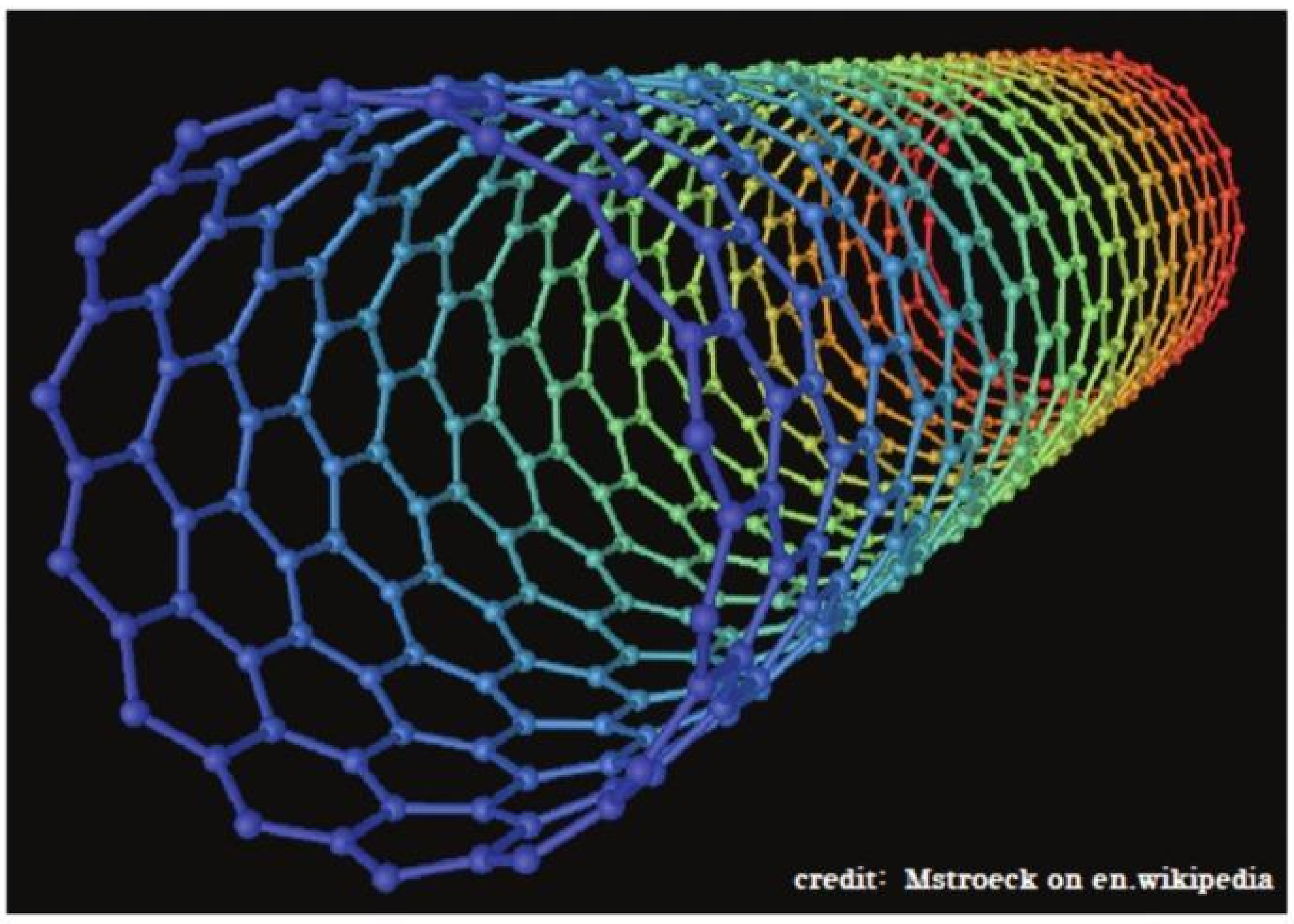
Of quantum vibrations



credit: Mstroeck on en.wikipedia

S ANANTHANARAYANAN

The twang of a nano-sized guitar string shows the graininess of nature

The Greeks thought matter must be made of atoms because they had to set a limit to how small things could get. The idea of infinite smallness presented a philosophical problem. If a distance could be divided without end, its length would consist of an infinite number of rapidly shrinking portions to be covered. It was then a wonder how we ever got from one place to another.

