticidal and acaricidal action, which reduces the population of sucking and mandibulate insects by the following spring. The defoliants used at present include calcium cyanamide, magnesium chlorate, calcium chlorate-chloride and butifos.

The first reports in the press on the ability of nicotine and certain other compounds to retard the growth of bean plants appeared at the end of the 1940s. Later, several compounds were separated that were capable of affecting the habitus of plants without any appreciable disruptions of their important physiological functions. At the end of the 1950s, the strong growth-retarding effect of 2-chloroethyltrimethylammonium chloride was noted, while in 1961 reports appeared on the prevention of the lodging of wheat on rich soils with the aid of this formulation, given the common name of chlormequat chloride or chlorcholine chloride.

At present, substances known as retardants, a class of plant growth regulators, are widely used in agriculture to control the growth of plants. Retardants are characterised by a low molecular mass, are readily soluble in water and penetrate freely into plants. A common chemical property of most retardants is the presence of organic cations that play a major role in the processes of energy exchange in cells.

Chlormequat chloride has come into especially great favour for preventing the lodging of cereal crops. It is used on crops on an area of about 10 million hectares, in vegetable growing and horticulture. Some other retardants are also used, as well as their combinations and mixtures with herbicides and fertilisers.

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