AFP

Doing better than guesswork

A mathematical modelling framework could chart the optimal course for release from lockdown

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Lockdown has retarded the spread of Covid-19. When and how it can be lifted is a question that administrations around the world are striving to answer.

In the current crisis, we do not have the benefits of smaller populations, lesser mobility and less globalised economics, which prevailed during past pandemics. However, we have more sophisticated capability in science and technology. A bit of math showed us where the spread of infection was headed – and got the world to act, with total lockdowns, more stringent than measures taken in the past. Math may again help optimise our crawl back to normalcy.

Thomas Rawson, Tom Brewer, Dessislava Veltcheva, Chris Huntingford, and Michael B Bonsall, from the University of Oxford and the UK Centre for Ecology and Hydrology, Wallingford, near Oxford, describe in the journal, *Frontiers in Public Health*, mathematical modelling of how different approaches to lifting the lockdown may pan out. The conclusions are not different from what can be imagined, but the formal exercise puts down the numbers that help time the decisions and trim the sails as the situation develops. "Although the simulations may lack absolute precision, predictions will have some level of robustness," the study says.

"As the number of new daily con?rmed cases begins to decrease, governments must decide how to release their populations from quarantine as ef?ciently as possible without overwhelming their health services," the report says. Quarantine has high economic costs and cannot continue for long. But lifting restrictions too soon would lead to increasing numbers that would go out of control. The problem of timing is hence one of optimising, which mathematical methods can solve.

The results show, as we can imagine, that release of the whole population would be disastrous. And gradual reintegration would be more reliable. Although the study deals with the case where the number of new infections has started falling, and daily new cases are below a threshold, the methods developed are useful to devise strategies even when cases are rising.

Optimisation problems are common in mathematics, economics, transport planning, etc., where the objective is to select the best from a range of solutions. Typical areas are in stocking raw materials -- buying in bulk at one time would lock up capital. Repeated, smaller purchases have higher costs and may increase the risk of stocks running out. A finance manager may need to keep cash assets in deposits and maximise interest. Short-term deposits would reduce the interest yield, while long-term, better paying deposits may lead to a liquidity crunch.

The classic transportation problem is to plan the routes that city buses should follow, so that passengers have the least travel time and the least waiting time and cost, given the number of coaches, people and places to reach!

The Oxford team modelled a population facing an epidemic as consisting of four groups – the Susceptible, the Exposed, the Infected and the Recovered (or dead) (SEIR framework) – to investigate the ef?cacy of two potential lockdown release strategies, focusing on the UK population as a test case. The gradual release strategy consists of allowing different fractions of those in lockdown to re-enter the working, non-quarantined population. Mathematical optimisation methods, combined with the SEIR model, lead to ways to maximise the number of those working while preventing the health service from being overwhelmed.

The other strategy modelled was "on-off", of releasing everyone, but re-establishing lockdown if infections become too high. The study concludes that the worst that can happen with a gradual release is more manageable than the worst possibility of an on-off strategy.

The modelling of how the numbers, S, E, I, R change with time was done separately for the population under quarantine and those who were not. In total lockdown, the second category consists of only front-line, essential workers, like medical staff, staff of utilities like power, water, etc.

The rate of change of the numbers was captured in eight relations – the number, S, of the susceptible, that is to say, those not yet exposed, would naturally reduce, depending both on the value of S and on the fraction of population that is infected. The number, E, of those exposed, would increase, depending on the same fraction as before, but tempered by its own increase. The same is true of I and R, depending on E and I, respectively, and tempered by their own increase. All these rates of change, separately for those in quarantine and the others, would then be affected by a factor that changes with time and reflects the policy of release of persons from quarantine.

The first factor of dependence to be considered, the transmission rate, of the conversion of the susceptible to the exposed, could be estimated from the data of Wuhan or Italy. As these rates, however, did not include the effect of asymptomatic persons, transmission rates that are twice as high have been considered. The relations take into account the natural death rate in the community and this is the rate that reduces the numbers of the recovered (R), even as the number increases as persons are cured. The lag, or the time that persons who are exposed (E), take to become infected (I) is considered, and then, how long the infected take to recover.

Solving the relations, for different policies of release of people from quarantine to work gives us the progression patterns of numbers, of the rise in the numbers infected persons, who would need medical attention. The model can thus show us the highest work force that we can release, given the medical facilities available. In affluent societies, ample medical facilities may allow large numbers to be released. This would help the economy, no doubt, but may be at the cost of many lives. The numbers released would hence be lesser and the results would enable refining the factors considered and hence more sensitive control.

The model developed considers cases where the increase in infections has begun to slow, or after methods of containment have shown effects. This is true of many countries like Iran, South Korea, the UK, France and Italy. The model, however, can be used in India too, where the numbers are continuing to rise.

We have three times the cases of China and are ahead of Italy. The daily increase, week to week, has risen every week, for the last 10 weeks. Against the time for doubling, 35 days in UK and USA, 55 days in Italy and 56 days in Spain, it is a quick 15 days in India. There are reasons – differences in the method of testing, criteria of considering a person infected, among others, – which make comparisons misleading, and that the testing in India is less, and limited to those at risk. And then, there is the large population – fertile ground for new infections. For all this, however, India's rate of mortality is low, at 2.8 per cent, compared to the global average of 6.8 per cent.