As algebra and the nature of converging series, which give us the answer, had not been developed, the Greeks said there was a limit to how far things could be divided. They must, then, reduce to something indivisible — the atoms. What we have now discovered is that atoms do have a structure and consist of smaller parts. But it turns out the Greeks were right — atoms, and hence all matter, consist of the so-called elementary particles.

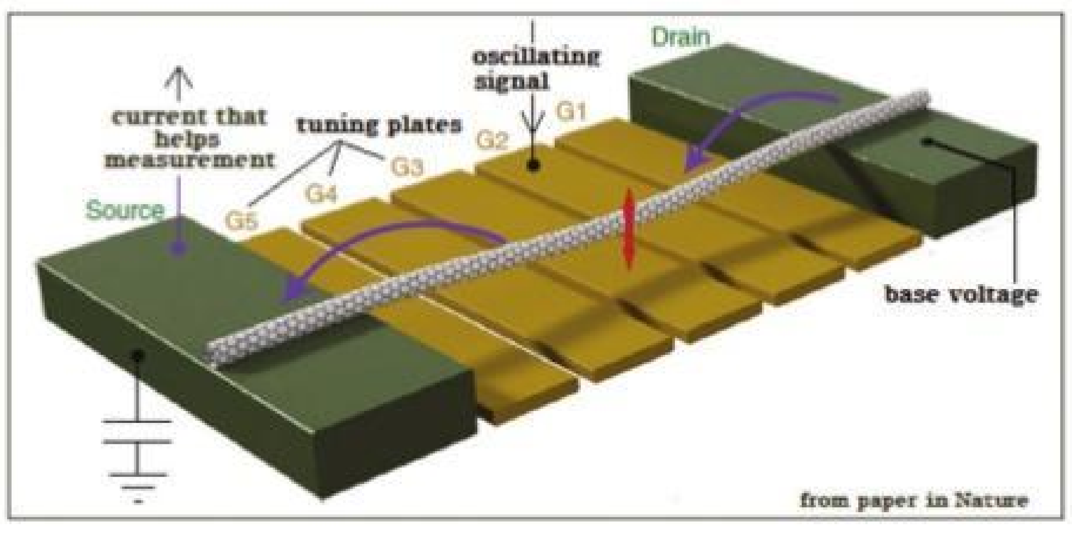
The maverick Nobel laureate, Richard Feynman, had an instructive angle to a thought experiment about very small particles. We now know that gases consist of molecules or submicroscopic particles in constant motion. It is because the particles are so small, and so many, that the pressure that their motion exerts on the walls of a container is not staccato but constant. And this is why the pressure is the same all over the volume of gas in a container.

The thought experiment Feynman spoke of is called Maxwell's demon, named after James Clerk Maxwell, its creator. The demon is imagined as a creature, about the size of the molecules of gas, controlling a trapdoor in the wall of a gas container. Now, as the demon can see the molecules, he can watch for each of them, as they approach the container wall, and open the trap door just when a molecule is headed straight for it. In this way, the demon can allow the fastest molecules to escape from the container, and the pressure and temperature within the container would steadily fall, although there was no refrigerator or exhauster at work.

Feynman shot down the idea of such a demon (which Maxwell did too) by considering what the effect of bombardment by high speed projectiles would be on the demon and the components of the trap door. Feynman quickly calculated that we cannot imagine that the dexterity of an agent operating such a mechanism in normal conditions would be the same in the very small world.

Yutian Wen, N Ares, FJ Schupp, T Pei, GAD Briggs and EA Laird, at the Universities of Oxford and Lancaster write in the journal, *Nature Physics*, of an experiment that brings into view the identity of individual electrons that make up an electric current. A nanotube of carbon, an electrical conductor of atom-sized dimensions, is set humming like a guitar string when a current is passed, an effect that has been shown to arise from the energy imparted to the carbon tube by staccato passage of electrons from the electrical connections of the nanotube.

