

## SNAPSHOTS



## Evolutionary history

Scientists have discovered three new species of toothed pterosaur - flying reptiles that inhabited the Sahara 100 million years ago. These were part of an ancient river ecosystem in Africa that was full of life, including fish, crocodiles, turtles and several predatory dinosaurs. The new fossils are described in the journal *Cretaceous Research*.



## Fish eating Neanderthals

Neanderthals were feeding regularly on mussels, fish and other marine life over 80,000 years ago, according to a study which suggests it was not just the modern humans who sourced food from the sea. The study, published in the journal *Science*, found the first robust evidence during an excavation in the cave of Figueira Brava in Portugal.

# Silent spread of novel coronavirus in Italy went undetected for weeks

By the time the first case was reported, the virus had already spread to most areas in southern Lombardy

R. PRASAD

Italy reported its first laboratory-confirmed case of novel coronavirus (SARS-CoV-2) on February 20. But according to a study posted in a preprint repository *arXiv*, people appear to have been infected in early January and started showing symptoms by January 14. There apparently seems to have been a silent spread of the virus in the community for nearly 50 days.

By the time the first case was reported, the virus had already spread to most areas in southern Lombardy. Lombardy region, a district of 10 million, is the epicentre of the epidemic in Italy. So a day after the first case was reported, 28 more cases were confirmed, confirming the silent spread of the virus in the community.

## Uncovering the trail

Contact tracing and testing of both symptomatic and asymptomatic exposures to positive cases helped uncover the ongoing transmission prior to the laboratory confirmation of the first case. The median age of people infected by the virus is 69 years and 47% of people who were infected required hospitalisation, of which 18% required intensive care. Each infected person spread it to 3.1 people, which started



**Quick spread:** Lombardy region, a district of 10 million, is the epicentre of the epidemic in Italy. • GETTY IMAGES

decreasing by end of the third week of February. The time between successive cases in the transmission chain, otherwise called as serial interval, was 6.6 days. "We did not observe significantly different viral loads in nasal swabs between symptomatic and asymptomatic," the authors say in the preprint. Manuscripts posted on preprint servers are yet to be peer-reviewed.

"The transmission potential of COVID-19 is very high and the number of critical cases may become largely un-

sustainable for the healthcare system in a very short-time horizon," the authors write. "Aggressive containment strategies are required to control COVID-19 spread."

## Progression of disease

If there were just 530 cases on February 28, it increased to 5,830 by March 8. By early March, cases were reported from several areas in Lombardy region, a district of 10 million, which is the epicentre of the epidemic in Italy. As on March 28, there have been

86,498 cases in Italy, which is nearly 5,000 cases more than China's (81,996), and 9,134 deaths, which is the highest in the world. The authors collected epidemiological data through standardised interviews of confirmed cases and their close contacts. The information gathered included dates of symptom onset, clinical features, respiratory tract specimen results, hospitalisation and contact tracing. The epidemiological analyses were carried out on 5,830 confirmed cases during the period January 14 and March 8.

## Immediate response

Contrary to what one might imagine, there has been "almost immediate initial response" by the Regional Health System. The focus was to collect epidemiological data and perform model-based predictions, increase in testing and providing hospital assistance for affected subjects.

The authors say that efforts were taken to limit the spread through contact tracing and isolation. Despite these efforts taken quickly, the number of new cases kept rising steadily leading to "rapid saturation of the health emergency system with a progressive difficulty" in treating COVID-19 patients.

## Possible transmission of novel coronavirus from mother to child

R. PRASAD

A possible case of transmission of novel coronavirus (SARS-CoV-2) from the mother to the child has been reported on March 26 in the *Journal of the American Medical Association* (JAMA). The researchers from the Renmin Hospital of Wuhan University and other hospitals found elevated levels of antibodies (IgM) against the coronavirus in a newborn.

The mother was laboratory confirmed to be positive for coronavirus on January 31. A chest CT showed typical signs of infection in both lungs. On February 2, the mother was admitted to the Renmin Hospital in Wuhan. Molecular tests carried out four times confirmed that she was positive for the virus.

## Caesarean section

On February 22, the infant was delivered by caesarean in a negative-pressure isolation room. The mother wore a N95 mask to reduce the chances of transmitting the virus to the newborn. The mother did not come in physical contact with the newborn after delivery. The mother's vaginal secretions were negative for the virus.

The newborn did not exhibit any symptoms of infection and molecular tests (RT-PCR) carried out five times - from two hours after birth to 16 days - were negative.

However, the newborn

showed elevated levels of antibodies against novel coronavirus even at two hours after birth and remained elevated till March 7, when the mother and child were discharged. However, molecular tests of the amniotic fluid and placenta were not done.