Large population and rising numbers are reasons for great caution while relaxing the lockdown, which could lead to spiralling numbers. On the one hand, in conditions of crowding, as in slums, the lockdown may even prevent social distancing. On the other, it is mobility that gives wings to infection. The SEIR framework, adapted to Indian conditions, could chart an optimal course that is based on objective criteria.

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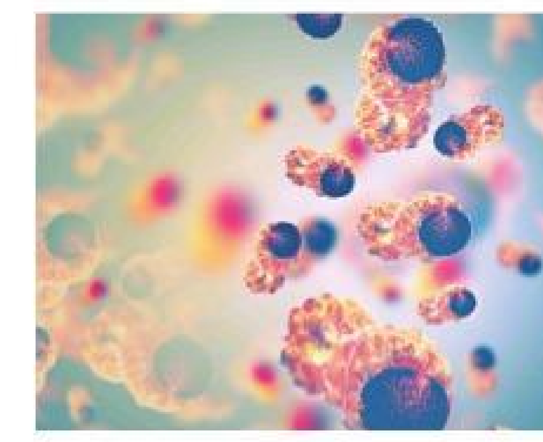
PLUS POINTS

Cancer therapy



Researchers have identified a specific micro RNA (miRNAs) called "miR-155" that is overexpressed in tongue cancer. This finding is important in that molecular strategies can potentially be devised to manipulate miR-155 expression to develop therapeutics for tongue cancer.

miRNAs affect cancer growth through inhibiting or enhancing the functions of certain proteins. For example, it has been shown that a type of protein called "programmed cell death 4" helps in stopping cancer cells from growing and spreading. Inhibition of this protein has been known to cause spread of oral, lung, breast, liver, brain and colon cancers.

A team of researchers lead by Devarajan Karunagaran, head, department of biotechnology, Indian Institute of Technology-Madras, and his research scholar Shabir Zargar collaborated with researchers from Cancer Institute and Sree Balaji Dental College and Hospital at Chennai and Indian Institute of Science at Bengaluru for this research. Their recent paper in this area has been published in the peer-reviewed journal *Molecular and Cellular biology*. It has been co-authored by Zargar, Vivek Tomar, Vidyarani Shyamsundar, Ramshankar Vijayalakshmi, Kumaravel Somasundaram, and Karunagaran.

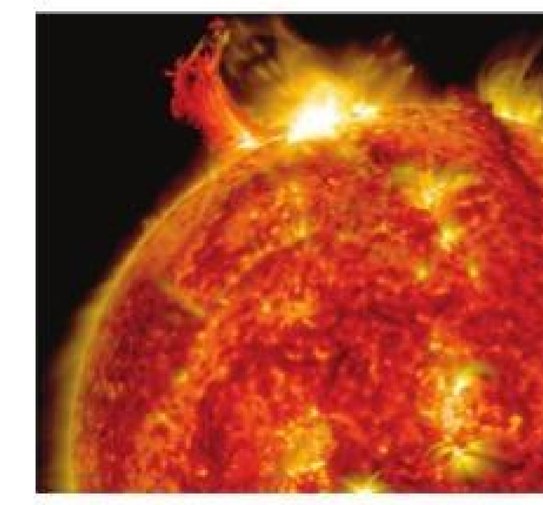
Elaborating about this research, Karunagaran said, "MicroRNAs are short non-coding RNAs containing 20-24 nucleotides that participate in virtually all biological pathways in animals. They have been found to play important roles in many cancers, in carcinogenesis (start of cancer), malignant transformation and metastasis – the development of secondary cancer. The miRNAs associated with cancer are called 'oncomirs'.

The team has gone beyond showing the connection between miR-155 and pdcd4. They have also shown that knocking out miR-155 causes death of cancer cells, arrests the cell cycle, and regresses tumour size in animal models and reduces cell viability and colony formation in bench top assays. Zargar said, "While it has been long suspected that miR-155 downregulates Pdcd4, there have, hitherto, been no evidence for such interaction."

The collaborative team has now shown beyond doubt that miR-155 is overexpressed in tongue cancer cells and tongue tumour tissues. This "overactivity" of miR-155 hinders the action of pdcd4, which in turn causes spread and growth of cancer of the tongue. "Our study has shown that the restoration of Pdcd4 levels through molecular manipulation of miR-155 can lead to potential therapeutic developments for cancers, especially tongue cancer," said Karunagaran.

miRNA manipulation is being combined with conventional cancer treatment methods such as chemotherapy, radiotherapy and immunotherapy, and the study reported by the team can enable such emerging therapeutics for cancer.

Solar flare



The Sun produced its largest solar flare since October 2017 in the last weekend of May this year, which could be an indication that its solar cycle is becoming more active. Such periods of activity can cause interference with radio equipment or satellites in space.