The paper in *Nature Physics* says that evidence of individual electrons has been observed in mechanical arrangements of nanometre dimensions, but the electrons disturb the delicate components and make it difficult to carry out measurements. In the current work, the authors used a carbon nanotube, 800 nanometres, or less than a micron in length, and they show that the passage of single electrons through the filament causes a sustained mechanical vibration, like a guitar string that has been plucked. And the vibration has the features of a laser but the result is mechanical vibration rather than emission of light.



Overtone	Frequency	Overtone	Frequency	Overtone	Frequency
Basic	440	7	28,160	14	3,604,480
1	880	8	56,320 ← insect limit	15	7,208,960
2	1,760	9	112,640	16	14,417,920
3	3,520	10	225,280	17	28,835,840
4	7,040	11	450,560	18	57,671,680
5	← human limit 14,080	12	901,120	19	115,343,360
6	28,160	13	1,802,240	20	230,686,720 231 million hertz

A nanotube of carbon is suitable for such work because of the properties of the carbon atom. It is the tendency for atoms to seek a stable state with eight electrons in their outer orbit. Atoms hence combine with other atoms and share electrons to make up the number. The carbon atom has six electrons, and four of them are in the outer orbit.

As this is half-way to eight electrons, carbon is able to form a variety of chemical bonds. And in a network of carbon atoms, each one can handhold with three or four other carbon atoms, to form structures of great mechanical strength. And one such structure is that of the nanotube, a microscopic connector, channel, with optical, electrical and mechanical properties that can be adapted for use in electronic microchips.

The group in Oxford and Lancaster suspended the carbon nanotube with electrical connectors at either end, so that a current could pass through. While the entry of single electrons affects the nanotube physically, changes in the nanotube would affect the current through the junctions at the ends. The result is that if the electrical and mechanical effects could find a match, one could feed the other, for sustained oscillation, the paper says.

Suitable electrical voltages, including a high-frequency, oscillating signal, were hence applied to the apparatus at the supports called the "source" and "drain". As thermal disturbances would obscure the effects being looked for, the apparatus was cooled practically down to -273°C or absolute zero. Mechanical movements of the nanotube were detected using the effect such motion had on the electrical currents flowing. And it was found that when the oscillating signal matched mechanical frequency, there was a peak in the level of vibration.

The remarkable feature noticed was that even when there was no oscillating signal applied but only a steady voltage was present, the nanotube was in vibration. And this vibration was the strongest near about the frequency of resonance when the oscillating signal was present. This vibration was apparently the result of the disturbance caused by single electrons crossing into the nanotube, and in the absence of the oscillating signal, these disturbances were not regular but staccato.

In the case of a laser, the medium collects packets of incoming energy and further packets of energy can induce or stimulate emission of more packets in a coherent fashion. In the case of the carbon nanotube, there was no "stimulated emission", but the vibration was "self-excited" and a result of the irregular arrival of electrons, modulated by the effect of the nano-tube deformations at the junctions.

The frequency at which the nanotube vibrates was found to be 231 million cycles per second. The frequency standard for tuning instruments in Western music is the "middle A", which is 440 cycles per second. The table shows the frequencies of the overtones or sounds with doubles frequencies. We can see that the nanotube vibrates at the 20th overtone of middle A. This is above the limit of our hearing, which is between the fifth and sixth overtones. Or even of animals and insects, which can hear till a little over the eighth overtone.

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PLUS POINTS

Waste to bio-bricks

Researchers from the Indian Institute of Technology Hyderabad and KIIT School of Architecture, Bhubaneshwar, have developed bio-bricks for construction from agricultural waste products. Their development serves the dual purposes of waste management and eco-friendly, sustainable building materials.

