對外合作組織與機構動態報導

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TACKLING DISEASE IN THREE DIMENSIONS: SUPERCOMPUTERS HELP DECODE RNA STRUCTURE

在三維條件下解決疾病：超級電腦解碼 RNA 結構

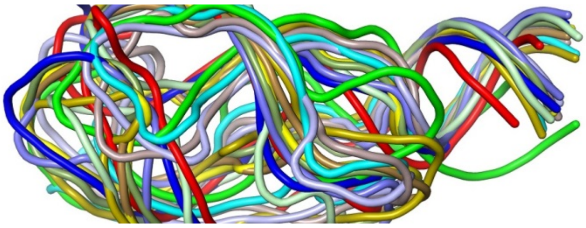
By Joan Koka • July 12, 2017

A cure for cancer, HIV and other stubborn diseases has evaded the brightest minds for generations. But with supercomputers – computing systems that can calculate, analyze and visualize extremely large amounts of data – researchers are gaining a leg up in the fight for better treatments and cures. Researchers at the National Cancer Institute (NCI) are using supercomputers at the U.S. Department of Energy's (DOE) Argonne

報告摘要(KEY INFORMATION)

1. 由於 RNA 極易折疊，要藉由實驗得知其功能性結構相當困難，因此該團隊決定使用電腦運算的方式，模擬數以千種的結構狀態，以找出具反應活性時可能性最高的結構。
2. 為瞭解各種環境作用以及環境污染的發生，科學家一直致力探究元素在環境中移動的過程，尤其是發生在水與礦物間介面的反應。實驗中，科學家將含銣溶液流經雲母，將雲母表層的鉀置換出來，再以含鈉溶液置換出銣。
3. 7 月 4 日，波蘭/捷克/德國工作坊於碳化學處理研究所舉行，其主題為：整合科技發展以最大運用褐煤與碳源。關鍵講題為「合作策略——研究發展整合」，討論碳的非能源應用相關科技發展。
4. 智慧型手機提供科學家統計大量數據的新方法。研究發現，肥胖問題多發生在「步數差距大」的國家。因此，如何打造一座「可行」城市，乃是不容忽視的公共衛生議題。
5. 目前應用的矽晶片為單層，且其邏輯與記憶體分離，使用上容易遇到資料傳輸壅塞情形。科學家使用非矽之新奈米材料，並將運算邏輯與記憶體層層堆高，以打破資料傳輸的壅塞現象。

National Laboratory to advance disease studies by enhancing our understanding of RNA, biological polymers that are fundamentally involved in health and disease.



In collaboration with staff from the Argonne Leadership Computing Facility (ALCF), researchers have perfected a technique that accurately computes the 3-D structure of RNA sequences. This method, which relies on a computer program known as RS3D and Mira – the ninth fastest supercomputer in the world – gives researchers studying cancer and other diseases structural insights about relevant RNAs that can be used to advance computer-assisted drug design and development.

RNA not only functions as a DNA interpretation messenger for protein fabrication, but also plays a multifaceted role in regulating gene expression – such as when, where and how efficiently a gene is expressed. For this reason, researchers are actively seeking to understand the functions of novel RNA sequences. And in order to get a complete picture, they need to know the biologically active forms of RNA, which are reflected in the complex 3-D structures that RNA sequences fold into after they're created.

"We already know the basic chemical groups for RNA and how they're composed, but what we don't know is what conformational structures they take," said Wei Jiang, a researcher at the Argonne Leadership Computing Facility who is one of the computational leads in the project.

"Getting the real functional structure, which is the 3-D structure, is very difficult to do experimentally, because the RNA polymer is too flexible," he said. "This is why we rely on computational simulation. Simulations can be used to explore hundreds or thousands of possible conformational states that would eventually lead us to the most likely 3-D structure."

The computer program RS3D was developed by a National Cancer Institute research team, led by researcher Yun-Xing Wang and postdoctoral fellow Yuba Bhandari, and optimized by ALCF researchers to run on Mira; Jiang played a central role in scaling the RS3D code to run on a large fraction of Mira, which improved its performance significantly.

As an input, RS3D uses known RNA sequence information and experimental data from small angle X-ray scattering, a technique that provides important structural information, such as particle size and shape, based on the scattering pattern that is generated when X-ray beams are applied to a target sample. With these inputs, RS3D outputs a low-resolution 3-D image of the topological structure of RNA that provides the most likely folding patterns.