A collection of sunspots, which are dark areas of the sun signifying complex magnetic fields, were spotted by a Nasa spacecraft. On 29 May, a relatively small solar flare came from these sunspots, sending harmful radiation into the atmosphere.

This flare was classified as M-class, which represents the middle in terms of solar flare strength. Each class is 10 times as powerful as before, divided into five classes – A, B, C, M and X. Even if a flare reaches X-class, there are 10 classifications within that measurement, each 10 times more powerful than the one previously, Nasa says. During the last solar maximum in 2003, the sensors cut out at X28.

This M-class flare did reportedly cause a small radio blackout, and was followed by a smaller C-class flare approximately three hours later. Although this flare was not strong enough to pass the marker at which point the National Oceanic and Atmospheric Administration would have to issue a warning for space weather forecasts, since the sun has been in a "solar minimum" this could be a sign that our closest star is becoming more active.

-THE INDEPENDENT

Climate-smart farming

Enriching agricultural soil with volcanic rock dust could help capture carbon from the air whilst boosting yields and protecting crops

MIKE E KELLAND

Substantial increases in global agricultural production are needed to provide food for the world's growing population. According to the latest United Nations projections, we must prepare to feed an additional two billion people by 2050 – an increase comparable to the present-day populations of India and Europe combined.

At the same time, greater efforts are required to minimise the risk of dangerous climate change this century, by aspiring to limit global warming to 1.5°C above pre-industrial temperatures. To meet this goal, the UN estimates that net global carbon dioxide (CO_2) emissions must now decrease by an extraordinary eight per cent every year, on average. For comparison, this is equivalent to the major decline in emissions predicted by the International Energy Agency for 2020, following an unprecedented shutdown of the global economy due to the coronavirus pandemic. Clearly, there is a pressing need both for aggressive climate policies to reduce emissions and new approaches to actively remove CO_2 from the atmosphere.

Enhanced Rock Weathering is one such strategy that could be used to capture CO_2 from the air, but which also has the potential to improve crop yields and reduce farmers' costs. The approach involves spreading powdered volcanic rock onto agricultural soils, using the same equipment that many farmers currently use to distribute powdered limestone onto their fields for soil acidity control.

As the volcanic rock breaks down (or "weathers"), a variety of beneficial elements are released into the soil. Some of these, such as phosphorous and potassium, are essential plant nutrients found in common fertilisers, whereas others, like calcium and magnesium, act to reduce soil acidity while triggering a chemical reaction that absorbs CO_2 from the air. Depending on the environmental conditions, the captured CO_2 can remain in the soil – in the form of a limestone-like mineral – or may instead be flushed into rivers and groundwater, before ultimately reaching the ocean where it will remain for millennia.

This mechanism for capturing and storing CO_2 is similar in operation to natural rock weathering, which has functioned as a sink for atmospheric CO_2 over hundreds of millions of years. ERW therefore seeks to accelerate this natural process by using a fast-reacting, powdered form of rock. The rock itself need not be mined especially for this purpose either, as substantial quantities of unwanted pulverised material are produced each year by the mining and aggregate industries. Much of this material, largely considered a waste product, could be suitable for repurposing as a valuable soil amendment.

Indeed, for my experiments at the University of Sheffield, I chose to use rock dust from a basalt quarry as the active ingredient. Basalt is ideal for ERW as it is found all over the world – notably in large volcanic provinces, such as India's Deccan Traps – and typically contains low quantities of potentially toxic metals but relatively high amounts of the plant nutrient phosphorus.

As a PhD researcher at the Leverhulme Centre for Climate Change Mitigation, my work focuses on the fundamental science behind ERW. By conducting controlled experiments within the university's world-class plant growth facilities, our research team investigates the potential for CO_2 capture via ERW and its effects on crop production. I use Sorghum bicolor for my experiments, which is one of the world's most widely cultivated cereal crops and the fifth most important crop for food and animal feed, with the US and India accounting for around half of global production.

In a recent paper published in *Global Change Biology*, my colleagues and I reported a 21 per cent increase in Sorghum (*jowar*) grain yield following a single application of pulverised basalt to an acidic UK agricultural soil. As basalt represented the only supplementary source of fertiliser and soil acidity regulator, this result should appeal to farmers looking to boost production or reduce their reliance on expensive chemical fertilisers and liming treatments.

Furthermore, we found that silicon – a key component of basalt – was readily absorbed by the plant, resulting in 26 per cent more silicon in the leaves and stem. This too should be of interest to producers, because increased silicon has been shown to improve plant protection from a range of pests and diseases, in a variety of crops.

Lastly, by fine-tuning computer simulations for our study, we estimated that the equivalent of two to four tonnes of CO_2 would be captured in every hectare of cropland, up to five years after applying the basalt. Given that no special processing of the rock was conducted prior to the experiment – the basalt quarry waste was merely washed with water – this outcome supports the notion that ERW can be an affordable and energy-efficient strategy for capturing CO_2.

Of course, further research is required to evaluate the effectiveness of ERW at larger scales, and such trials are currently underway at the University of Sheffield, however these initial results indicate fantastic prospects for climate change mitigation and food production.

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