TIB: Catalyzing Greener and Cooler Growth

By SONG Jianlan (Staff Reporter)

The ideas glittering in the labs of TIB might catalyze a revolution in industrial manufacturing, and hence blaze a novel way out from the carbon-economy dilemma.

Photo by SONG J.

It has long been disputed whether efforts to curb carbon emissions could slow down economic growth and hence social development; meanwhile the accelerating depletion of fossil fuel reserves has also raised concerns about energy crisis. Plus their crucial role as a source of raw materials for petrochemical industry and other sectors, it has become more and more pressing to find substitutes for these resources.

To address these global issues, scientists have been working from different perspectives, ranging from fundamental research in mechanisms underlying the incredibly efficient harvesting and transformation of solar energy built in photosynthesis of plants/bacteria, to applied research for renewable energy sources. Unfortunately, so far still no non-fossil energy sources can substitute fossil fuels to offer stable and affordable energy flow, with the only exception of nuclear energy, whose safety has remained a dubious issue for ordinary people. Seems that humanity has been trapped into an inevitable dilemma in which no compromise can be made.

Isn't there anywhere else to go? A newly established institute under the umbrella of CAS might have the answer.

Officially established in late November 2012 after three years of preparation with joint efforts from CAS and the Tianjin Municipal Government, the Tianjin Institute of Industrial Biotechnology (TIB), CAS is striving to carve out "the third road", a greener and cooler way to bypass the energy-growth dilemma, breaking through with industrial biotechnology.

Take It Light

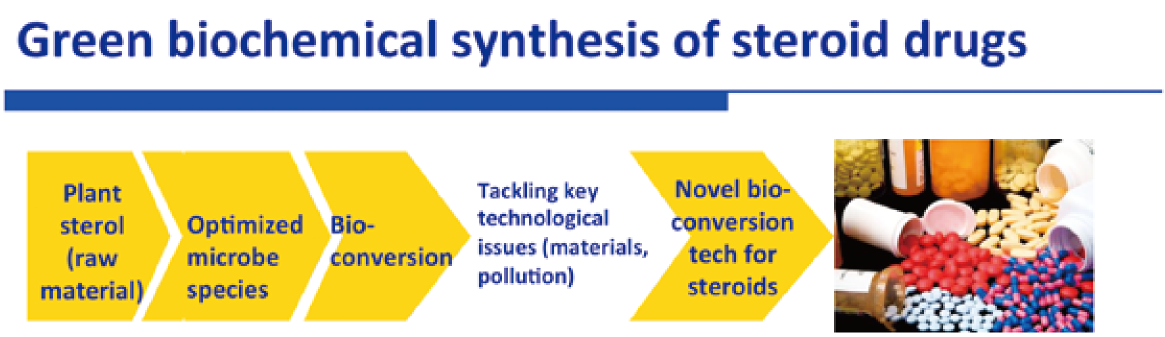
"The establishment of TIB represents an effort to implement a novel strategy for green, low-carbon development," remarks Prof. LI Yin, Deputy Director-General of TIB. The new entity, he introduces, aims to blaze a trail from the upper reach of the industrial chain for green economy, namely fundamental research, to the lower reaches, the transfer and commercialization of green technologies. "We are not directly working to unveil the mystery of photosynthesis, that is hard," jokes LI: "instead, we take the lighter way to arrive at the same destination."


A TIB employee works in lab. (Photo by SONG J.)

"Lately China offered to peak its carbon emissions by 2030, and to raise the compositions of clean energy sources to 20% in her portfolio. It is a very demanding goal, and naturally will pose some challenges to our economy, which to a great extent is driven by fossil fuels," comments SUN Jibin, Deputy Director-General of TIB. "Therefore we hope to help our country to shift from the traditional mode to a greener one for development, by proposing and promoting a new strategy for green economy."

What this strategy hinges on is biotechnology, a versatile pathway capable of turning impossible materials like straw, organic trash or even air into basic industrial materials like propylene glycol, artificial fibers, and even medicine. More importantly, this pathway can significantly decrease the release of poisonous gases, wastewater or waste residues, therefore is highly friendly to the natural environment, according to TIB experts.