"Since the biologically active form of RNA is a 3-D structure, going from understanding the primary sequence and the two-dimensional layout of an RNA to understanding the 3-D form is a big stepping-stone that gives us a lot of useful information about biological functions," said Bhandari, one of the leaders of the project. "Understanding the structural basis provides a foundation for further investigating molecular interactions and biological pathways in various diseases."

The researchers validated their technique by using it to compute the 3-D structure of 18 RNA polymers whose structures are known. These select RNAs fold into a wide variety of structures that represent common folding architectures. Additionally, researchers used R3SD along with experimental data recorded at the synchrotron light source at Argonne, the Advanced Photon Source, to compute the structure of adenine riboswitch, an RNA structure known to regulate gene expression.

"One of the unique and advantageous features of this technique is the fact that it's fully automated, meaning it does not require the user to input an initial 3-D structural template to work. This sets it apart from other methods that perform similar calculations," Bhandari said. "This helps us eliminate any potential limitations or biases that could be introduced through a template, and make the whole approach easier to apply."

The researchers are now in the process of publishing their technique; the source code will be made available to researchers thereafter. A brief summary of their computational work, presented in an article titled "Modeling RNA topological structures using small angle X-ray scattering," is published in Methods.

This work is funded by the Intramural Research Programs of the National Cancer Institute. This work employed resources at the Argonne Leadership Computing Facility and the Advanced Photon Source, both DOE Office of Science User Facilities. Experimental data for adenine riboswitch RNA was recorded at Sector 12 of the Advanced Photon Source. Computing time was awarded through the ALCF's Director's Discretionary Program.

MICA PROVIDES CLUE TO HOW WATER TRANSPORTS MINERALS
由雲母一窺水在礦物中的運輸過程

By Jared Sagoff • July 13, 2017

In order to understand various environmental processes and learn to better address the effects of pollution, scientists have been interested in tracking the movement of elements through the environment, particularly at interfaces between water and minerals. In a new study from the U.S. Department of Energy's (DOE) Argonne National Laboratory, in collaboration with the University of Illinois and Chicago and the University of Delaware, chemists have been able to look at the interface between water and muscovite mica, a flat mineral commonly found in granite, soils and many sediments. In particular, the researchers looked at the capture and release of rubidium – a metal closely related to but more easily singled out than common elements like potassium and sodium.

In the experiment, the researchers flowed a rubidium-containing solution over the mica, which caused rubidium atoms to replace the potassium that occurs naturally near the surface of the mica. Then the rubidium solution was replaced for one containing sodium, which in turn replaced the rubidium atoms.

According to Argonne chemist Sang Soo Lee, who led the study, the dynamics of the ion transport were largely controlled by electrostatic properties at the interface between the mica and the water. Essentially, the rubidium atoms “clung” to the mica’s surface similarly to how lint clings to clothing. The strength of the clinging behavior was determined mainly by how many water molecules were in between the mica’s surface and the rubidium – the fewer water molecules, the tighter the cling.

Lee and his Argonne colleague, chemist Paul Fenter, used Argonne’s Advanced Photon Source, a DOE Office of Science User Facility, to observe the activity of the rubidium using a technique called resonant anomalous X-ray reflectivity. This technique allows scientists to probe the position of a single element at an interface.

“Essentially, it’s like looking for a goldfinch in a tree, and using a technique that only shows you where yellow things are,” Fenter said.

By using the technique, the researchers were able to condense the timeframe it takes to measure the signal from the data. “Normally these data take hours to measure, but now we can have a time resolution of one or two seconds,” Fenter said.

Having a picture of the real-time dynamics of these kinds of interfaces give scientists a new view of how ions sense surfaces energetically. “If you think of our experiments like watching planes at an airport, then previously we were able to only know how many Boeings or Cessnas there were,” Lee said. “Now, we have a way to watch the planes actually take off and land.”

The research was funded by DOE’s Office of Science (Office of Basic Energy Sciences).

A paper based on the research, “Real-time observations of cation exchange kinetics and dynamics at the muscovite-water interface,” was published in *Nature Communications* on June 9.

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INTEGRATED TECHNOLOGY DEVELOPMENT FOR EFFECTIVE UTILIZATION OF LIGNITE AND COAL RESOURCES

波蘭/捷克/德國工作坊：整合科技發展以最大運用褐煤與碳源

On 4 July 2017, Poland – Czech Republic – Germany Workshop took place in Institute of Chemical Processing of Coal. The workshop was entitled "Integrated Technology Development for Effective Utilization of Lignite and Coal Resources" The meeting was attended by representatives of science and industry representing Germany, the Czech Republic and Poland. The representatives of the Ministry of Energy and the Ministry of Development of Republic of Poland have also participated in the meeting.

