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Special Feature Silk Vascular Grafts Attract Attention in the Field of Regenerative Medicine

Silk Vascular Grafts Attract Attention in the Field of **Regenerative Medicine**

Silk is called the "queen of fibers" because of its smooth touch and pearl-like luster. In Japan, researchers are taking on the challenge of making small-diameter vascular grafts using silk as the main material. Professor Tetsuo Asakura at Tokyo University of Agriculture and Technology is advancing the research and development of these silk vascular grafts. We asked him about his work in the forefront of this field.

Surprising use of silk that benefits mankind

Silk is an animal fiber taken from the cocoon of the silkworm. Although people associate the fiber with luxury textiles, it has long been used for surgical sutures and therefore is known to be a potential candidate for use as a regenerative medical material. Dr. Tetsuo Asakura, Professor Emeritus at Tokyo University of Agriculture and Technology, studied the structure of silk for years and has



Dr. Tetsuo Asakura Emeritus Professor and Specially Appointed Professor, Tokyo University of Agriculture and Technology Graduated from a doctoral program at Tokyo Institute of Technology in 1977. Research subjects: Structural analysis of polymers using NMR, basic science and application of silk, and regenerative medical engineering.

succeeded in developing silk vascular grafts.

When it becomes necessary to surgically replace crucial blood vessels that no longer function, the options are to use artificial vascular grafts, to transplant blood vessels from another part of the body or to transplant donated human blood vessels. There are various types of commercial vascular grafts such as synthetic fibers and vessels made of polytetrafluoroethylene (PTFE) knitted in tubular form, but vascular grafts made of natural materials such as silk have never been used in clinical practice.

Professor Asakura describes the remarkable characteristics of silk that make it suitable for vascular grafts-impressive biocompatibility, controllable biodegradability, minimal inflammation, suitable mechanical properties, and its ability to be tailored into various forms such as films, fibers, tubes and porous sponges.

For example, when a silk vascular graft is implanted into an animal such as a rat or dog, early formation of blood clots does not occur. The surrounding cells stick to the silk and proliferate, and replacement of the graft's inner wall can be observed. The silk content then decreases gradually over the course of a year after implantation, resulting in a smooth inner vascular surface with no

signs of blood clotting. "This phenomenon of 'remodeling' does not occur with vascular grafts made of conventional synthetic fibers," explains Professor Asakura.

Molecular structural analysis using NMR paved the way for the utilization of silk

Professor Asakura's original research was the structural analysis of polymers using nuclear magnetic resonance (NMR), which is an analytical method of looking at the structure and dynamics of materials at the molecular level. "When I was conducting NMR research at Tokyo Institute of Technology as a student, I was greatly inspired by presentations at the meeting of the NMR Society on attempts to take direct NMR measurements of living animals and plants in an NMR tube. In 1980, I started silk research at Tokyo University of Agriculture and Technology and began in vivo NMR measurements of living silkworms."

Professor Asakura then focused on determining silk's structure in the agueous solution stored in silkworms. It was believed that the structure before spinning was the key to understanding how silkworms can produce such a strong fiber. Professor Asakura said that it took 20 years to determine the structure before spinning. He also used NMR to de-

Cross section of a vascular graft transplanted into a rat



With time, the white part (silk) of the cross section of the vascular graft disappears as it is replaced with the rat's own blood vessel component (collagen).

termine the structure after spinning and the mechanism of fiber formation. Based on that research, he started to use silk in practical applications.

Use of small-diameter vascular grafts in clinical practice was the dream of researchers all over the world

Currently, large- and medium-diameter vascular grafts with diameters of 6 mm or more, which are used in clinical practice, are made of synthetic fiber material and have almost attained a satisfactory level of performance. However, small-diameter vascular grafts-those with a diameter of less than 6 mm-would be useful to bypass the coronary arteries to the heart or the artery under the knee but are not commercially available because of the high probability of blood clotting. Many researchers around the world have tried to develop such smalldiameter vascular grafts for use in clinical practice without success.

disease in modern society has made it an urgent necessity to develop blood vessel substitutes, especially those with a small diameter, to replace damaged blood vessels. Professor Asakura explains, "I began such development because I thought that I might find a clue as to why silk has been used for many years for sutures without any problems. I began to tackle this difficult task based on the knowledge I accumulated on the structure and processing methods of silk."