This research was undertaken by Priyabrata Rautray, PhD scholar, design department, IIT Hyderabad and Avik Roy, assistant professor, KIIT School of Architecture, Bhubaneshwar. The results of this research work, which was guided by Deepak John Mathew, Head, design department, IIT Hyderabad and Boris Eisenbart from Swinburne University of Technology, Australia, have been presented at the International Conference on Engineering Design (ICED-2019) at TU Delft, Netherlands. The team's bio-brick also received a special recognition trophy for sustainable housing at Rural Innovators Start-Up Conclave 2019 organised recently by the National Institute of Rural Development and Panchayati Raj, Hyderabad.

Repurposing of agricultural waste is particularly important in India. More than 500 million tons of agricultural waste is produced in the country every year. While some of this is reused as fodder, 84 to 141 million-tons are burnt, which results in severe air pollution.

The process of making bio-bricks starts with careful selection of dry agro-waste like paddy straws, wheat straws, sugarcane bagasse and cotton plant. The team decided to use dry sugarcane bagasse for the first sample. The bagasse is first chopped to the desired size. A lime-based slurry is prepared, and the chopped agro-waste is added to the slurry and mixed thoroughly by hand or mechanical mixer, to create a homogenous mixture.

This mixture is poured into moulds and rammed with a wooden block to make a compact brick. These moulds are left to dry for a day or two, after which the sides of the moulds are removed, and the brick is allowed to dry for 15-20 days. It takes approximately a month's time for these bio-bricks to attain its working strength by air drying.

Although these bio-bricks are not as strong as burnt clay bricks and cannot be used directly to build load-bearing structures, they can be used in low-cost housing with combination of wooden or metal structural frameworks. Besides, these bricks provide good insulation to heat and sound and help in maintaining humidity of buildings, making these houses suitable for a hot and humid climate like India's.

"Other than as bio-bricks, this material can be used as panel boards or insulation boards and designers could explore such applications for this sustainable material," said Rautray. The team continues to study the designs and also seeks ways in which the load-bearing capacity of the bricks can be improved.

Skin for devices

Scientists have developed an "artificial skin" that they say can wrap around devices such as smartphones and make them ticklish. The prototype, which has been designed to look like and mimic human skin, responds to different forms of human contact such as tickling, caressing and pinching. Called Skin-On interface, it can be attached to mobile phones, wearable devices and laptop touchpads.

One of the things the researchers said they were able to demonstrate was "tactile emotions" with use of emojis. "A strong grip conveys anger while tickling the skin displays a laughing emoji and tapping creates a surprised emoji," said the study's lead author, Marc Teyssier, a PhD student at Telecomm ParisTech. "This skin has a subtle surface texture — the sensing is performed in the dermis and the hypodermis layer (fat layer) and the elasticity is what allows us to perform expressive gestures such as pinching."

The technology was developed by researchers at the University of Bristol in partnership with Telecomm ParisTech and Sorbonne University in Paris. The team says their work opens the door for a possible future with "anthropomorphic devices" — where gadgets have human characteristics.

The Independent

Battling toxicity

Are anti-cancer drugs defeating the deadly disease but damaging the heart?

SUSAN CURRIE

Cardiovascular disease remains the leading cause of death worldwide. This trend is mirrored in India, where estimated deaths due to CVD have risen from 25.6 million in 1990 to 54.6 million in 2016. Dorairaj Prabhakaran from the Public Health Foundation of India and Centre for Chronic Disease Control in Gurgaon has linked this to population growth, ageing and a stable age-adjusted CVD mortality rate. Importantly, the need for fundamental research to uncover the underlying reasons for progressive CVD in India has been highlighted by Prabhakaran.

An emerging and now recognised contributory factor to the global burden of CVD is the impact that certain chronic medications may have on cardiovascular function. Indeed, the possibility of non-specific or off-target effects of non-cardiac drugs on the heart is an ongoing concern for safety pharmacology in the pharmaceutical industry and may have enormous long term effects both socially and economically.

Anti-cancer drugs in particular have received widespread attention due to reports of off-target detrimental effects on cardiovascular function. Although many new anti-cancer drugs have significantly improved survival rates from cancer, there is growing evidence that some patients can, over time, develop cardiovascular complications. Depending on the anti-cancer agent in question, these effects can range from hypertension to arrhythmias to left ventricular failure and can occur in patients who have no prior history of CVD.