The workshop was devoted to new and effective technologies for the use of coal and the prospects of their development under the European Union conditions. The purpose of the meeting was to develop a vision for the development of sustainable coal technologies, and to create the basis for creating new research areas in Europe.

The workshop was opened by prof. M. Ściążko from Institute for Chemical Processing of Coal, with the plenary presentation on "Megatrends in global development". Another lecture was given by prof. R. Wehrspohn from the IMWS Institute for Microstructure of Materials and Systems, co-authored by T. Dickert from Zentrale der Fraunhofer-Gesellschaft ZV from Germany, who has discussed on "Fraunhofer International – Worldwide Initiatives in Applied Research"

The workshop contained two discussion panels entitled "Role and place of lignite and coal in the economy", and "Status of research into carbon resources and circular carbon economy". Panel I was opened by Deputy Director of GIG, dr. eng. Z. Lubosik who has discussed on "Recourses, production and consumption of hard coal and lignite in Poland" subject. In summary, Director of IChPW dr. eng. A. Sobolewski discussed "Coal as feedstock for the production of chemicals and fuels".

The key discussion of the meeting, which was realized in the form of a panel entitled "Collaboration strategy – integration of R&D" concerned the development of future technologies for the use of coal for non-energetic applications.

Then participants of the meeting had an opportunity to be familiarized with the infrastructure of the Center for Clean Coal Technologies (CCTW), where prof. J. Zuwała has presented unique pilot scale installations that enable pilot scale research.

Workshop gathered a total number of 35 participants. The international representatives were 15 representatives from universities and research institutes (Fraunhofer Institute, University Hamburg & Fraunhofer, Technische Universität Chemnitz, TU Bergakademie Freiberg, Research Institute for lignite (brown) coal, s.c., Most, Czech Republic, The Institute of Chemical Process Fundamentals (ICPF), Czech Academy of Sciences, VŠB, Technical University of Ostrava) and also one industrial representative (RWE Power AG).

Polish partners representatives were: IChPW, GIG, AGH Faculty of Energy and Fuels, Silesian University of Technology, Poltegor and Azoty Kędzierzyn Group – ZAK, TAURON Polska Energia SA, PGE Polska Grupa Energetyczna SA, PGE Polska Grupa Energetyczna SA and JSW Innowacje

BY COUNTING STEPS, RESEARCHERS DISCOVER 'ACTIVITY INEQUALITY'

由計步看出活動力的不均等

By Tom Abate, July 10, 2017

Stanford researchers using smartphones to track the activity levels of hundreds of thousands of people around the globe made an intriguing discovery: in countries with little obesity, people mostly walked a similar amount per day. But big gaps between people who walked a lot and those who walked very little coincided with much higher levels of obesity.

Considering that an estimated 5.3 million people die from causes associated with physical inactivity every year, these researchers looked for a simple and convenient way to measure activity across millions of people to help figure out why obesity is a bigger problem in some countries than others.

The ground-breaking study, appearing in *Nature,* used data captured from smartphones to analyze the habits of 717,000 men and women from 111 countries, whose steps were studied for an average of 95 days.

The researchers, led by computer scientist Jure Leskovec and bioengineer Scott Delp, dubbed this phenomenon "activity inequality" to evoke the well-established concept of income inequality. "If you think about some people in a country as 'activity rich' and others as 'activity poor,' the size of the gap between them is a strong indicator of obesity levels in that society," Delp said.

A related finding was the powerful role that gender played in country-to-country differences. Prior studies of physical activity, done mainly in the United States, have shown that men walk more than women, and this was borne out in the global findings. What surprised researchers, however, was how greatly this gender step gap varied from country to country with negative consequences for women. "When activity inequality is greatest, women's activity is reduced much more dramatically than men's activity, and thus the negative connections to obesity can affect women more greatly," Leskovec said.

The researchers, who are sharing their findings on an activity inequality website, hope their work will help improve public health campaigns against obesity and support policies to make cities more "walkable."

Smartphones and steps

Smartphones are equipped with tiny sensors called accelerometers that can automatically record stepping motions. The researchers acquired the data for this study from the Azumio Argus app, which tracks physical activity and other health behaviors. Azumio anonymized the data but provided key health demographics: age, gender, height and weight. The last two data points enabled the researchers to calculate each person's body mass index.

