Persistence isn't always a virtue

GAMBLERS ARE SUITORS WHO WILL NOT TAKE NO FOR AN ANSWER, WRITES **S ANANTHANARAYANAN**

As gambling systems are usually with the odds slightly against the player, in the "long run" it is certain that the player will lose. And yet generations of gamblers have tossed fortunes away in the belief that the outcome in their own case would be different.

Luke Clark, Bettina Studer, Joel Bruss, Daniel Tranel and Antoine Bechara of the Universities of Cambridge, Iowa and California report in the journal *Proceedings of the National Academy of Sciences* of the USA that it may be a part of the brain that drives tendencies that make us human, that is hyperactive in the case of compulsive gamblers.

The fact of the matter is that most people are gamblers to some degree. "Seventy-three per cent of people in the UK report some gambling involvement in the past year," says a study conducted in 2010. Even governments promote gambling through state lotteries and moderate chance taking is viewed as stress relieving behaviour. And then, many gambling schemes are presented like "opportunities" and the accounts of people who were ruined are viewed as cases where the victims made a "mistake" while playing, rather than a reason to stay away from the casino.

Mumbai's own *matka*

In this ingenious money-spinner for the underworld, players (read victims) placed bets on an "opening" or a "closing" number, which could be zero to nine, for the chance to win nine times the money staked. It is obvious that the *matka* operator would win in the "long run", because he would receive 10 units for every nine units he paid out. Yet, generations in Mumbai and elsewhere by "trunk call" played *matka* with zeal and determination. How did they expect to profit? A number of "systems" were developed.

If a player took it that he/she would win once every 10 times he/she played, and the amount was one rupee each time, he/she had to be just a little lucky to win nine rupees before having invested the full Rs 10. And once he/she had won that nine rupees, it could be taken that a new series had started. A popular system was when a punter doubled his/her bet every time they played. Then, no matter when the individual won, he/she would cover well over everything lost till then. Such high investors must have been popular with the operators.

The trouble is that it is far from certain that a punter will win once in every 10 tries. This is because in 10 tries, there are all kinds of possible outcomes — no wins at all, exactly one win, exactly two wins, three wins and so on. To have no wins means to *lose* every time. Losing any one time has a nine in 10 chance, or 0.9. For this to happen 10 times in a row, the chance works out to 0.35. Winning exactly once is to lose nine times. It works out that to win in exactly one of the 10 times round and to lose all the others has a chance of 0.39.

Expectation goes awry

When we think of winning more times, like exactly three times, four times and so on, the high figure, or 0.9, the losing chance, enters the reckoning a less number of times and the probability comes crashing down (see Table I). It turns out that the chance of winning *at least* once, which is the total of the chances of winning once, twice, and so on, which is also just the chance of *avoiding* losing every time, comes to 0.65 (notice, this is 1-0.35). Now this is hardly the expectation of the average punter of being sure to win once every 10 tries!

Luke Clark

TABLE IN CHANCES OF WINS IN 10 TRIES

No of wins (N) in 10 tries	0 wins	one win	two wins	three wins	four wins
Chance of exactly N wins	0.35	0.39	0.19	0.06	0.01
Chance of at least N wins	1.0	0.65	0.25	0.07	0.01
Chance of at most N wins (ie, N or less than N wins)	0.35	0.74	0.93	0.99	0.99

TABLE II-CHANCES OF WINS IN 100 TRIES

No of wins (N) in 100 tries	0 wins	10 win	20 wins	30 wins	40 wins
Chance of exactly N wins	0	0.13	0	0	0
Chance of at least N wins	1.0	0.55	0	0	0
Chance of at most N wins	0	0.58	0.99	0.99	0.99

The chances of winning at least once in 10 tries gets even lower as the total number of tries is increased. In Table II, for instance, the chance of at least 10 wins in 100 tries is 0.55. In 100 tries, in fact, it is almost certain that one would win at least five times, but the chance of winning at least even 11 times drops to 0.42.

Even if the ordinary visitor to the casino did not know the mathematics of the thing, losing a few thousands at the table should help drive home the same lesson. But because some wins keep happening and the winners celebrate in view of everyone around, the others think they are just having a "bad patch" and take lessons in patience. But the organisers of the racket know that the more the players, the more stable their assured income.

Research findings

The researchers features in *PNAS* take note that persistent gamblers often treat "near misses" as different from any other outcome or that they act out the *gambler's fallacy* of viewing a series of losses as a reason for the next play to fall outside the series, in the form of success. Gamblers "display an array of cognitive biases that create a distorted expectancy of winning," the researchers say in the paper. The group then conducted trials to see if it were a feature of the brain that was behind this error of judgment in habitual gamblers. Rather than try to seek out the part of the brain that was responsible, the researchers studied the behaviour of patients with injuries in different parts of the brain. "While neuro-imaging studies can tell us a great deal about the brain's response to complex events, it's only by studying patients with brain injury that we can see if a brain region is actually needed to perform a given task," says Dr Clark.