At the core of this magical pathway lies the tiny but powerful bio-machinery built in the cells of



Bio-manufacture offers clean and highly efficient conversion technology for synthesis of important medicine, such as steroid, a large category of medicine frequently used in daily life. (Image by courtesy of TIB) microorganisms, called the "cell factory". Some species of microorganisms can decompose coarse fibers like straw, and turn them into short-chain hydrocarbons like alcohol. Some others can further produce more complex products like amino acids as the result of their metabolic process. Moreover, microorganisms reproduce themselves rapidly: through fermentation a population can increase the number of its individuals by orders of magnitudes in a few hours.

These traits offer great promise in industrial applications. "Based on the functions we know of such species, we can design, optimize or even synthesize an appropriate species, and produce preconceived industrial products using such cell factories," explains LI. With help from fermentation, such goods could be efficiently produced in a well-designed bioreactor at very low costs, leading to a conversion rate much higher than what traditional industrial manufacturing can offer.

Taking this "light" way, TIB is catalyzing an ambitious revolution in industrial manufacturing, to largely reduce energy consumption, pollution discharge, and carbon emissions.

Handle It Safe

"Optimization or 'synthesis' of the species might involve genes transferred from other species than the host. It is safe, however, because it is easy to avoid gene escapes, given that the end products are actually secretion from the transgenetic/synthesized organisms, hence they themselves do not contain any genetic matter of the species at all," assures LI.

"Actually the fermentation tanks we use in industrial processes are air-tight vessels that can prevent the microbes from escaping; after the fermentation/culturing, we adopt strict procedures for sterilization and the subsequent wastewater processing. Therefore there is no risk of leakage as long as the entreprise strictly follows the procedures," he continues.

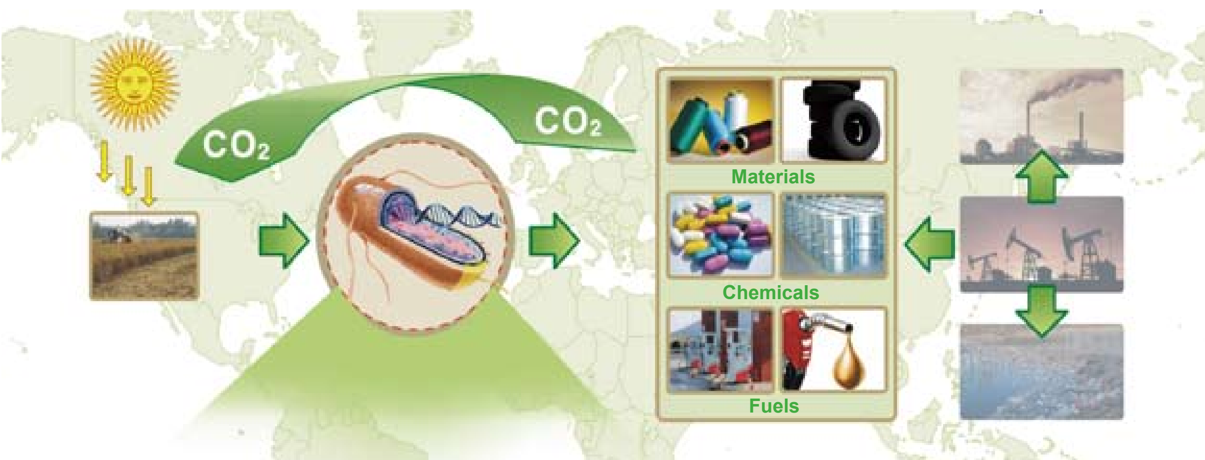
"What we deal with at TIB for biotech R&D are microbes – a category of organisms which is a far cry from human beings – rather than higher plants or animals. In this domain, biosecurity issues brought about by synthetic biology, like gene escape and spread, are just similarly challenging as those by genetic engineering when the latter emerged about three decades ago. As a proactive response to potential risks, TIB is developing necessary technologies to prevent the synthesized genetic matter from escaping or being stolen," LI adds.

