Using human sweat as diagnostic tool and source of power

A recent breakthrough brings in an e-skin patch with six sensor probes

• Recall those early days when the family physician was called home to treat a patient. The first thing he’d do was to touch the skin on your face, temples and chest. This would let him diagnose quickly. If the skin feels hotter than usual, you have fever; if it is paler than the usual, you are dehydrated and must drink more water; if it has a bluish tinge, you need to breathe more oxygen; and if it feels wet, you need to exercise less or cut your physical stress and so on. Then you are given what he considers the appropriate medicine as pills or potion, or an injection. Alas, we have now replaced him with a doctor sitting in a clinic, who asks you to go to a commercial centre for diagnostics and prescribes the medicine based on the report. Skin-based diagnosis is a gone thing for general practitioners.

• These days, skin specialists do an interesting procedure, in which they attach a thin polymer-based sheet which contains the desired drug, stick it to the skin on your arm or chest and deliver the drug past the sweat fluid directly into the body, using a tiny electric current on the patch. This is thus a wearable technology for personalised medicine — no pills or potions. And with the advent of microelectronics and bio-compatible polymers, we now have ‘electronic skin’ (e-skin), and nanoscale wires that can be attached and an external electric power supply using micro-scale batteries.

Role of sweat
• Notice in all this, the active body fluid, namely, the sweat, is ignored or treated as an inert carrier of no other value. The role of sweat fluid in our body and the chemicals it contains are becoming
increasingly understood and utilised only recently. Sweat comes out of three types of glands distributed across all over our skin, secreting water and substances that help keep our body at the optimum temperature of 37 degrees C (or 98.4 degrees F). Our brain has temperature-sensitive nerve cells (neurons) which control the sweat glands in releasing the fluid depending on the temperature and physical and metabolic activity of the body. Sweat is thus our body’s thermo-regulator.

What does sweat contain? It is 99% water containing sodium, potassium, calcium, magnesium and chloride ions, ammonium ions, urea, lactic acid, glucose and other minor components. An analysis of the sweat fluid in a patient and how it compares with that of a ‘normal’ individual will thus be of diagnostic value (just as much as other body fluids do). For example, in the illness called cystic fibrosis, the ratio of the sodium to chloride ions in the sweat is different from that of a normal individual. Likewise, the amount of glucose in the sweat of a diabetic is higher than normal. But the problem is the amount of sweat available from the skin.

Diagnosis based on e-skin

It is here that modern-day technology has become of value. Now that microelectronics and e-skin patches are both available, scientists have been using them for real-time measurements of some chosen component in the sweat, using the appropriate probe (sensor) in the patch in order to detect and measure the level of the component. But would it not be much better if we can measure as many components as we desire if the e-skin patch be loaded with probes not for one but several components simultaneously? A breakthrough on this was made by a group of biologists, material scientists, computer experts and electrical engineers from California (Stanford and Berkeley), and was published with the title: “Fully integrated wearable sensor arrays for multiplexed in situ perspiration analysis” (Nature 2016 January 28; 529(7587): 509-514. doi:10.1038/nature16521. free access on the web). They put in not just one but six sensor probes — for Na, K, Cl ions, lactate, glucose and the temperature of the sweat — all six of them embedded on a e-skin patch, such that a stable sensor-skin contact is maintained. Signals coming from each sensor measuring the sweat component as a tiny electrical signal are then converted into a digital form, and sent to a micro-controller, and from there to a Bluetooth transceiver, which can be seen on a mobile phone or other screen, and passed on through SMS, email, or uploaded to the Cloud interface.

The Californian Group followed it up with another paper in 2017 titled: “Autonomous sweat extraction and analysis applied to cystic fibrosis and glucose monitoring using a fully integrated wearable platform” in Proceedings of the National Academy of Science, 114(18), 4525-4630; https://www.pnas.org/content/114/18/4625. Since the amount of sweat accessible in sedentary people is too low, the group resorted to what is called iontophoresis, wherein one can stimulate local secretion of sweat at chosen sites, thus getting enough of the fluid, analysing its relevant components in normal (control) individuals, and people with cystic fibrosis and also monitoring glucose levels in the sweat — all this in a similar integrated platform as was used in their Nature e
In a control individual, they found 26.7 mM of Na ions and 21.2 mM of Cl ions (note that the Na level is higher than Cl level here), while in a CF patient, Na level was 2.3 mM and Cl level 95.7 mM (far higher than the Na level), in keeping with what CF specialists have found in their routine (“classical”) practice. The group further found that oral glucose consumption while fasting led to increased glucose levels in sweat and in blood.