Patients with injuries to specific parts of the brain were presented with two gambling situations, one a slot machine where there were "near misses" and another, a roulette table with a series of losses, to suggest that the next play would be different. The parts of the brain affected were the frontal part, which is involved in cognition, the *amygdala*, a tiny organ involved in emotion and aggression, or the *insula*, a part in the centre of the brain now thought of as the seat of social emotions, like lust and disgust, pride and humiliation, guilt and atonement. And then there were subjects with injuries to other parts of the brain and also subjects with no injuries.

The remarkable result was that all subjects, but one category, were motivated to keep playing when they got "near misses" at the slot machine or "continuous losses" at roulette. And the category that did not respond in this way was the one with injury to the insula. The insula may thus be the part of the brain that has evolved in humans to endow us with unique emotional features, including the tendency to take chances. "Based on these results, we believe that the insula could be hyperactive in problem gamblers, making them more susceptible to these errors of thinking. Future treatments for gambling addiction could seek to reduce this hyperactivity, either by drugs or by psychological techniques like mindfulness therapies," says Dr Clark.

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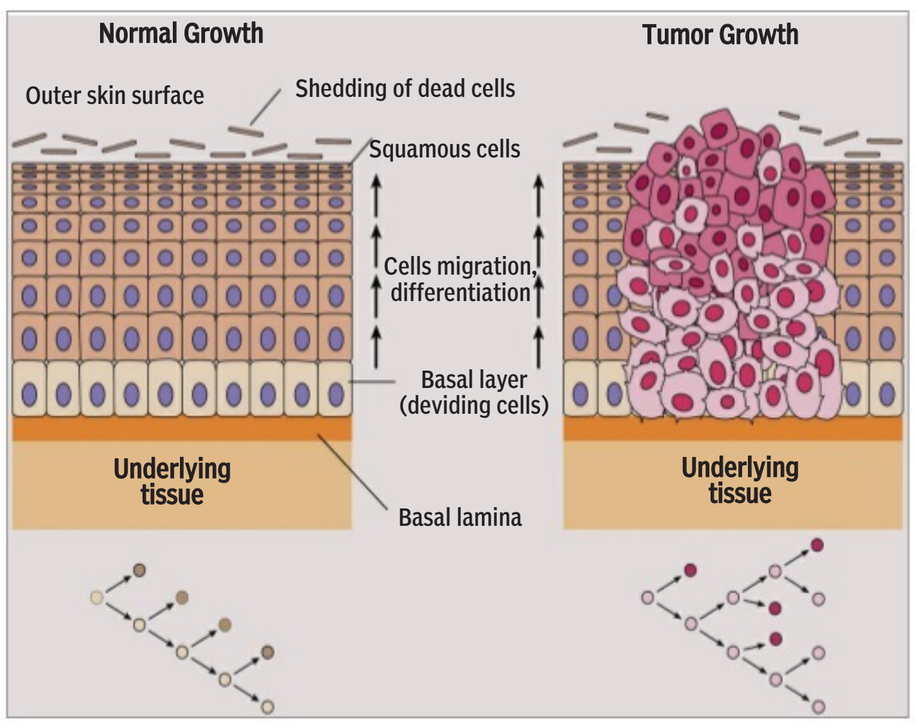
DISTINCTIVE TRAITS

CANCER CELL PROLIFERATION IS ANCHORAGE-INDEPENDENT AND INSENSITIVE TO POPULATION DENSITY, SAYS **TAPAN KUMAR MAITRA**

A cancer is an abnormal type of tissue growth in which cells divide in an uncontrolled, relatively autonomous fashion, leading to a progressive increase in the number of dividing cells. The resulting mass of growing tissue is called a tumor (or *neoplasm).* Although tumors have escaped from normal controls on cell proliferation, tumor cells do not always divide more rapidly than normal cells. The crucial issue is not the rate of cell division but, rather, the balance between cell division and cell differentiation.

Cancer cell proliferation exhibits a number of distinctive traits that distinguish it from normal cell proliferation. One trait, of course, is the ability to form tumors. With human cancer cells, it is difficult to study tumor formation experimentally because it is unethical to inject cancer cells into humans for research purposes. In addition, injecting human cells into animals is not generally practical because the animal's immune system will reject human cells simply because these are of foreign origin. One way around the problem is to inject human cells into mutant strains of mice whose immune systems are unable to attack and destroy foreign cells. Human cancer cells injected into such immunologically deficient animals will usually grow into tumors without being rejected. Cancer cells also exhibit a number of other distinctive growth properties that allow them to be distinguished from normal cells. For example, normal cells don't grow well in culture if they are suspended in a liquid medium or a semi-solid material such as soft agar; but when they are provided with a solid surface to which they can become anchored, the cells attach to the surface, spread out and begin to proliferate. In contrast, cancer cells grow well not only when they are anchored to a solid surface but also when they are freely suspended in a liquid or semi-solid medium. Cancer cells are, therefore, said to exhibit anchorage-independent growth.