According to LI, when designing and synthesizing a microbe or a cell factory for industrial use, scientists can cut off some "redundant genes" from the genome of the model microbe – those genes that are "redundant" for industrial manufacturing but indispensible for the organism to survive in a natural environment. As a result such artificial cells, which can only survive in an artificial medium for culturing, will be strictly isolated from the natural environment.

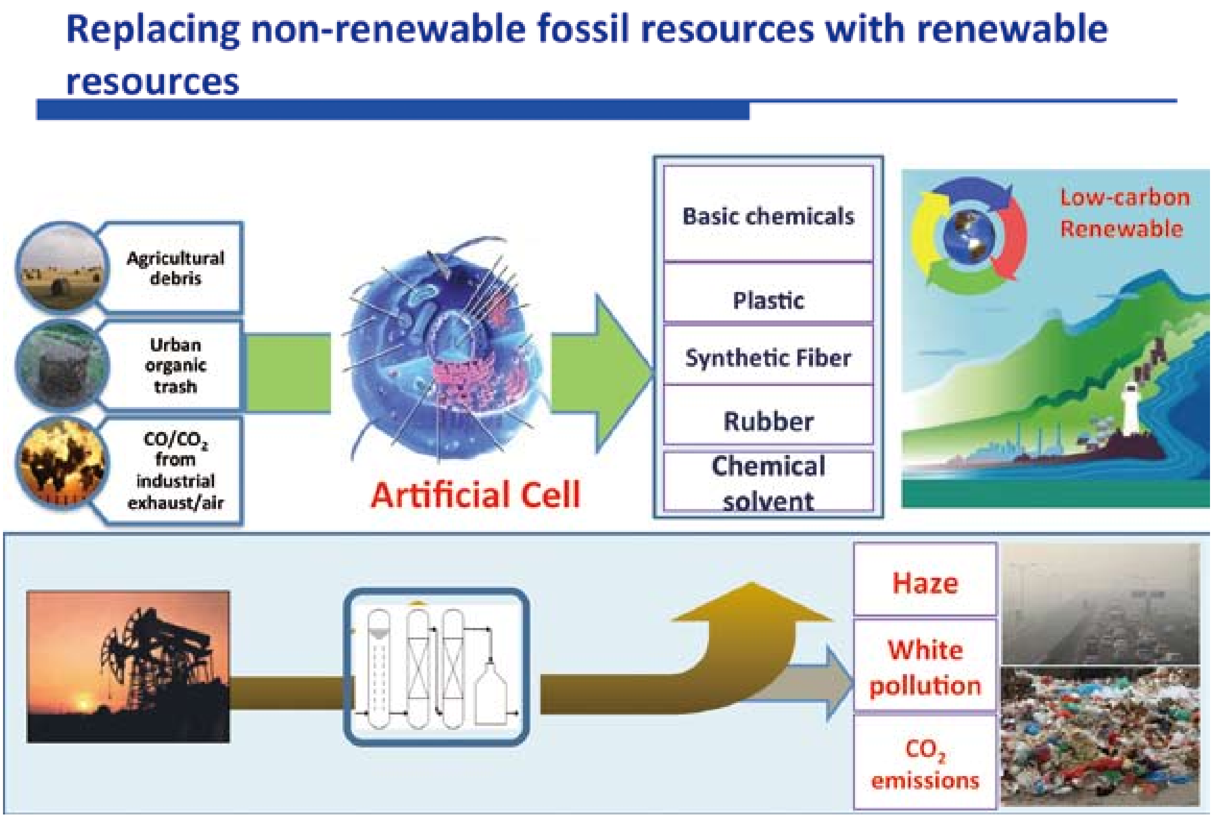
"This will eradicate the potential risks of gene escape and spread," says LI.