The authors say that the antibodies (IgM) cannot be transferred to the foetus through the placenta. So in all possibility the foetus was exposed to the virus for at least 23 days from the day the mother was diagnosed positive for the virus.

Although the baby was delivered by caesarean, infection with the virus at the time of delivery cannot be completely ruled out, the authors say. But even if the baby was infected to the virus during the time of delivery, it takes three-seven days for antibodies to the virus to start appearing. However, in this case, antibodies were seen just two hours after delivery.

"The elevated IgM antibody level suggests that the neonate was infected *in utero*," the authors write. "IgG antibodies can be transmitted to the foetus through the placenta and appear later than IgM. Therefore, the elevated IgG level may reflect maternal or infant infection."

However, only when molecular tests of the amniotic fluid and placenta (which were not done in this case) show positive can one be certain of vertical transmission.

## How population size shapes evolution patterns in *E. coli*

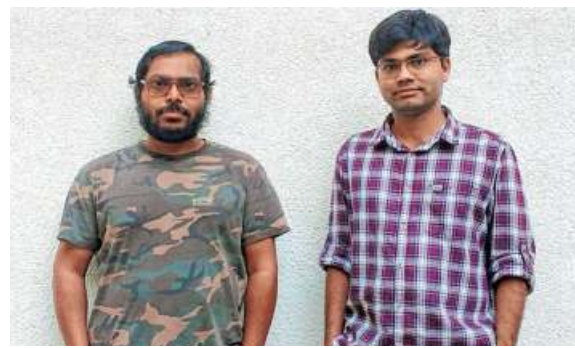
Large populations tend to evolve into exercising fitness trade-offs

SHUBASHREE DESIKAN

Studying cultures of *E. coli* bacteria, a group of evolutionary biologists from Indian Institute of Science Education and Research (IISER), Pune, has found that the population size determines the kind of fitness trade-offs the microbes adopt. Fitness trade-off may be understood in the following manner: Organisms do not have the capacity to maximise all their functions at the same time. Often when they enhance one function, another function suffers, or when they adapt to survive well in one environment, they cannot survive or reproduce well in another environments. This is called a fitness trade-off. This concept has been used by evolutionary biologists to explain why species prefer one environment to another.

## Generalists, specialists

There are several ways in which the concept of fitness trade-off originates. Evolution causes some organisms to be generalists, by which it is meant that they can survive in different environments, and basically they will have a tolerable level of fitness in all environments. The other option is



**Weakness within:** Owing to higher extent of specialisation, larger populations can become more vulnerable to sudden environmental changes, say Suthir Dey (left) and his collaborator Yashraj Chavhan.

they evolve into specialists, where the organism will have a high degree of fitness in a particular environment while having low fitness in other environments. An example of this is in the context of antibiotic resistance - generalists tolerate a wide range of distinct antibiotics (for example, multidrug resistant bacteria). On the other hand, specialist bacteria have to show a fitness trade-off. They resist one antibiotic (for instance, rifampicin) but become susceptible to another (for instance, tetracycline). From the example itself, it is clear that understanding how evolution brings about difference between specialists and generalists, for instance, is very important.

The study shows that large populations tend to evolve into specialists, exercising fitness trade-offs, whereas small populations evolve into generalists.

## Environmental changes

"Ours is the first study to demonstrate a relationship between population size and fitness trade-offs and the results are important in understanding the population genetics of ecological specialization and vulnerability to environmental changes," says Suthir Dey of IISER Pune's Department of Biological Sciences and the corresponding author of the paper published in the journal *Hereditas*.

The study experimentally affirms the link between

population size and evolution of fitness trade-offs. Apart from this there are practical implications. An example is described by Prof. Dey: "Owing to their higher extent of specialisation, larger populations can become more vulnerable to sudden changes in the environment."

If the environment abruptly shifts between two states that show fitness trade-offs with each other, then populations with a history of evolution at larger numbers would be at a greater disadvantage than historically smaller populations. "For example, costs of antimicrobial resistance are expected to check the spread of resistant microbes if antimicrobials are removed abruptly from the environments. Moreover, pathogens are also expected to experience fitness trade-offs when they migrate across different hosts," explains Prof. Dey.

The group next plans to study the response in fluctuating environments. "We are now studying more complex links between population size and trade-offs, combining fitness data with population genomics, in both constant and fluctuating environments," says Prof. Dey.