When growing in the body, most normal cells meet the anchorage requirement by binding to the extracellular matrix through cell surface proteins called *integrins.* If attachment to the matrix is artificially prevented using chemicals that block the binding of cell surface integrins to components of the matrix, normal cells usually lose the ability to divide and, in many cases, they self-destruct by *apoptosis.* Triggering apoptosis in the absence of proper anchorage is one of the safeguards that prevents normal cells from successfully floating away and setting up housekeeping in another tissue. Because cancer cells are anchorage-independent, they circumvent this safeguard.



Another property that distinguishes cancer cells from normal cells is their response to crowded conditions in culture. When normal cells are grown in the laboratory, they divide until the surface of the culture vessel is covered by a single layer of cells. Once this *monolayer stage* is reached, cell division stops — a phenomenon referred to as density-dependent inhibition of growth.

Cancer cells exhibit reduced sensitivity to density-dependent inhibition of growth and, therefore, do not usually stop dividing when they reach the monolayer stage. Instead, these cells continue to divide and gradually begin piling up on top of each other.

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The hidden menace

CURING HIV MEANS FINDING AND ERADICATING VIRUSES STILL LURKING IN THE SHADOWS. **GENEVIEVE MARTIN, MATTHEW PACE** AND **JOHN FRATER** REPORT

Since the early 1980s, when HIV was first identified, our knowledge of the virus — how it causes disease, how it interacts with our immune system, how it responds to drugs — has grown by the year. Drugs specifically designed to target HIV and given as a cocktail of different agents — known as combination Antiretroviral Therapy (Art) — have decreased the mortality associated with infection to the point where, for newly diagnosed individuals today, life expectancies are comparable to those who are HIV-negative.

But of the 35 million people currently living with HIV, the World Health Organisation estimates that only around 40 percent use Art, partly because about half do not know they are infected. Providing Art to all who need it is a major challenge and even when the drugs are available they are not a panacea. Regardless of treatment, there is increasing evidence that HIV-infected individuals may be at greater risk of non-Aids comorbidities, for example, cardiovascular disease and dementia. Moreover, Art has to be taken for life: if the drugs are stopped, virus production quickly ramps up and the disease can progress, a phenomenon known as rebound.

Rebound occurs because HIV forms a reservoir in long-lived T cells that persist despite treatment. As with all retroviruses, a key aspect of the HIV replication cycle is the reverse transcription of the viral genome into DNA, followed by integration of this viral DNA, known as the provirus, into the host genome. In activated cells, this proviral DNA can give rise to viral mRNA, proteins and infectious viral particles. However, in some infected cells, the virus enters a resting state, termed latent infection, in which transcription or translation is restricted but integrated HIV is still present. These latently infected cells make up the HIV reservoir and, eventually, may be stimulated to produce infectious virus.

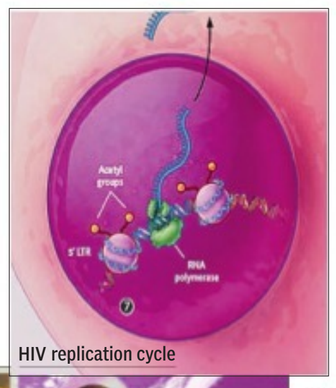
The HIV reservoir consists largely of resting CD4+ T cells, but other cells, such as macrophages, may also contribute. In patients who have been treated for many years with Art, these latently infected cells are rare but still present. It has been estimated that the proportion of latently infected cells capable of giving rise to rebound virus production is approximately one in a million resting CD4+ T cells in patients on Art. However, the difficulty of reliably measuring the reservoir means this number could be significantly higher or lower.

Regardless, the HIV reservoir is a major barrier to virus eradication and its existence raises several questions for cure strategies. Is it possible to completely eradicate latently infected cells from the body, or can we keep them silent to prevent viral rebound? Even more to the point, is it possible to prevent the reservoir from forming in the first place?

Due to the assimilation of viral genetic elements into the host genome, researchers previously assumed that once infection has taken hold, HIV could never be completely eliminated. Yet in 2009, German clinicians announced the case of an apparent HIV cure in Timothy Ray Brown, also known as "the Berlin patient." He underwent a bone marrow transplant following unsuccessful treatment for acute myeloid leukemia with conventional chemotherapy. Following the transplant, Brown ceased taking Art and the virus did not rebound. More than six years later, researchers have been unable to find evidence of replication-competent HIV in blood or tissues from this patient; it appears that any viral reservoir has been cleared. Despite the exceptional circumstances surrounding this case, many believe that the Berlin patient serves as proof of the concept that HIV can be cured.