The photographs above show the change over time in the cross-section of a silk vascular graft implanted into a rat. The time span is two to 48 weeks (almost one year) after implantation. The white silk component gradually decreases while the red collagen component constituting the regenerated blood vessel increases. This shows that remodeling of the silk grafts occurred-that is, the silk component disintegrated and was replaced with the rat's own regener-

The increasing rate of cardiovascular

Utilization of silk in regenerative medicine



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ated blood vessel. It was this type of research that confirmed silk to be an ex-

from 1 to 6 mm and have a delicate, yet strong,

structure

cellent material for vascular grafts. Additionally, silk has the superb characteristic of preventing blood clotting.

Apart from vascular grafts, Professor Asakura is researching the use of silk to regenerate bones, teeth, ears, corneas, and wounded skin.

"There are various ways of using silk because of its unique properties. For example, it has excellent oxygen and water-vapor permeability in its hydrated state and the release rate of medicine wrapped in it can be easily controlled. In addition, by using genetically modified silkworms, it is possible to produce modified silk with functions more suitable for specific purposes."

Sometimes, familiar creatures that we regard casually possess fantastic abilities. By drawing upon the innate wisdom of these creatures, we may be able to develop healthier and more prosperous lifestyles for ourselves.





Case Study

Gaysorn Tower







1 Exterior of Gaysorn Tower 2 A savic-net G5 monitoring screer the central monitoring room. The system's graphical and userriendly interface allows the desired information to be accessed

Gaysorn Group, headquartered in Bangkok, has opened Gaysorn Tower, a 30-story office and commercial building, in the city's Ratchaprasong district, which is known as the busiest commercial area in Thailand. To ensure efficient and smooth building operation, Gaysorn Group selected Azbil's building management system for the Tower, its latest building, because Azbil has a proven track record in energy conservation. Gaysorn Group also expects to partner with Azbil to promote energy-saving measures throughout the Ratchaprasong district.

Selecting the best partner based on energy conservation results

Thailand is located in the heart of mainland Southeast Asia. Its economy and Japan's are deeply connected, with about 5,500 Japanese companies are doing business there. Gaysorn Group has expanded its real estate development and management business, since its founding in the 1960s, to food and pet food manufacturing, health care, beauty, etc., contributing in various ways to the enrichment of people's lives in Thailand.

Gaysorn Property Co., Ltd. is a Gaysorn Group company that develops and manages real estate. In September 2017, it opened the



Digital display next to the reception desk for Gaysorn Tower's office floors. The display usually shows an information screen, but it can be switched to display the savicnet G5 monitoring screen during tours focused on Gavsorn Tower's building management.

30-story Gaysorn Tower in the Ratchaprasong district, a bustling commercial area filled with large-scale shopping malls and high-class hotels and located in the center of the capital city of Bangkok.

"The office zones on the 14th and higher floors house the offices of many well-known global enterprises," says Charn Srivikorn, Gaysorn Property's chairman. "The lower floors have commercial facilities, including popular restaurants, shops for brand-name goods, and hot springs and spas. This new building integrates office and commercial functions."

"Gaysorn Tower was designed to be an environmentally friendly building with energy-efficiency in mind, and was certified as 'Gold' class by LEED*1, which rates buildings for their environmental performance," adds Fafuen Temboonkiat, the company's managing director.

Around 2014, Gaysorn Property initiated the process of selecting a partner for the Gaysorn Tower construction project. In the Ratchaprasong district, the Group operates another largescale office and commercial building called Amarin Plaza. Since 2014, Gaysorn Property has improved the energy efficiency of Amarin Plaza with the assistance of Azbil Thailand Co.,

Ltd. Based on this successful implementation, Azbil was selected as the partner to assist with Gaysorn Tower operation and management and to make it energy-efficient.

"For Amarin Plaza, we initially set the expected payback period at 3.2 years, but that was shortened to 2.8 years as a result of continuous good energy savings. This success led us to trust in the capabilities of Azbil, allowing us to choose them again without hesitation from among the globally competitive candidates recommended by our consultants," explains Mr. Srivikorn.

Laying the foundations for energy conservation with the latest BEMS

In 2015, Gaysorn Property welcomed Azbil as the BEMS*2 vendor for the Gavsorn Tower proiect, and construction began in 2016. By September 2017 the building was fully operational.