This phenomenon of "anti-cancer drug cardiotoxicity" has given birth to a new clinical discipline called cardio-oncology. This interdisciplinary approach to patient care combines cardiology and oncology and has resulted in more effective patient management going forward.

That said anti-cancer drug cardiotoxicity is a growing global challenge. The number of new anti-cancer drugs continues to increase and we still do not fully understand why or how many of these drugs will be cardiotoxic. Going forward we need to prioritise which cancer patients are most likely to be susceptible to chemotherapy-induced cardiotoxicity and how we may reduce any cardiotoxic effects while maintaining the effectiveness of the treatment.

In India there were estimated to be 1.15 million new cancer patients in 2018 and this is predicted to double due to demographic changes by 2040 (Smith and Mallath, 2019). The inevitability of increased reliance on chemotherapy and radiotherapy is clear. Reported tolerance to these therapies is variable and depends upon the anti-cancer agent used (some anti-cancer agents such as anthracyclines exhibit more cardiotoxic effects than others), whether the patient may have a pre-disposition to cardiovascular risk and what the patient's overall general nutritional status is like. Indian cancer patients have a higher prevalence of malnutrition at diagnosis than those from a Western population and this may impact upon drug tolerance.

In order to overcome anti-cancer drug cardiotoxicity we need an improved understanding of how these drugs exert their effects on the cells of the heart and blood vessels. If we can understand the underlying cellular mechanism of cardiotoxicity, we can then develop a strategy to reduce or reverse it.

The approach we have taken at the University of Strathclyde is to first examine the effects of clinical doses of selected anti-cancer drugs on cardiovascular function in rodents. We have used a technique called echocardiography (the same technique that is used in patients) to image the heart and measure how well the chambers of the heart are pumping blood. In rodents treated with the anti-cancer agents, there is a significant reduction in cardiac contractile function. This is similar to what we see in heart disease.

The functional parallels between anti-cancer drug-induced cardiotoxicity and heart disease made us question whether similar cellular changes

might be happening in both scenarios. There is an enzyme present in cardiac cells called calcium/calmodulin dependent protein kinase II (CaMKII) that we know is vital in regulating the balance between cardiac cell health and disease. In CVD we know that CaMKII becomes hyperactive and switches on a whole series of pathological effects.

Previous work has shown that if we specifically reduce CaMKII activation, we can reduce or reverse disease progression and restore a healthy balance. We have found that in rodents treated over a period of weeks with anti-cancer agents, CaMKII becomes activated, similar to what we observe during disease. Interestingly, CaMKII is activated early on (within hours) after starting drug treatment before we observe any measurable reduction in cardiac output. This early onset of activation could possibly be used as a marker to indicate susceptibility to progressive cardiovascular dysfunction in response to drug treatment.

We have recently extended our work to focus on isolated primary cardiac cells (both contractile and non-contractile cell types) and have shown that anti-cancer drug treatment at clinical doses does not only affect contractile muscle cells of the heart but also significantly impairs the function of cells called fibroblasts that are essential in providing a structural matrix to the heart. The drugs cause significant increases in substances called reactive oxygen species across both cell types and we are currently examining alterations in specific cellular patterns of ROS expression. We are exploring how ROS activation may be linked to CaMKII and aim to develop cell-based strategies that will allow us to selectively prevent anti-cancer drug activation of these molecules.

We believe there are strong parallels between the cellular mechanisms responsible for drug-induced cardiotoxicity and those responsible for progression of CVD. We believe that CaMKII could serve as a novel marker of cardiotoxicity, given its early onset of activation and also as a target for intervention, given its recognised role for longer-term pathological effects in the cardiovascular system.

Ultimately, the field of cardio-oncology requires collaboration across cardiology, oncology and basic science. Going forward, our work has highlighted CaMKII activation as a potential mechanism underlying drug-induced cardiotoxicity. This may provide a strategy for future intervention to reduce the detrimental effects of anti-cancer therapy on the global burden of CVD.

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