Sweat as power supply

• Note that in all these assays, the probes and sensors need to be powered externally using microbatteries. If these e-skin platforms are to be used in robotics and other devices, can we do away with this external, and have the material in the sweat itself be used as a biofuel generator of electric power? The group showed in their paper that just appeared 10 days ago in the journal Science Robotics (Yu et al., Sci. Robot. 5, eaaz7946(2020)). On a patch on the individual’s e-skin patch they added the enzyme Lox which would react with the lactate in the sweat and oxidise it to pyruvate in a bioanode, and reduce the oxygen into water in a biocathode, thus generating electrical energy that is sufficient to drive the patch with no external energy source — what a brilliant idea!

• Finally, in these COVID-19 days, it is good to know that sweat does not carry any pathogen (bacteria or virus); on the contrary it carries a germ-killer protein called dermcidin (Schittek et al, BMJ 2001, 323(7323);1206). One wonders if dermcidin or its modification can be anti-viral.

Coronavirus | Can antibody tests help tackle COVID-19?

Why have States complained about the tests being inaccurate in many cases? And, should India use both RT-PCR and antibody tests?

• The story so far: In the COVID-19 fight, the Indian Council of Medical Research (ICMR) had advised States to use antibody testing for surveillance and reiterated that the focus has always been on real time RT-PCR (or real-time reverse transcription-polymerase chain reaction) tests for diagnosis. The rapid testing kits that State governments had been using to detect antibodies to the novel coronavirus were throwing up unreliable results. In Rajasthan for example, rapid testing kits failed to detect antibodies even when the laboratories had confirmed patients to be COVID-19 positive.

What is the difference between rapid antibody tests and the RT-PCR tests?

• There are two ways to detect the presence of a virus, directly or indirectly. Antibody
tests, also called serological tests, have usually been the time-tested approach to finding out the presence of a virus in the body. They do so by detecting the presence and quantity of antibodies that are produced by the immune system to battle an infection. It is an indirect test because it cannot find the virus, but it can determine if the immune system has encountered it.

• Antibodies can show up between nine to 28 days after an infection has set in; by that time, an infected person, if not isolated, can spread the disease. Sometimes the antibodies may be produced in response to a closely-related pathogen and sometimes they may not be the right kind to counter the infection. These are the factors that can make an antibody test erroneous.

• In an RT-PCR test, a nasal or throat swab is taken from a patient suspected of having the disease. The test involves extracting RNA or ribonucleic acid, the genetic material of the virus, and checking if it shares the same genetic sequence as the SARS-CoV-2 virus. If it is a match, the sample is deemed positive. The only way such tests turn negative is if the actual sample does not have the virus or the swab was not properly administered and too little of the virus was gleaned.

• As the sequencing of genomes is now widespread and the technology well understood by experts in several countries, China, and subsequently others, were quickly able to determine the structure of the SARS-CoV-2 coronavirus and learn what differentiates it from related viruses. This is why it was possible to prepare accurate tests to detect the virus relatively quickly, almost in the middle of a pandemic, and the RT-PCR tests began to be followed as the ‘gold standard’ in detecting the virus. As not enough research hours have been spent studying the antibodies and the profile of recovered patients, the antibody tests we have for COVID-19 are imperfect.

Why is there a clamour for antibody kits?