Dream It Big

With help from modern biotechnology, TIB has committed itself to three ambitious missions aimed at the cause of green economy: to replace fossil resources with renewable and affordable carbon sources including straw, trash, and even carbon dioxide, as raw materials for industrial production; to replace the traditional chemical processes for industrial manufacture, which features poisonous emissions and pollution, with biological



Committed itself to three ambitious missions, TIB aims to promote a greener and cleaner mode for industrial manufacturing. Its missions include: 1) To replace fossil resources with renewable carbon sources as raw materials; 2) To replace traditional chemical process with biotechnological production; and 3) To elevate the quality of industrial production via modern biotechnology. (Image by courtesy of TIB)



The novel strategy promises great potential for carbon and pollutant reduction. (Image by courtesy of TIB)

processes, which are mild and much more compatible with the ecosystem of our planet; and finally, to elevate the current industrial manufacturing with aid from biotechnology, improving its productivity.

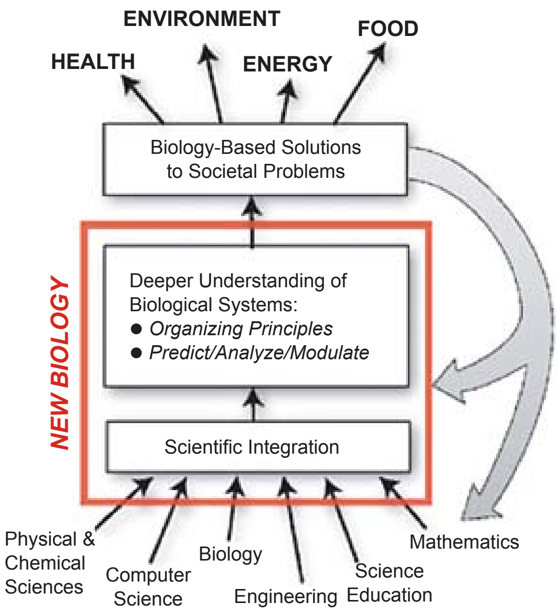
"In short, what we want to do is: TWO REPLACEMENTS, and ONE ELEVATION," summarizes Prof. SUN.

"The replacements will also make contributions to environment conservation, including biodiversity conservation," Prof. LI adds: "Our efforts include replacing endangered medicinal plants with cell factories, producing unlimited amount of effective compounds for healthcare. Industrial biotechnology can further offer a bonus, namely a greatly increased output compared with traditional methods. Generally such effective compounds are very rare contents in plants; due to their extremely low concentrations it is very hard to extract them from the raw plant materials. This in turn deteriorates the availability of the involved medicinal plants and leads to over exploitation of them. Replacing traditional manufacturing processes with industrial biotech processes will free many of such natural resources from depletion; very probably, it will even save many endangered plants from extinction. So far we have already succeeded in some cases like TAX (Taxol), the effective constituent of an anti-cancer drug first discovered in ground hemlock, an endangered plant."

"Another successful case is producing ginsenosides (protopanaxadiol, the effective constituent of an anti-cancer drug found in Ginseng) via fermentation," LI continues: "We only need a factory of only 1,000 m^2 floor space to produce as much of protopanaxadiol as what can be extracted from Ginseng grown in a plantation of about 7,000 hectares."

When asked of what TIB can do in terms of the "ONE ELEVATION", Prof. SUN explains that with aid from new biology, TIB experts are able to greatly improve the productivity and meanwhile greatly reduce the pollution. "For example, traditionally, L-alanine, a popular amino acid, has to be produced from decomposition of benzene, a poisonous chemical. The production undergoes a very long pathway and discharges a lot of carbon dioxide, wastewater and pollutants including heavy-metal catalysts. One of our scientist makes a change and adopts a biological method – through fermentation of a special species of microorganism, glucose is turned into alanine at one step, giving off much less pollutants or carbon dioxide. A small, obscure company adopted this technology and has since grown rapidly into the biggest manufacturer in the world, enjoying the largest market share, amounting 50%. To think, it used to hold just a negligible share!