Gaysorn Tower adopted Azbil's savicnet™G5, its latest building management system, which was developed in consideration of global market needs, based on the cumulative know-how and expertise gained by Azbil in the building market. Since savic-net G5 is compati-

ble with BACnet*3, it can easily connect to various devices from different manufacturers. With a broader range of equipment options available for combination with Azbil's control system, Gaysorn Tower was ready to create an ideal indoor environment. Gaysorn Tower also installed VAV*4 controllers that maintain, in each area, finely-tuned room temperature suited to the needs of the occupants. The office areas on the upper floors of the tower are divided into small zones where proper airflow is maintained by the VAV controllers according to preset temperatures, so that a higher value-added indoor environment can be provided to office users.

"There are still some vacant floors in the building," says Mr. Temboonkiat. "On these floors, air conditioning is running in necessary areas only, and the air conditioning throughout the whole building is optimally controlled according to the tenant occupancy rate. We are impressed with the technology and also very satisfied with Azbil Thailand's high-guality services for system management and maintenance."

For additional energy efficiency, a system was prepared to understand and manage energy usage peaks, waste, etc., based on the operational data on electricity, heating/cooling source, air conditioning, etc., that is accumulated by the BEMS. Based on the data. Gavsorn Group will plan energy-conservation measures and consider how to put them into practice.

Collaboration on energy-saving and environmentally friendly city development

Based on the results at Amarin Plaza and Gaysorn Tower, Gaysorn Group intends to continue

collaborating with Azbil. For example, with Azbil's cooperation, Gaysorn Group plans to implement energy efficiency measures for Gaysorn Plaza, an existing building complex next to Gavsorn Tower.

"In addition to building management, a beverage manufacturer in our Group decided to install Azbil's industrial monitoring systems in its factory, and construction is currently ongoing," says Chai Srivikorn, director of Gaysorn Private Equity Company Limited.

Gaysorn Group has many large buildings in the Ratchaprasong district and plays a leading role in driving urban development, including energy and environmental conservation efforts. In cooperation with other local real estate management companies, the Group hopes to involve the entire district and redouble its efforts toward energy efficiency and environmental conservation. It has high expectations of Azbil as a partner in these efforts.

In the Ratchaprasong district, a large commercial facility called The Market is currently under construction. With the urging of Gaysorn Group, the facility has decided to use Azbil's BEMS.

"In Thailand, the birthrate is decreasing and the population is aging," explains Director Srivikorn. "If various facilities in the district install the same vendor's systems, they can benefit by sharing personnel, as a way of dealing with the decreasing labor force. Other than providing products and services to buildings, we would like Azbil to use its abundant experience and expertise to help us to improve energy efficiency and environmental conservation throughout the whole town."

Gaysorn Property Co., Ltd.





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Beginning of Ope 2000

Business

Real estate development and management



Chai Srivikorn Gaysorn Private Equity Co., Ltd.



glossary

*1 ► LEED (Leadership in Energy and Environmental Design) An environmental performance evaluation system based of how buildings and sites are used. The system was developed by the U.S. Green Building Council and is operated by Green Business Certification, Inc. In this system, energy-efficient and environmentally friendly buildings and sites are rated as be-ing on one of four levels: Certified, Silver, Gold, and Platinum.

★2 ► BEMS (Building Energy Management System)

A system that automates the energy-saving monitoring and control of all energy-consuming equipment in buildings, factories, and district heating and cooling plants. With this system, the energy consumption for an entire building can be minimized.

*3▶ BACnet (Building Automation and Control Networking Protocol)

A communication protocol for intelligent buildings. BACnet connects and monitors various devices from different manufacturers through the same interface, allowing it to be used for the compr control of facilities such as air conditioning, lighting, access control,

*4 ► VAV (Variable Air Volume)

A type of HVAC system that keeps a constant airflow temperature but adjusts the air conditioning by changing the airflow volume. This makes the control of individual areas easier, which in turn reduces the power used for transport and results in energy savings.



Using the IoT to Create **New Value in Manufacturing**

The Japanese manufacturing industry has seen an increasing demand for safety, dependability, reliable operation, and further productivity improvement because of changes in the business environment, such as aging plants and a labor force that is decreasing due to the low birthrate and aging population. Azbil has long contributed to customers' production sites with its measurement and control technology and its pioneering initiatives for "smart industrial safety." Now Azbil is undertaking new initiatives aiming for "a new dimension of productivity" that boosts manufacturers' businesses more comprehensively.