• Antibody tests are fast and relatively inexpensive. The current RT-PCR technology requires RNA extracting machines, a specialised laboratory, and trained technicians. And at least a minimum of 30 samples are needed to make the process economically viable. The tests are done in batches and it can take up to four hours to confidently test for the presence of a virus from a batch. If one adds the time taken to isolate the RNA from swabs, this could again take a couple of hours. The scale of logistics involved can mean that it can practically take a day for results from a sample to be known. If one adds the cost of chemicals needed to perform these tests and the vagaries of importing practically every element of the paraphernalia involved, in the midst of a pandemic when demand far exceeds supply, it results in the test not being cheap. It can cost at least ₹4,500 depending on whether one is tested at a public or privately-run facility. Antibody tests are portable, can be administered on-site, conducted en masse and give quick answers. However, these answers are useful in-so-far as those who are using them are asking the right questions.

What do antibody tests reveal?
Given that they are not useful for directly detecting the presence of the virus, antibody tests can be used to gauge the extent of infection in a community or a large group of people who may have had exposure to the virus. Much like pregnancy detection kits, rapid-test kits change colour when particular molecules are detected. Two kinds of antibodies result from an infection: Immunoglobulin M and Immunoglobulin G (IgM and IgG). In response to an infection, the IgM is first produced within a week of infection. Two weeks later, the levels of IgM reduce and are replaced by IgG. The latter is a longer-lasting antibody and, depending on the infectious agent involved, can offer different durations of immunity. Antibodies to the chickenpox virus last for decades. Those to influenza viruses and even other coronaviruses (that cause the common cold) last no more than a year or two. This is why people need flu shots at regular intervals, and one of the reasons why it is practically pointless to have a vaccine for the common cold. It is too early in the course of the COVID-19 pandemic to determine how long immunity lasts. Nevertheless the presence of IgM, IgG can in a sample of the population determine whether the virus is present in certain clusters. Ideally, this can help government authorities decide on what regions in a lockdown can be opened up if the aim is to get regular life back on track as soon as possible.

This is what happened when infections had reached frightening proportions in the United States and Europe. It was apparent that the limitations of the RT-PCR combined with the virus’s ability to spread even through those who were not visibly sick would mean large numbers would be infected without being detected. Rapid antibody tests can also play a role in determining the degree of “herd immunity” in a population. That is, the true number who may have been infected; when a sizeable fraction of the population has been infected, the virus ceases its pace of spread. Current research expects herd immunity to have been achieved when 55% to 80% of the population has been infected — only careful serological surveys can establish that. Studies in India too have shown that for every symptomatic positive, there are two asymptomatic or presymptomatics (those who do not visibly manifest the disease). Thus, antibody tests could also be used for such estimates in India. The ICMR had laid out the strategy to use antibody tests to gauge the degree of COVID-19 presence in the country. The plan involved using a combination of both RT-PCR and antibody tests to establish infection levels.

What happened to India’s rapid testing plan?

Two Chinese companies, Wondfo and Livzon, got licences to sell 500,000 rapid antibody kits to the ICMR. Several of these were to be given to States and some were for the ICMR’s own use. A first batch was deployed in some States and soon complaints began pouring in over inaccurate results. The ICMR then asked States to stop using these kits for two days. After two days, the ICMR advised States to stop using the kits altogether. The Health Ministry has cancelled the licences given to the companies that were importing these kits from China. So far, the ICMR has not clarified what was wrong with the kits. The Chinese companies have also claimed that the kits were validated by the ICMR’s expert body, the National Institute of Virology (NIV). However, the NIV only clears batches of
kits that are submitted for testing. It is possible that even if a company’s kits get cleared, it ends up supplying kits on the field that are not up to the mark.

Another feature of the kits is their sensitivity (in percentage terms, the times the tests correctly identify people as positive for an infection) and specificity (in percentage terms, the times the test correctly rules out those not carrying the virus). Specificity refers to its ability to accurately distinguish between the target virus and other viruses. It is a well-established feature of tests that in regions of low actual prevalence of a disease, they can, depending on the kit’s specificity and sensitivity, misclassify vast numbers of those tested. It is not clear if these were factored in in tests using kits blamed as faulty by States. India is not the only place where complaints over Chinese kits have been raised. The United Kingdom and Spain have also raised such issues with these kits. In either event, there is no clarity if the ICMR has ordered more kits. The Health Minister, Dr. Harsh Vardhan, has said that by the end of May, the country will have kits that are made in India for antibody and RT-PCR tests.