"Again, for another amino acid representing a highly profitable industry valued dozens of billions yuan a year," he continues: "We invented a new biotechnology to raise its conversion rate from a little bit over 60% to around 80%, hence greatly lowered the costs of the production. Now we have thrown this technology into industrialization and conducted necessary R&D for its commercial application.



The concept of new biology. (Image adapted from Committee on A New Biology for the 21st Century: *A New Biology for the 21st Century*, p18, 2009.)

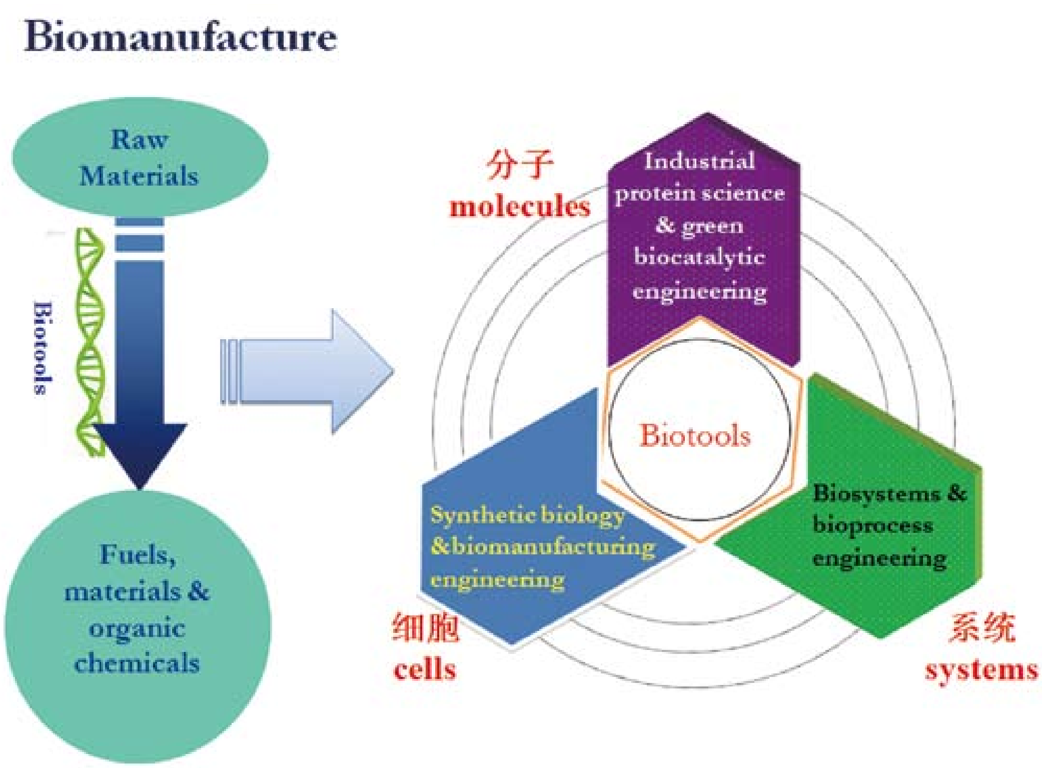
"Therefore the biotech pathway can represent a future mode of manufacturing, and we can give the industries in China a push to make the change," SUN suggests.

"Many industries in China feature very large scales, for example the industries of textile and antibiotic – China owns the biggest gross capacity of antibiotic production, which even exceeds the overall demand of the world," he laughs. "These industries, however," he continues in a solemn tone: "suffer from lower productivity and give off more pollutants, if compared with those of developed countries. As a result, our enterprises suffer from lower profit rates, and our people suffer deteriorating environment.

"Therefore what we need to do is, to elevate the quality of our industries, lower the costs, raise the productivity, and to improve the competitiveness of our enterprises," SUN concludes.