Researchers have since attempted bone marrow transplants from donors carrying the same CCR5 mutation in six other cases of HIV-positive patients. Unfortunately, all of these individuals died within a year from relapsed malignancy or transplantation complications. In one of these individuals, rebound occurred after an HIV variant used an alternative T-cell coreceptor, CXCR4, suggesting a potential limitation to targeting only CCR5.

These cases demonstrate the intrinsic dangers and difficulties of the Berlin patient strategy, which could never be realistically scaled up to help all those infected with HIV. Researchers have now turned to another strategy to eradicate HIV: using gene therapy to turn off **CCR5** expression. If successful, such a treatment could prevent additional cells from being infected with HIV, thwarting disease progression even in the presence of a viral reservoir.



HIV replication cycle

Significant work remains to be done in the development of a potential cure and it is an exciting time in the field, with interventional trials running in parallel with continued basic research into the mechanisms of HIV infection and pathology.

THE SCIENTIST

PLUS POINTS

A picture posted to Twitter of the space espresso, served in a specially-developed cup.

First coffee in space

Astronauts have made the first cup of coffee in space — using technology that had to be painstakingly devised on earth and then transported up to the International Space Station in a rocket. Yes, the ISS crew finally got to use a specially-devised Espresso machine, dubbed the ISSpresso.

Samantha Cristoforetti's tweets were packed with references to *Star Trek*, as *The Washington Post* noted. It brings to an end months of waiting for the space coffee — the machine had been expected to arrive on a rocket last year but the SpaceX rocket carrying it exploded. That meant that non-essential items were delayed, which the National Aeronautics and Space Administration judged the espresso machine to be.

It finally arrived on a SpaceX Dragon ship, along with Italy's first woman astronaut and 450 grams of caviar for the team's new year feast. (That Italian astronaut was Cristoforetti, sent up by the European Space Agency, who posted the pictures of herself with the machine.)

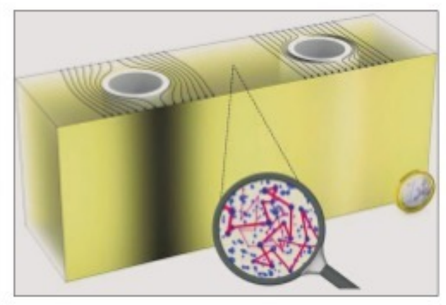
The machine was made by the Italian Space Agency's engineering firm Argotec and coffee company Lavazza. It required special technology to be built because normal coffee machines rely on gravity and any spillages could lead to boiling water being thrown around the space station or coffee grounds getting thrown around into the specialist equipment.

Nasa has only sent up 20 coffee capsules and hasn't yet worked out how to dispose of the used ones. Because each of them are individually wrapped, they are creating a lot of rubbish that the agency is unable to throw away. But those behind the mission to get coffee into space hope the same technologies can eventually be used for making and consuming other important things, like medicines.

ANDREW GRIFFIN/THE INDEPENDENT

Invisibility cloak

Scientists have built systems that hide objects by bending light around them so that they can't be seen — but they have previously only been tiny and worked at small wavelength ranges. Now scientists from the German Karlsruhe Institute of Technology claim to have built an invisibility cloak big enough to hide small objects, like phones, keys or a wheel of cheese.



In a diffusive light-scattering medium, light moves on random paths. A normal object casts a shadow, an object with an invisibility cloak does not.

To use the cloak, objects are put inside a small, long box that is coated with a special paint. The box bends light around it, meaning that the objects placed in it disappear from sight. Like previous versions, the invisibility cloak works by bending light around the box. But doing that forces it to take a longer route that it normally would, posing a problem for the technology because it's not possible to speed the light up.

But the KIT scientists have got round that issue by covering the whole box in a light-scattering material. In effect, that material slows down all of the light — which means that it can be sped back up again. "As we seemingly slow down the light everywhere, speeding it up again in the cloak to make up for the longer path around the core is not a problem," said Robert Schittny, who led the research project.

And because of the way it is built, the team behind the cloak says that it can be easily transported and so could be taken to classrooms to inspire students. "It is a macroscopic cloak that you can look at with your bare eyes and hold in your hands," said Schittny. "With a reasonably strong flashlight in a not too bright room, it is very easy to demonstrate the cloaking. That means no fancy lab equipment, no microscopes, no post-processing of measurement data. The effect is just there for everyone to see."

THE INDEPENDENT