Why has the Reserve Bank of India opened a liquidity window for mutual funds?

What are the concerns about the mutual funds industry?

The story so far: In view of the possible redemption pressure that the mutual fund industry may face after the abrupt winding up of six debt schemes of Franklin Templeton Mutual Fund, the Reserve Bank of India (RBI) on Monday announced a special liquidity window of ₹50,000 crore for mutual funds. Under the scheme, the RBI will conduct repo (repurchase agreement) operations of 90-day tenor at a fixed repo rate of 4.40% for banks. According to the RBI, banks can avail funds under this facility exclusively for meeting the liquidity requirements of mutual fund houses by extending loans and undertaking outright purchase of and/or repos against the collateral of investment grade corporate bonds, commercial papers (CPs), debentures and certificates of deposit (CDs) held by the fund houses. The scheme will be open till May 11 or up to utilisation of the allocated amount, whichever is earlier.

Why was it needed?

The trigger for the liquidity window was Franklin Templeton Mutual Fund’s decision to wind up six debt funds that had a combined assets under management (AUM) of almost ₹26,000 crore. The fund house said that it decided to wind up the schemes to preserve the value at prevailing levels — their value had eroded because of redemption pressures and mark-to-market losses due to lack of liquidity on account of the COVID-19 pandemic. That led to fears that the debt funds of many other fund
houses could face redemption pressure accentuated by the panic sparked by Franklin Templeton Mutual Fund’s sudden move.

Are mutual funds’ debt schemes under pressure?

• While the mutual fund industry clarified that what had happened at Franklin Templeton Mutual Fund was an isolated case, wider liquidity and other concerns persist. A couple of fund houses have already seen huge erosion in the net asset values of a few debt schemes post the Franklin Templeton episode due to mark-downs of their holdings. Incidentally, till date, banks have borrowed about ₹2,000 crore through the RBI liquidity window for mutual funds. Market observers say debt schemes are under pressure due to a combination of factors.

How much debt assets do mutual funds manage?

• The AUM of debt schemes of the mutual fund industry is about ₹15-lakh crore, which is more than half of the total AUM of Indian fund houses. The worst affected sub-category of debt funds is Credit Risk funds that account for only 5% of the overall debt assets. Investors, however, are sceptical about the overall credit quality of the assets; hence debt schemes are likely to see a spike in redemptions. Mutual funds are allowed to borrow up to 20% of their assets to meet liquidity needs for redemption or dividend payout. As of April 23, four mutual funds — of a total of 42 fund houses — had a cumulative borrowing of ₹4,427.68 crore, according to the Association of Mutual Funds in India (AMFI). Fund managers say that while such borrowings are common in March — there are huge redemptions due to advance tax payment and other quarter-end obligations — a spillover of such borrowings to April is a cause for concern.

What is the quality of debt securities held by mutual funds?

• Fund managers are of the view that more than half of the assets in debt schemes have a rating of AA or above. They say that while about 20% to 30% of total debt AUM would be AAA rated or in cash, another 30% to 50% would be in AA+ or AA rating. While the overall debt quality, based on current ratings, looks good on paper, the ongoing nationwide lockdown has impacted cash flows of most corporates, and investors are expecting defaults especially from the mid and small-sized corporate segment.

What are the regulators doing?

• The regulators are aware of the potential risk and are monitoring the situation closely. Market participants have already written to the Securities and Exchange Board of India (SEBI) to take action against Franklin Templeton Mutual Fund including appointing a highpowered committee to
take over the management of the fund house while examining its investment decisions. The
Association of National Exchanges Members of India (ANMI), an umbrella body representing about
900 brokers, has written to the Ministry of Finance and SEBI that as much as 64.73% of the total AUM
of Franklin India Low Duration Fund was in securities rated A or below, while in Franklin India Short
Term Income Plan, such securities accounted for almost 59% of total assets. The brokers’ association
says Franklin Templeton Mutual Fund invested in long duration securities even though SEBI norms
state that ultra short duration funds can only have bonds with a tenure between three and six
months.