Cleaner, Greener, and Cooler

Traditional chemical engineering generally gives people a "dirty" impression: it is the pronoun of poisonous wastes and pollution, involving high-



Bio-manufacture might represent a future mode of industrial manufacturing. (Image by courtesy of TIB) temperature and high-pressure reaction conditions, organic solvents and heavy-metal catalysts, all burdening the natural environment with stress.

"These emissions, all non-biological, are very difficult for nature to decompose. Our Mother Nature still needs some time to evolve needed strategies to deal with them," SUN comments. "Things will be very different with the biological pathway of industrial manufacturing, however," he asserts.

"Humanity and microorganisms alike are organisms, and we undergo lots of bioprocesses very similar to our microbe friends. For example many of human metabolic processes are highly similar to those in microorganisms, based on the same fundamental biochemical reactions," explains Prof. SUN. "And these essential metabolic processes depend on the same enzymes to catalyze the biochemical reactions; even their reaction conditions are the same. For example the pH value in human cells are almost neutral, the same as that in microorganisms. Moreover, the material we 'burn' in our metabolism to supply our cells with energy is sugar, the same as many microorganisms," he continues.

"This high level of conservation means," SUN emphasizes: "if we utilize a microbial process to produce industrial goods, it could be highly compatible with us human beings. After all, microorganisms do not like heavy metals and organic solvents, either."

"Many cases have illustrated its safety," SUN furthers: "Our practice has proven that replacing the chemical engineering process with the bio-pathway is highly environment-friendly. Moreover, bio-manufacture can provide better efficiency or productivity."

"We all know that fossil resources are non-renewable, therefore it is not sustainable to rely on them as primary energy sources. Nor is it sustainable to rely on them as raw materials for industrial manufacturing. Replacing them with renewable carbon sources including biomass will save such valuable resources from depletion. To think what will happen if we can create clothes and tables, say, from thin air," he anticipates with an optimistic smile: "It is a dream coming true – we are really working on a project to capture carbon dioxide from the air, and turn it into hydrocarbons."

"Aside from saving fossil resources from depletion, this strategy presents a low-carbon solution for economic growth," SUN continues: "Consumption of fossil fuels means releasing ancient carbon sources of our planet, which were condensed and reserved deeply into the strata by geological movements, back into the atmosphere, producing extra carbon emissions. Using renewable carbon materials like biomass as raw materials, however, means neutral or even negative carbon emissions. Therefore this strategy will greatly reduce the carbon footprint of industrial manufacturing and represents a promising way out for low-carbon growth."

Make Difference

The missions of TIB, also the original intention of its founding, differentiate it from most other CAS institutes. "Traditionally, an institute under the umbrella of CAS focuses on explorations in a certain scientific discipline like physics, chemistry, or microbiology. Our institute, however, aims to construct a complete industrial system for a greener economy, and to remove technological barriers in the way, utilizing biological devices as tools," introduces SUN, passion sparkling in eyes.

Indeed, the whole institute has been built revolving around the above-mentioned three missions, with R&D teams devoted to the full spectrum of disciplines along the industrial chain, all oriented towards an elevated industrial mode for green growth.

"We are to fulfil these missions through 'new biology', an interdisciplinary science that integrates protein science, systems biology, synthetic biology, and fermentation engineering, drawing on know-hows from biology, chemistry, mathematics, engineering science and computing science. More specifically, we are pursuing these goals with some biological devices, particularly the design of synthetic biocatalysts," SUN introduces.

TIB attaches special importance to fundamental and applied fundamental research in three areas, namely industrial protein science and biocatalytic engineering, synthetic biology and microbial manufacturing, and biosystems and bioprocess engineering. Its operation features a sandwich-like structure integrating the R&D system consisting of teams devoted to a spectrum of disciplines, a coordinating department called the "Department of Strategic and Integrative Research (SIR)", and an infrastructure platform integrating core facilities. The three parts work altogether to assume roles of different hierarchy, including science research, technological innovation, industrial incubation and postgraduate education.

Outstanding in this sandwich-like structure is the coordinating department SIR, which bridges the industrial sectors and the R&D activities of TIB, making sure that the latter's output is market-oriented.