Manufacturing industry change generates a greater need for safety, dependability, and productivity

n the Japanese manufacturing industry, the importance of safety, dependability, reliable operation, and improved productivity has received much attention. There are several reasons for this, one of which is aging plants. There are guite a few in Japan that have been operating for over 50 years. Under these circumstances, many of the experienced operators who assisted in production during that time have reached retirement age, and in some cases their knowledge and expertise are being lost. Because the working population is decreasing due to a declining birthrate—a situation that will accelerate in the future-plant operation must be handled by a smaller number of employees.

Dealing with this challenge is increasingly important, especially for chemical plants. Based on the azbil Group philosophy of "human-centered automation," the Advanced Automation Company (AAC) is developing products and services to further improve productivity and quality. These efforts include the area called smart industrial safety, which uses advanced technologies such as the Internet of Things (IoT), big data, and artificial intelligence (AI).

With smart industrial safety, stable operation follows

zbil offers a variety of solutions for smart industrial safety at plants. By using smart valve positioners and simple valve diagnostic equipment, we monitor the operating status of valves and their diagnostic parameters in order to catch valve anomalies at an early stage. In addition, we provide products that collect operational data in real time. Together with these products, we offer services in which our professional engineers analyze the collected data in order to recommend, for example, which valve should be replaced first. The result is more efficient, optimized maintenance.

One of our latest products uses technology such as machine learning to analyze large amounts of data (big data) that is collected from each piece of equipment in a facility, so that unusual equipment behavior, which is an advance warning sign of



Azbil AAC's young employees are discussing new product development

problems, can be detected in real time. This is known as our online anomaly monitoring system. Another product, which provides advanced critical trend monitoring for safety, predicts future fluctuations based on past data, and issues alarms to prevent future trouble.

Azbil has a proven track record of delivering products and services for smart industrial safety to a large number of customers in Japan. Its leadership in this area has received high praise from all quarters. According to a report released by Japan's Ministry of Economy, Trade and Industry in April 2017, which examined smart industrial safety initiatives at 25 leading companies, Azbil is involved in the initiatives of seven of those companies. An explanation of our smart in-

A new dimension of productivity



dustrial safety using the IoT was given at the fourth Future Investment Meeting^{*1}, which was held at the Prime Minister's official residence on January 27, 2017, and at a panel discussion at the Thailand 4.0*2 symposium held in Bangkok, Thailand, on September 12, 2017. Our initiatives attracted a great deal of attention.

Advancing a new vision for achieving a new dimension of productivity

any factories and plants have already introduced automation into their production lines. Therefore, Azbil is aiming at a new dimension of productivity that makes factories and plants more productive than ever, and is much more than a small step forward from previous improvements.

Conventional automation plays a role in controlling equipment and transporting items. In addition to these conventional functions, Azbil believes that it is also necessary to provide products and services fulfilling the new roles of advanced information processing and decision-making, and we are now developing such automation products and services. This advanced automation will provide the manufacturing industry with an environment where customers can focus more on creative business activities, which is something only human beings can do, including accelerated product development, service improvement, and globalization.

Azbil is the right company to develop this vision because it is in the business of contributing to factory operations based on the azbil Group philosophy of "creating value together with customers at their sites" by providing measurement and control for particular equipment or lines, optimizing overall production planning and operation by mathematical programming and multivariable model predictive control, and developing applications and providing operational assistance

productivity, it is essential to develop new technology and also to sense and predict the current and future needs of customers, so we are making efforts from a variety of perspectives. As an example, we continually hold IoT technology exchange meetings with customers who are undertaking advanced production initiatives. These kinds of meetings are places where we can understand

To achieve a new dimension of

customers' needs and problems, which is that necessary step in achieving that new dimension of productivity. Topics are not limited to production facilities, but also include management issues, which must be considered from a broad perspective. We create this type of opportunity so that we can use the resulting findings to create new products and services.

Azbil intends to continue to make contributions to the manufacturing industry by utilizing the measurement and control technology and expertise we have cultivated over many years, and to achieve a new dimension of productivity in line with the Group philosophy of "human-centered automation."

