DEEP EARTH REVELATIONS

HKUST deep earth discoveries have thrown fresh light on how the extremely high temperatures and pressures at work in our planet's mantle may alter fundamental assumptions of how carbon, the building block of life, operates many kilometers beneath our feet. The findings by Prof Ding Pan, a cross-disciplinary expert in physics and chemistry, have contributed to a new understanding of the deep carbon cycle, which in turn could provide further insights into carbon-related hot topics, ranging from diamond formation to controversial proposals on inorganic petroleum formation.

Prof Pan used quantum mechanics simulations to determine, for the first time, the dielectric constant of water in the upper mantle. Having gauged this basic property governing the solvation of water, significant water and carbon interactions and reactions could then be explored, for example, the amount of carbon that can be stored and transported at such depths.

These measurements were previously not possible to accurately ascertain, given the challenges of simulating the mantle's extreme environment experimentally. In utilizing quantum mechanics, Prof Pan was able to calculate forces applied to atomic-level interactions, which could then be scaled up. To do so, he used one of the world's largest parallel supercomputers, Tianhe-2, housed in the National Supercomputer Center in Guangzhou as well as high-performance clusters at HKUST.

Prof Pan went on to reveal that carbon in the water-rich fluids, or geofluids, in the upper mantle transports carbon primarily as highly active ions rather than carbon dioxide, as previously thought. The finding enhances the possibility of carbon species reacting with other minerals, such as silicates and iron.

In 2018, the young scientist was awarded a prestigious Croucher Innovation Award. He is using the funding it provides over five years to develop novel theoretical tools, such as Raman and infrared spectroscopy using first-principles molecular dynamics.

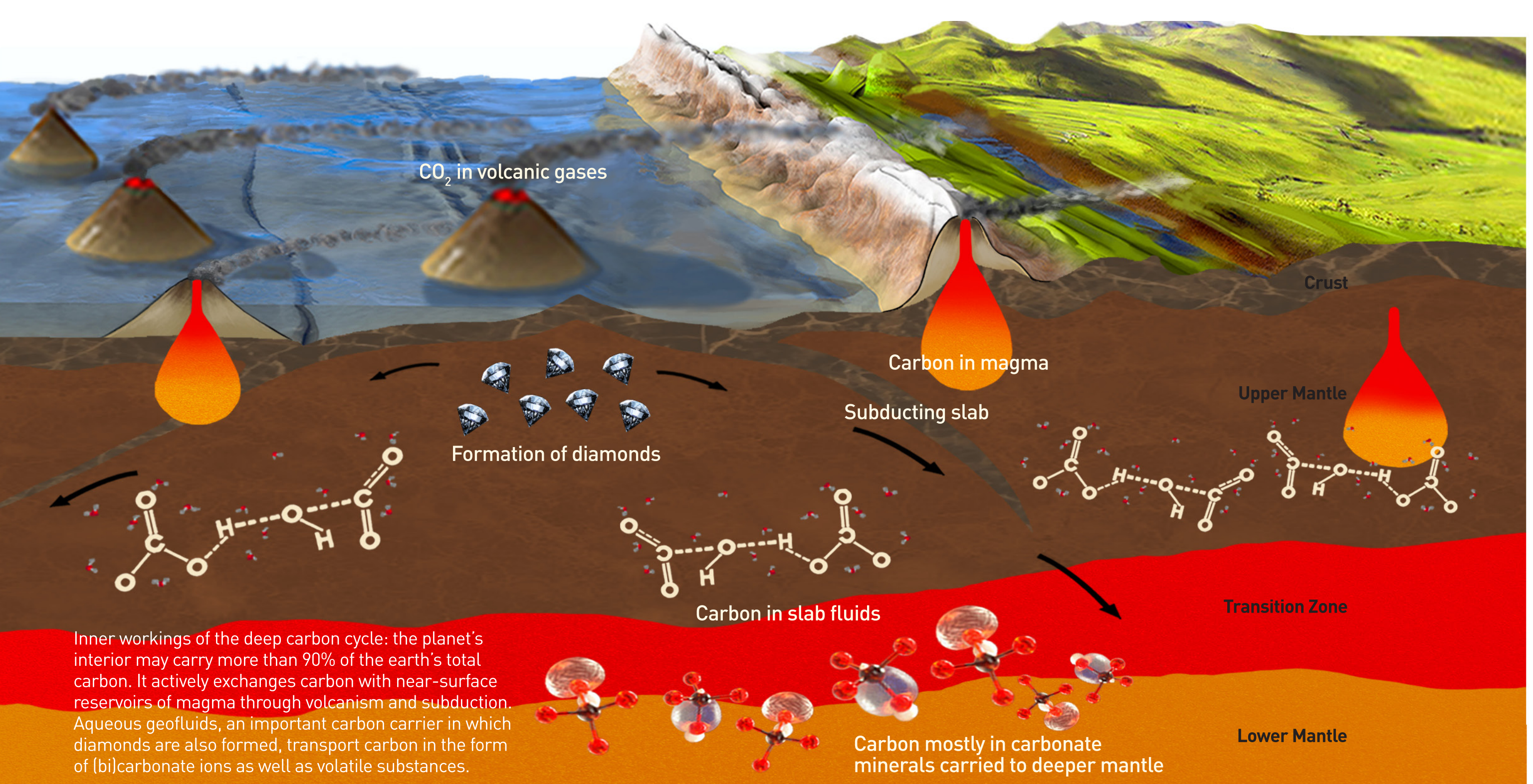
With these tools, he aims to provide an atomic picture of how carbon takes its diamond form, and contribute to the highly debated hypothesis of abiogenic petroleum formation during the carbon cycle, as opposed to fossil fuels being solely derived from ancient organic materials.