Throughout the whole process of its R&D activities, according to Prof. LI, TIB pays great attention to make sure the end products meet the current demands of the market. "It is important to give the industry due incentive to use green technologies," he reaffirms: "Otherwise these technologies would be left in oblivion and all the R&D investment become a waste; as a result we would fail to promote our strategy for green growth."

The key to keep all the R&D on a market-oriented track is the SIR department, an epitome of TIB operation.

Responsibilities of this department include initiation of projects, recruiting internal or external groups to build up R&D teams, monitoring the R&D progress, and evaluation of the performance of the team members. Research groups at TIB, each focusing on a specific area, are encouraged to attend the projects initiated by SIR and subject to its guidance and assessment.

Under this system, fundamental research at TIB has gained a special role: to serve the consequent applied fundamental and technological research, and beyond.

Some research groups at TIB focus on "pure" biology like genome analysis. According to Prof. SUN, they are all positioned at certain nodes of the innovation chain and respectively have their own outlets for industrial applications.

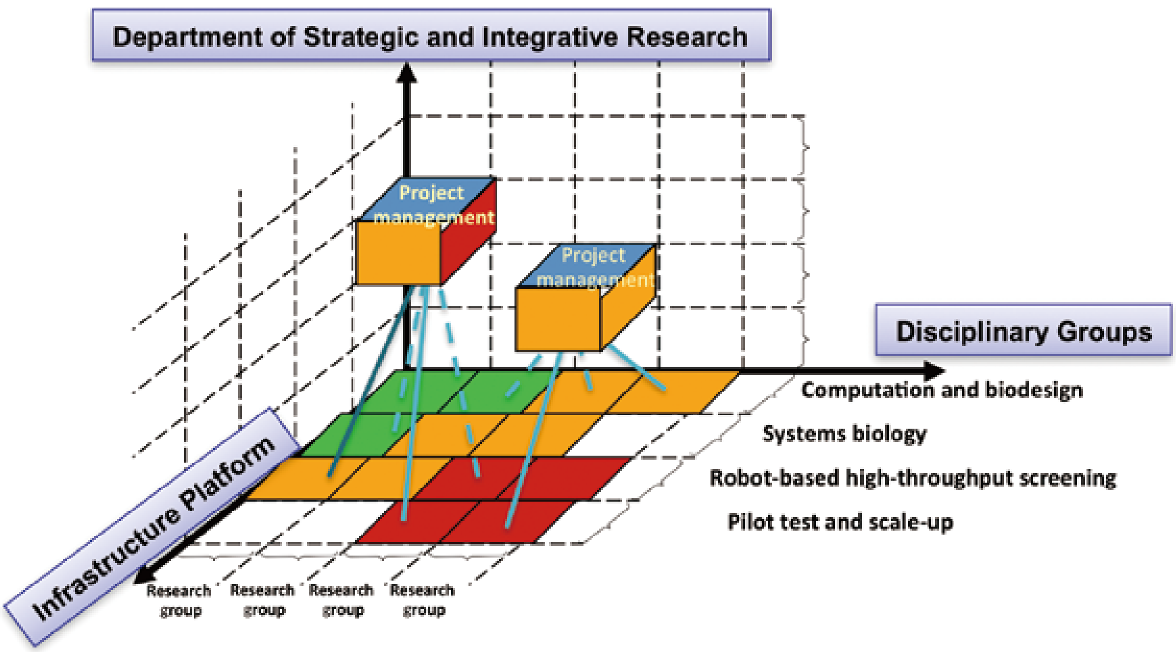
"The industrial microbe species we employ might involve some mutants leading to very efficient functions and hence better productivity. Through genomic analysis we can understand the detailed changes in its genes, and based on this we can further study the mechanism underlying its excellent performance. More idealistically we might break through the potential bottlenecks and optimize the species. This has made it necessary to include pure biological studies in house," explains SUN.