*1 ► Future Investment Meeting

This meeting combines an industrial competitiveness meeting with a public-private dialogue for future investment, and serves as a "control tower" for a growth strategy that promotes investment by public-private partnership in areas where investment will help future growth, expand future investment, and accelerate structural reform. The chairman of the meeting is the Prime Minister of Japan.

*2▶ Thailand 4.0

An economic model created by the Thai government. Its aim is to create, within 20 years, an economy and society that continuously creates added value, with keywords such as innovation, productivity, and trade in services

Keywords to Vol. 20

Keyword Deep Learning

Deep learning, a machine-learning method aimed at achieving artificial intelligence (AI), has recently received much attention. It is hoped that by having a multilayered neural network learn a vast amount of data, versatile intelligence like that of humans can be created.

Just as babies learn words, Al itself learns and makes judgments

Do you think that AI has become increasingly smart in recent years? AI helps make our lives convenient with a variety of services such as the voice assistants and automatic translation available on smartphones.

It is said that advances in AI such as these have been brought about by deep learning, a term we have often heard in recent years. It is a type of machine learning that uses a neural network. Deep learning is a method aimed at deriving an optimal solution from a machine that is repeatedly trained using a large amount of data. A neural network is a machine-learning method intended to mimic the mechanism by which neurons in the brain transmit information. Given an enormous amount of data consisting of questions and correct answers, a neural network will learn relationships between the questions and correct answers and will be able to give the correct answer to a new question.

This is like babies who learn words by hearing their parents speaking them repeatedly. For example, parents repeatedly say to their babies, "Look, it's a doggy" until the baby



can identify a dog. At first babies say "doggy" when they see a cat, but after seeing many dogs and cats they learn to differentiate them.

The word "dog" includes animals that are quite different in color, size, body shape, hair length, etc., and yet we can tell whether the animal before us is a dog. This is because we have seen many dogs and have a knowledge of their characteristics. So the mechanism of deep learning is very similar to how babies learn the names of things.

Extracting relationships from large amounts of labeled data using multilayer neural networks

Having the largest possible pool of questions and answers is the key to deep learning. It would be meaningless, though, to have plenty of questions without answers, or to have plenty of images without tags. In other words, using the example above, learning is possible only when there are a large number of dog images with labels.

With conventional AI, taking a tomato as an example, it was necessary to tell the computer each characteristic, such as the color, roundness, and green stem. However, teaching all the characteristics is not a feasible method because some tomatoes are yellow and others are not round.

In that respect, deep learning has the revolutionary capability of extracting features by itself. Drawing features from a large amount of image or voice data, which can now be easily acquired (but previously was difficult to get), deep learning can answer questions.

Using a multilayered neural network, it can learn from a given set of data, extract features, and recognize complicated information.

The input image data is analyzed down to the individual pixel level and classified into "layers" for color, shape, and more complicated features. The data in each layer is connected to the data in the next layer. From these many layers, complicated features are extracted based on combinations of color, shape, etc. The term "deep" refers to the depth of these layers.

The main reason that it is possible to analyze data in multiple layers in this way is the dramatic increase in the computational ability of computers. Today's personal computers have a processing capability equal to that of supercomputers in the past. The accuracy of feature extraction, which requires a large amount of data processing, has also improved rapidly.

More applications for consumers as vast amounts of data become readily available

Typical applications of deep learning are smart speakers with voice recognition and self-driving cars that recognize the surroundings based on information from cameras and GPS. In addition, deep learning is used in various fields such as web search technology and automatic photo tagging on social networking sites. These functions and services, which are available because large amounts of labeled data can be acquired easily via the Internet, are mainly for consumers.

Some efforts to use deep learning for industry are underway, but the applications and necessary data vary according to the industry or company. Unlike the situation for consumers, it is difficult to collect a large enough amount of labeled data to operate a service because the volume of available data is limited. In order to solve this problem, research on algorithms that can successfully extract features from a small amount of data is underway.

As computer processing capability further improves in the future, it may become possible to solve more complicated problems. Or, perhaps a type of AI using a totally different mechanism will appear. As the use of AI increasingly becomes a part of our lives, we have to wonder what future developments in AI will bring.

Cover photo: Pinnawala, Sri Lanka, by Koji Mizutani, Merry Project representative director

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Yamatake Corporation changed its name to Azbil Corporation on April 1, 2012.

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