## How artificial intelligence can aid eye testing

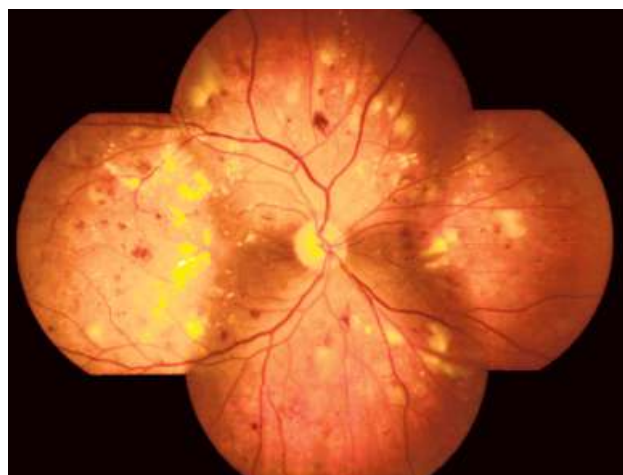
A tool to detect diabetic retinopathy has been developed by Google and an international team of researchers

ASWATHI PACHIA

From diagnostics to drug development, artificial intelligence (AI) today has become a valuable extension of the medical field. A new addition to its long list of uses is a hi-tech screening tool developed by Google and an international team of researchers for detecting diabetic retinopathy a diabetic complication in the eye.

A study conducted at two eye care centres in India - Aravind Eye Hospital, Madurai and Sankara Nethralaya, Chennai - which screened over 3,000 patients with diabetes, has shown that the AI's performance exceeded the conventionally used manual grading method used to identify diabetic retinopathy. The AI had a specificity and sensitivity of around 90%. The results were published in *JAMA Ophthalmology*.

A specialised retinal fundus camera was used to take



**Specialised camera:** A montage of images of the retina taken using fundus photography. •

photos of the eye. "Usually when we need to evaluate the retina, we dilate the pupil to allow more light to enter the eye and illuminate the back of the eye. But in this fundus photography it is not necessary as a coherent beam of light can enter the small gap (Pupil) and take an image in

just two to three minutes," explains Dr. Rajiv Raman from Sankara Nethralaya, Chennai and one of the authors of the paper.

He adds that it is very easy to operate and the cost of the camera has also significantly reduced in the recent past. Tamil Nadu and Kerala go-

vernments already have over 150 of these cameras currently in use.

Once the images are taken, it is fed into the computer and the AI tool screens it for diabetic retinopathy. A previous paper published by the team in 2016 in *JAMA* explains how the AI tool was shown over 120,000 images of the retina and taught to identify what each lesion meant. According to the International Clinical Diabetic Retinopathy scale, the AI tool was taught to grade the severity (none, mild, moderate, severe or proliferative) and give an instant report along with the recommendations.

## Early intervention

"Diabetic patients are normally asymptomatic when the eye is concerned until the late stages or advanced stage when treatment is difficult or not so effective. So it is important to find the patient at an early stage and help prevent

loss of vision," explains Dr. Kim Ramasamy from Aravind Eye Hospital in Madurai.

"What we have deployed here is an opportunistic screening. We placed the camera at the diabetologist's clinic and trained their technician to take a picture of the back of the eye (retina) and upload it to the AI tool. In about two minutes, the patient can get their eye test report along with the other regular diabetic test reports. Based on this report, the diabetologist can further refer the patient to an ophthalmologist if needed," he adds.

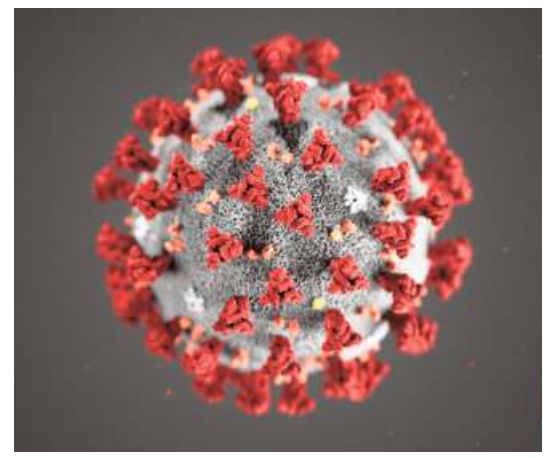
Dr. Ramasamy explains how the team has been testing this AI at even small Health Centres in Tamil Nadu. "When about 100 patients are screened, about 20 will have any level of diabetic retinopathy and only four to five might need intervention. But to track down this small number we absolutely need to screen all the diabetics, and

we currently don't have the facilities now. It would be great if we can have these opportunistic screenings at offices, railway stations or other public places," adds Dr. Ramasamy.

## Detecting breast cancer

The corresponding author of the paper Lily Peng adds in an email to *The Hindu*: "Beyond diabetic retinopathy we are also working on a number of other research projects using AI to tackle healthcare problems. Earlier this year, we showed in a research paper that AI models can help detect breast cancer in mammography images more accurately than doctors. Our research is still in the early stages, but it shows that AI can be a path forward to improve screenings for breast cancer and boost the chances of survival."