On the macro level, he hopes to answer challenging questions on carbon transportation inside the earth, energy implications of the carbon cycle, and carbon's role in the beginning of life. Working in affiliation with the HKUST Energy Institute, he will also assist research into sustainable e-fuel energy storage.

Prof Pan's quantum mechanics simulations have been developed in collaboration with fellow researchers in the Deep Carbon Observatory (DCO), a leading international collaboration involving over 1,000 scientists. He is the only member from Hong Kong and was awarded a 2019 DCO Emerging Leader Award.

> "Now we can use the fundamental laws of physics to help us understand carbon in the deep earth"

PROF DING PAN
Assistant Professor of Physics and Chemistry



Inner workings of the deep carbon cycle: the planet's interior may carry more than 90% of the earth's total carbon. It actively exchanges carbon with near-surface reservoirs of magma through volcanism and subduction. Aqueous geofluids, an important carbon carrier in which diamonds are also formed, transport carbon in the form of (bi)carbonate ions as well as volatile substances.

THE SECRETS OF MICRORNA BIOGENESIS

Human cells have more than 2,000 microRNAs (miRNAs), tiny structures playing critical roles in the regulation of gene expression, and a greater understanding of their functions holds clues for future control of many medical conditions, from infections to cancers and neurodegeneration.

miRNAs affect numerous biological processes, such as cell death, stem cell differentiation, and metabolism, among others. They can also be significant actors in human diseases, if their expression level in cells is not kept under strict control, with miRNA biogenesis among the most important regulatory mechanisms, according to biochemist Prof Tuan Anh Nguyen. The different factors involved in biogenesis, the process of miRNA synthesis, are the focus for Prof Nguyen's lab at HKUST.

Such exploration is built on numerous studies, including Prof Nguyen's, investigating the role of the human Microprocessor protein complex, which is responsible for the maturation of miRNAs. His past research has contributed to elucidating the cleaving mechanism initiating miRNA production and also overturned previous theories on the composition of the Microprocessor. These discoveries served as the basis for a 2018 Croucher Innovation Award.

Prof Nguyen's research adopted a combination of challenging methodologies involving the purification of protein components in the Microprocessor and, for the first time, observation of its biochemical activity when mixed in an assay of RNA. Bioinformatics and single-molecule technology were used to affirm the results, analyzing the behavior of the Microprocessor with different RNA precursors. X-ray crystallography helped identify the structure of the proteins, reinforcing initial findings.

Given the numerous types of miRNA precursors (pri-miRNAs), Prof Nguyen believes that the complex requires the collaboration of many more proteins and other factors. The recent work from his group at HKUST has discovered that heme, a critical small molecule playing an important role in oxygen transfer in human blood, along with SRSF3, an RNA splicing factor, is responsible for orienting the Microprocessor on pri-miRNAs to the precise position for cleaving.