The findings leaned most heavily on data from the 46 countries for which Azumio provided at least a thousand anonymized users, enough to form the basis for statistically valid inferences. The analysis disclosed strong correlations among activity inequality, the gender-activity gap, and obesity levels. "For instance, Sweden had one of the smallest gaps between activity rich and activity poor, and the smallest disparity between male and female steps," said Tim Althoff, a doctoral candidate in computer science and first author on the *Nature* paper. "It also had one of the lowest rates of obesity."

Meanwhile, the United States ranked fourth from the bottom in overall activity inequality, indicating a large gap between activity rich and activity poor. It was fifth from the bottom in the gender step gap and it has high levels of obesity.

Walkable cities

To better understand the causes and consequences of activity inequality in urban settings, the researchers analyzed a large subset of data from the United States to investigate how the built environments of 69 cities related to activity, obesity and health. Prior research had scored each city by how walkable and pedestrian-friendly it is, using factors such as ease of walking to shops, restaurants, parks and other destinations. The researchers then correlated this walkability index to their smartphone activity data.

Team member Jennifer Hicks, director of data science for the Mobilize Center at Stanford, said the results make clear that city design has health impacts: the cities that were most conducive to walking had the lowest activity inequality. "Looking at three California cities in close geographic proximity – San Francisco, San Jose and Fremont – we determined that San Francisco had both the highest walkability score and the lowest level of activity inequality," she said. "In cities that are more walkable everyone tends to take more daily steps, whether male or female, young or old, healthy weight or obese."

A new research instrument?

The technological star of the project was the increasingly ubiquitous smartphone. Nearly 70 percent of adults in developed countries now carry smartphones; in developing nations, the percentage is close to half. "This opens the door to new ways of doing science at a much larger scale," Delp said.

But qualifying the smartphone as a tool for this type of research was no cakewalk. "The methodology was so new that the reviewers were dubious at first," Leskovec said.

However, strong data and rigorous computational methods ultimately proved the validity of this new approach. Now, having qualified the smartphone for research of this sort, the Stanford researchers are looking for new ways to leverage this tool. "With the appropriate apps and sensors we can push this research in exciting directions," said team member Abby King, a professor of medicine and health research and policy. "We could better link activity within and across populations with food intake, or examine the ways activity and inactivity may affect stress or mental health, as well as investigating how best to fine-tune our environments to promote increased activity."

A NEW 'HIGH RISE' CHIP BREAKS COMPUTING'S DATA BOTTLENECK IN TWO WAYS

新型「高樓」晶片以二種方法突破運算資料傳輸瓶頸

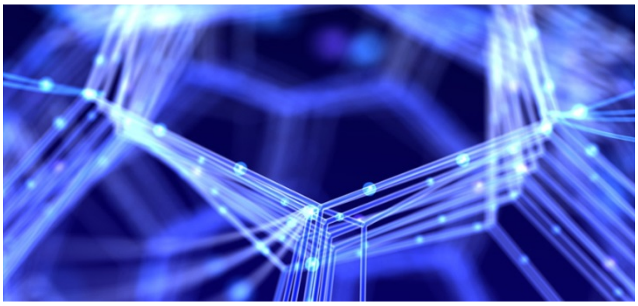
By Taylor Kubota, June 29, 2017

One day soon we may live in smart houses that cater to our habits and needs, or ride in autonomous cars that rely on embedded sensors to provide safety and convenience. But today's electronic devices may not be able handle the deluge of data such applications portend because of limitations in their materials and design, according to the authors of a Stanford-led experiment recently published in *Nature*.

To begin with, silicon transistors are no longer improving at their historic rate, which threatens to end the promise of smaller, faster computing known as Moore's Law. A second and related reason is computer design, say senior authors and Stanford professors Subhasish Mitra and H.-S. Philip Wong. Today's computers rely on separate logic and memory chips. These are laid out in two dimensions, like houses in a suburb, and connected by tiny wires, or interconnects, that become bottlenecked with data traffic.

Now, the Stanford team has created a chip that breaks this bottleneck in two ways: first, by using nanomaterials not based on silicon for both logic and memory, and second, by stacking these computation and storage layers vertically, like floors in a high-rise, with a plethora of elevator-like interconnects between the "floors" to eliminate delays. "This is the largest and most complex nanoelectronic system that has so far been made using the materials and nanotechnologies that are emerging to leapfrog silicon," said Mitra.