Ms Peng is a Product Manager at Google Health, California



**Spiky ball:** This illustration provided by the Centers for Disease Control and Prevention (CDC) shows the 2019 novel coronavirus. • AP

## Strike at the spike and win the war

The spikes made of a glycoprotein are the business end of the virus



## SPEAKING OF SCIENCE

D. BALASUBRAMANIAN

During the last six weeks, a series of research papers have appeared that offer medical solutions to defeat the life-threatening coronavirus infection - COVID 19. These are apart from the attempts to produce a protective vaccine against it.

The picture of how the novel coronavirus (scientists also call it SARS-CoV-2) looks is by now familiar to all of us (see the picture above). It is a roundish ball with spikes covering its entire body. These spikes, which are the business end of the virus, are made up of a glycoprotein, and the detailed structure of the spike protein and how it helps in entering the host (what an unwelcome name! but scientists are polite people) cell of the infected individual is seen by a Seattle-based group, using cryo-electron microscopy (<https://doi.org/2020.02.19.956851>) and also in the journal *Cell* < [cell.doi.org/10.1016/j.cell.2020.02.058](https://doi.org/10.1016/j.cell.2020.02.058)>. The spike protein recognises a specific enzyme called ACE2 on the cell surface, kills its activity and enters the host cell, and wreaks damage.

## Learn from the past

Go back in literature, and one finds that this activity of the novel coronavirus is actually a historical one. People have studied the catastrophe caused in 1918 by the Spanish Flu pandemic, wherein millions died. The patients suffered severe lung damage, pneumonia, and acute respiratory syndrome, which has recently been seen again in severe acute respiratory syndrome (SARS) by the pathogen named SARS (called SARS-CoV coronavirus virus). Research here showed that the enzyme called Angiotensin Converting Enzyme or ACE2 fights against the viral attack and protects against damage (see: "good ACE, bad ACE do battle in lung injury, SARS" <https://doi.org/10.1038/nm0805-821>, and also that ACE2 is beneficial for hypertension, diabetes and cardiovascular diseases (Tikellis C, Thomas MC. Angiotensin-Converting Enzyme 2 (ACE2) Is a Key Modulator of the Renin Angiotensin System in Health and Disease., *International Journal of Peptide Research* 2012, doi:10.1155/2012/256294).

Hence this repeated request by public health officials to senior citizens across the world, and to those with these problems to stay safe at home.

## Molecular and genetic basis

Most recently, a very important paper appeared from the Wuhan-based CAS lab for special pathogens, which revealed the genetic sequence of the novel coronavirus, its entry through deactivating ACE2 of the affected individual, plus another important point, namely, treatment of the affected by using the serum of a recently recovered patient. (This is important since it was shown as early as in 2006 by Liu and co-workers, < <https://doi.org/10.1086/500469>> when the SARS infected the world, treating the affected with the sera of recovered patients offered them the protective antibody IgG.) Hence the suggestion made across the world by some scientists that this can be followed in the present instance of COVID 19, too.

About the same time that this Wuhan work came about, comes another paper in the journal *Cell* from Leibniz, Germany (<https://doi.org/10.1016/j.cell.2020.02.052>), where the group confirmed that the novel coronavirus' cell entry depends not only of ACE2 but another molecule (and enzyme) in the host cell, called TMPRSS2. They suggest further that the latter can be blocked by a clinically proven protease inhibitor! This is an important advance, since we may now look for such blocking molecules as drugs against the dreaded enemy the novel coronavirus SARS-CoV-2!

## Take Home Lessons

We thus see four different ways of overcoming the enemy. The very first is what people must do (use protective devices and methods, do not allow community spread, stay home and safe); the second is to attempt to use the serum from recovered patients to boost the immunity of the afflicted; the third is to look for drugs to treat the affected and the fourth is to devise successful vaccines. These take time - but hopefully in months and not in years. Let us therefore attempt all of these methods.

A few words about SARS-CoV-2 and COVID 19. Two days ago, the newspaper *The Guardian* of U.K. points out that as many as 35 companies worldwide are racing towards such a vaccine, and at least 4 of them have tested their products on animals. Some have repurposed and modified their earlier vaccines against SARS and MERS to try on COVID 19. And two companies are building vaccines based on the messenger RNA that COVID19 has. But clinical trials on humans will take time to check on their efficacies and side effects, which may be as long as a year or more. Let us therefore attempt all of these methods.

We know by experience that where there is distress, there is hope; where there is hope, there are efforts; where there are efforts, there are solutions; and where there are solutions, there is success.

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