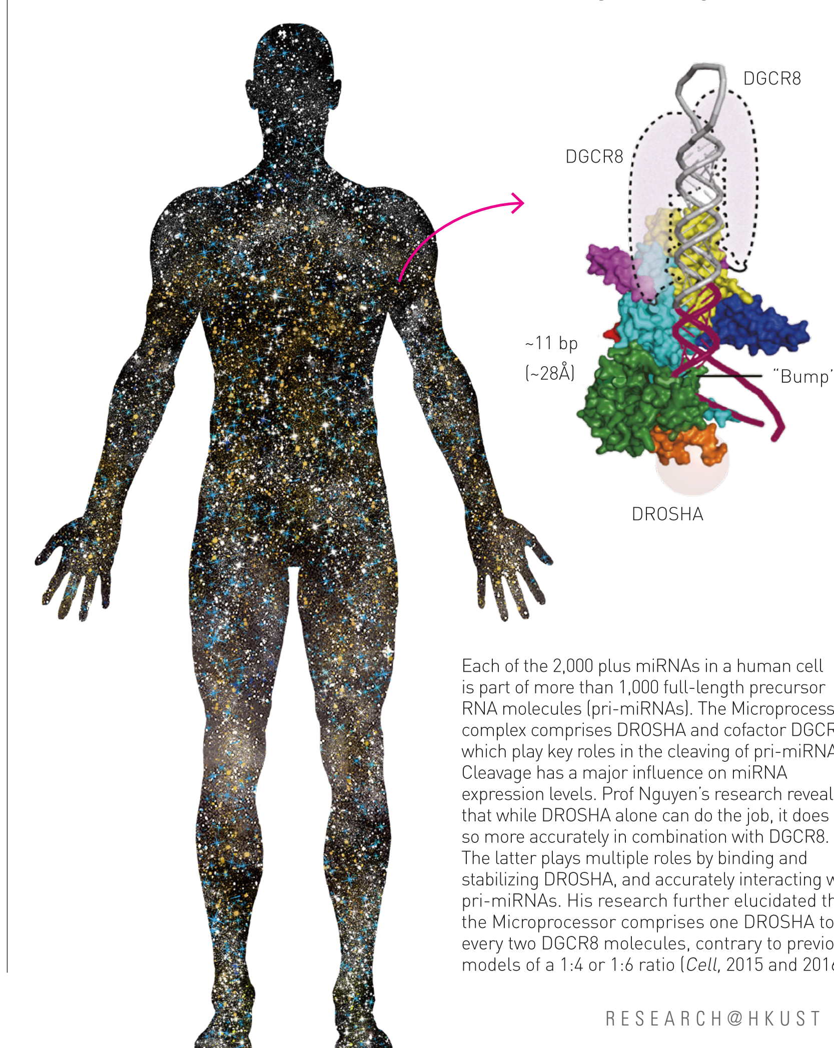
Prof Nguyen will use his five-year Croucher funding to investigate links between human RNA-binding proteins (RBPs) and miRNA production. His group is integrating core biochemistry and bioinformatics to investigate the enzymology and functions of RBPs. Previous enzymology research methods were limited to studying one enzyme with one or several substrates at a time. "Now we can work with thousands of substrates," he said. This work has implications for controlling diseases such as Severe Acute Respiratory Syndrome (SARS) and HIV.

Prof Nguyen joined HKUST in 2017 after completing his PhD at the Korea Advanced Institute of Science and Technology (KAIST) and his postdoctoral fellowship at Seoul National University. He received the Young Scientist Award from the Korean Society for Structural Biology in 2015.

In the longer term, the rising star's dream is to build a set of human RBPs for use in drug screening.

> "We can now study RNA-interacting enzymes in a high throughput manner, allowing us to understand enzyme functions and characteristics rapidly"

PROF TUAN ANH NGUYEN
Assistant Professor of Life Science



Each of the 2,000 plus miRNAs in a human cell is part of more than 1,000 full-length precursor RNA molecules (pri-miRNAs). The Microprocessor complex comprises DROSHA and cofactor DGCR8, which play key roles in the cleaving of pri-miRNAs. Cleavage has a major influence on miRNA expression levels. Prof Nguyen's research revealed that while DROSHA alone can do the job, it does so more accurately in combination with DGCR8. The latter plays multiple roles by binding and stabilizing DROSHA, and accurately interacting with pri-miRNAs. His research further elucidated that the Microprocessor comprises one DROSHA to every two DGCR8 molecules, contrary to previous models of a 1:4 or 1:6 ratio (*Cell*, 2015 and 2016).