The team, whose other Stanford members include professors Roger Howe and Krishna Saraswat, integrated over 2 million non-silicon transistors and 1 million memory cells, in addition to on-chip sensors for detecting gases – a proof of principle for other tasks yet to be devised. "Electronic devices of these materials and three-dimensional design could ultimately give us computational systems 1,000 times more energy-efficient than anything we can build of silicon," Wong said.



First author Max Shulaker, who performed this work while a PhD candidate at Stanford, is now an assistant professor at MIT and core member of its Microsystems Technology Laboratories. He explained in a single word why the team had to use emerging nanotechnologies and not conventional silicon technologies to achieve the high-rise design: heat. "Building silicon transistors involves temperatures of over 1,000 degrees Celsius," Shulaker said. "If you try to build a second layer on top of the first, you'll damage the bottom layer. This is why chips today have a single layer of circuitry."

The magic of the materials

The new prototype chip is a radical change from today's chips because it uses multiple nanotechnologies that can be fabricated at relatively low heat, Shulaker explained. Instead of relying on silicon-based transistors, the new chip uses carbon nanotubes, or CNTs, to perform computations. CNTs are sheets of 2-D carbon formed into nanocylinders. The new *Nature* paper incorporates prior ground-breaking work by this team in developing the world's first all-CNT computer.

The memory component of the new chip also relied on new processes and materials improved upon by this team. Called resistive random-access memory (RRAM), this is a type of nonvolatile memory – meaning that it doesn't lose data when the power is turned off – that operates by changing the resistance of a solid dielectric material.

The key in this work is that CNT circuits and RRAM memory can be fabricated at temperatures below 200 Celsius. "This means they can be built up in layers without harming the circuits beneath," Shulaker says. "This truly is a remarkable feat of engineering," says Barbara De Salvo, scientific director at CEA-LETI, France, an international expert not connected with this project.

The RRAM and carbon nanotubes are built vertically over one another, making a new, dense 3-D computer architecture with interleaving layers of logic and memory. By inserting a plethora of wires between these layers, this 3-D architecture promises to address the communication bottleneck. "In addition to improved devices, 3-D integration can address another key consideration in systems: the interconnects within and between chips," Saraswat said.

To demonstrate the potential of the technology, the researchers placed over a million carbon nanotube-based sensors on the surface of the chip, which they used to detect and classify ambient gases.

Due to the layering of sensing, data storage and computing, the chip was able to measure each of the sensors in parallel and then write directly into its memory, generating huge bandwidth without risk of hitting a bottleneck, because the 3-D design made it unnecessary to move data between chips. In fact, even though Shulaker built the chip using the limited capabilities of an academic fabrication facility, the peak bandwidth between vertical layers of the chip could potentially approach and exceed the peak memory bandwidth of the most sophisticated silicon-based technologies available today.

System benefits

This provides several simultaneous benefits for future computing systems.

"The new 3-D computer architecture provides dense and fine-grained integration of computing and data storage, drastically overcoming the bottleneck from moving data between chips," Mitra says. "As a result, the chip is able to store massive amounts of data and perform on-chip processing to transform a data deluge into useful information."

Energy efficiency is another benefit. “Logic made from carbon nanotubes will be ten times more energy efficient as today’s logic made from silicon,” Wong said. “RRAM can also be denser, faster and more energy-efficient than the memory we use today.”

Thanks to the ground-breaking approach embodied by the *Nature* paper, the work is getting attention from leading scientists who are not directly connected with the research. Jan Rabaey, a professor of electrical engineering and computer sciences at the University of California, Berkeley, said 3-D chip architecture is such a fundamentally different approach that it may have other, more futuristic benefits to the advance of computing. “These [3-D] structures may be particularly suited for alternative learning-based computational paradigms such as brain-inspired systems and deep neural nets,” Rabaey said, adding, “The approach presented by the authors is definitely a great first step in that direction.”

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Subhasish Mitra is a professor of electrical engineering and of computer science, and a member of Stanford Bio-X and the Stanford Neurosciences Institute. H.-S. Philip Wong is the Willard R. and Inez Kerr Bell Professor in the School of Engineering, an affiliate of the Precourt Institute for Energy and a member of Bio-X and the Stanford Neurosciences Institute. Roger Howe is the William E. Ayer Professor in Electrical Engineering and a member of Bio-X and the Stanford Neurosciences Institute. Krishna Saraswat is the Rickey/Nielsen Professor in the School of Engineering and professor, by courtesy, of materials science and engineering, and an affiliate of the Precourt Institute for Energy. This story is a revised version of a press release by MIT News correspondent Helen Knight.