"For example, the group led by Prof. GUO Ruiting, a PI recruited from Taiwan Region, is adept in spatial structure characterization of proteins. His team has characterized the structures of many industrial proteins, or enzymes, to understand their catalysis process. Such studies are essentially fundamental, targeted at the underlying mechanisms, but at the same time they are also highly valuable for industrial application. Without knowing the underlying mechanisms we will not be able to optimize the functioning of the species, say changing their substrate specificity, improving their stability and catalytic speed. On the contrary, with a sound understanding of their structures, we can do a lot of things.

"Aside from groups focusing on fundamental research, we also have groups engaged in technology support, applied research and other R&D aimed at industrialization and commercialization. On the campus we have a large center for computation and biodesign; and we have deployed teams for protein design, pathway analysis and design, cell simulation, fermentation process optimization, and product extraction. For a certain product (technology), we cover all the R&D along the innovation chain from genomic analysis to industrialization, and as the result what we provide the enterprises with is a complete package of technologies together with microbial species.

"And what keeps coordinating in between is the SIR," introduces SUN: "It takes the lead to organize the R&D for a project, recruiting teams and experts at different areas."

This operational mode has proven successful. So far TIB has established far-reaching and close ties with industries at home and abroad. It has also established



The Department of Strategic and Integrative Research plays an important role in the sandwich-like structure of TIB, bridging the R&D and the demands of the market. (Image by courtesy of TIB) partnerships with more than 60 companies for S&T cooperation, to help them overcome barriers in terms of technology transfer. It has also inked a number of agreements for strategic collaborations with the Tianjin Municipal Government and also local governments in Shandong, Jiangxi, and Sichuan provinces, among others.

On top of its market-oriented R&D and technology transfer, TIB has also made efforts to help enterprises incubate technologies that have promise in industrial application, aiming to make difference in industrial manufacture and further the mode of economic development.

Incubator of Institutional Innovations

The newly born entity is currently staffed with 280 employees recruited from all over the world. To meet its ambitious goals, the Institute is still hungry for talents – according to Prof. SUN, they are expecting to double the number of their employees in two or three years.

"We need more talents to join us," says SUN: "and to this end we are making the best from current talent policies to recruit people and, more importantly, inspire their passion via suitable human resources management. Still, institutional innovations are needed here to establish an optimal system of personnel procedure."

As a brand-new institution, TIB adopts a performance assessment system distinctive from other CAS institutes, with emphasis placed on the employee's substantial contribution and influence. Subsequently, the annual evaluation of a research group stresses less on the number of publications and patents; instead it gives more weight to their contributions to the Institute and society, as well as influence on the community as a measure of quality.

TIB scientists at work. (Photo by SONG J.)

"The contribution of an individual employee could be unique and covers a wide range," SUN explains: "it could be theoretic innovation, including new methods, new theories and new understanding; it could also be economic value created by or derived from his/her innovations."

"A seemingly good publication list might not mean good contributions," SUN indicates in particular. "Your publications in a highly influential journal, or even your wonderful citation record as well, could be merely the result of intended 'dilution' into the literature with repeated ideas. You can define yourself as a scientist devoted to fundamental research and take publication list as the primary form of your output, but you have to make clear what exactly your contribution is," he asserts.

"The reform in performance assessment and evaluation, from my view, lies at the core of the deepening institutional reform of CAS, the Pioneer Initiative under implementation," SUN remarks: "Now the headquarters is dividing the affiliated institutes into four categories, and to assess their performance in differentiated ways. The essential idea is, to change the traditional system of assessment, which gives excessive importance to papers and impact factors. Papers cannot fully represent the contribution of a CAS employee, therefore the traditional system is a bit misleading."

To recognize the employees' contributions, TIB has established a policy to share benefits from technology transfers with its employees. Once a technology is successfully transferred, the inventors will be awarded with a significant portion of the profits. This incentive further encourages the scientists to pay attention to the demands of the market.

"As a new-type institute, the establishment and dynamic adjustment/optimization of a reasonable system of performance evaluation constitutes an important part of our work," SUN says when envisioning the future of TIB.