EXPLORING NEW FRONTIERS

SHIMADZU GROUP 130th

Developing Technology That Satisfies the Needs of 21st Century High-Growth Industries

The life science, environmental solutions, and semiconductor/flat panel display markets are clearly the high-growth industries of the 21st century. Shimadzu is moving aggressively into these markets backed by its management principle "Realizing Our Wishes for the Well-being of Mankind and the Earth." The question Shimadzu faces today is how to apply the company's unique technologies and expertise to these highly volatile growth industries. We believe the answer lies in what Shimadzu has accomplished to date and in the challenges that the company has faced along the way.

Life Science

Environmental Solutions

Semiconductors/Flat Panel Displays

Life Science

Discovering What Lies Ahead for Life Science

Creating an R&D System that Integrates Some of the Most Advanced Equipment and Best Minds in the World

Exploring New Frontiers

The successful decoding of the human genome has placed life science on the fast track for growth. This means that applications in this field are rapidly developing in a variety of areas, such as fundamental research, gene therapy, drug discovery, and disease diagnosis. Shimadzu has been on the cutting edge of bio-business for over 20 years and first ventured into the business in 1984, together with the development of bio-support equipment. Later, in 2000, the company added out-sourcing services for genetic and protein analysis. Next, as part of an overall strategy to develop and provide analytical equipment and system solutions for life science researchers, in 2001 Shimadzu established the Life Science Laboratory to conduct research on reagents and analytical techniques.

Decoding the Essence of Life

Research institutes and corporations around the world are conducting extensive research on protein analysis. It is widely believed that understanding how proteins work will tell us what causes disease as well as the types of drugs and treatments that should be administered. Perhaps it will also help us decode the fundamental structure of life. If genes are the blueprints for life, then proteins are the products made from those blueprints. Proteins produced from information stored in genes are used to create the cells and cellular systems that form a unique tapestry. We could go so far as to say that proteins are the essence of life.

Research in this area, however, has never been easy. It would have been simple if one gene always manufactured the same protein, but it is now understood that one gene can produce a multitude of proteins. Since there are more than a hundred thousand proteins in the human body, it is virtually impossible to grasp the overall picture, particularly in light of the staggering number of possible protein interaction combinations.

Shimadzu's life science program has a two-fold mission that is essential to protein research. The first is to develop the most advanced reagents and life science support equipment. The second is to deploy out-sourcing services for gene and protein analysis.

Pooling the Best and Brightest for Protein Research

The Life Science Laboratory at Shimadzu has brought together a group of highly talented individuals who are among the top in their field. The leader of the Laboratory, Osamu Nishimura, came to Shimadzu from the pharmaceutical industry and serves as the Deputy General Manager of the Analytical and Measuring Instruments Division. Dr. Nishimura began supervising the Life Science Laboratory four years ago and, prior to his appointment, had specialized in drug discovery at a major pharmaceutical firm. Dr. Nishimura was among the first to stress the importance of protein research just when genome-based drug discovery was taking over the mainstream in the pharmaceutical industry. He theorized that the inner workings of proteins had to be studied to produce really effective medicines. Since Shimadzu was already committed to protein research as a matter of policy, the move to Shimadzu made perfect sense for Dr.

Nishimura.

Susumu Tsunazawa is a Senior Manager at the Life Science Laboratory who has been conducting protein-related research non-stop for 40 years, including the analysis of amino acid sequences in proteins. This was an ideal pairing since Dr. Nishimura was interested in developing new medicines from proteins and Dr. Tsunazawa was an expert in protein analysis. Dr. Tsunazawa watched as one colleague after another headed into genome research during the genome boom, however he resolutely believed in his theories and refused to give up protein research. He dreamed that the analytical techniques he had devoted his life to would eventually be incorporated into practical devices, which is what brought him to Shimadzu three years ago.

Tsutomu Nishine is an R&D Manager at the Life Science Laboratory. He majored in pharmaceutical science and joined Shimadzu in 1986. Mr. Nishine was involved in developing and evaluating the RISA-384 Multi-capillary DNA Sequencer when genome research came of age.

Koji Tanimizu is a Product Manager at the Life Science Laboratory who joined Shimadzu in 1981. Mr. Tanimizu has spent his entire career at Shimadzu on the manufacturing side producing primarily clinical testing equipment. His job is to turn successful research results into practical devices. Mr. Tanimizu sees to it that completed devices conform to applicable laws and regulations, and that the devices are 100% user-friendly before they are shipped to actual clinical laboratories. His extensive first-hand knowledge of customer sites makes him an invaluable member of the Shimadzu team.

Shimadzu has recruited personnel with different backgrounds and different areas of expertise from inside and outside the company to take on the very ambitious goal of unlocking the biomechanics of proteins. They are without question the best and the brightest. Dr. Tsunazawa describes it aptly this way, "Our greatest strength is right here, where day in and day out you see researchers working side-by-side with instrument builders."

Securing the Most Powerful Equipment Available

No one questions the important role that equipment plays. After all, proteins are formidable adversaries for analysts and cannot be taken on without some kind of help. At Shimadzu that help came in the form of a mass spectrometer.

In the past Japan lagged behind the U.S. in genome analysis. Right from the early development stage, American equipment manufacturers pooled a team of distinguished geneticists and a group of highly-talented engineers to work together on the project. This joint effort produced superior analytical systems that were easy to use and it was not long before genome research took off in the U.S.

Tsutomu Nishine (left)
R&D Manager and
Koji Tanimizu (right)
Project Manager, Life Science Laboratory, stand in front of the Xcise Automated Gel Processing Platform for proteome analysis.

The Transdirect Insect Cell is a cell-free protein synthesis kit that greatly simplifies in-vitro protein synthesis using insect cell extract.

Around the world, everyone seems to be heading down the exact same road in protein analysis. This stage is a critical juncture for creating an environment sooner rather than later where research specialists are working side-by-side with equipment specialists.

Dr. Nishimura notes enthusiastically, "It's hard to believe that we are using cutting-edge measuring instruments that are so new that they are still prototypes. We can peer into worlds where no one else on the planet can go. This is a huge advantage that will give us the edge for years to come."

Letting the Development Cycle Take Its Course

While Shimadzu's Life Science Laboratory has successfully integrated the production and academic worlds into a cohesive research program, the Laboratory is also conducting this same research in cooperation with various outside research institutions. Mr. Nishine explains, "Equipment sales are not the end of the story for manufacturers. The real concern comes after the sale. Manufacturers will hold serious discussions and entertain suggestions to address the concerns of researchers who have done such a great job against

worldwide competition. These researchers have said that while they really enjoyed the work, they were wondering what was next for them. Others wanted to do more extensive research, but were not sure how to go about it. Still others were concerned about the significance of their data. Additionally, Shimadzu and other manufacturers must also accommodate customer demands and will likely find the best solution is by feeding back information about difficult issues to specialists from various fields. New analytical techniques and equipment are sure to be created from this type of back-and-forth exchange."

New drug discovery and analytical techniques have already yielded an array of innovations. One was a cell-free protein synthesis reagent. This was the first time ever that a reagent was developed using an extract derived from cultured insect cells and that genes were used to artificially synthesize proteins. The development has drawn considerable interest since it was first announced because it produces proteins more efficiently than conventional products.

Pictured from the left are Senior Manager Dr. Susumu Tsunazawa of the Life Science Laboratory in the Analytical and Measuring Instruments Division, Product Manager Koji Tanimizu, R&D Manager Tsutomu Nishine, and Division Deputy General Manager Dr. Osamu Nishimura.

Entering the Diagnostic Business

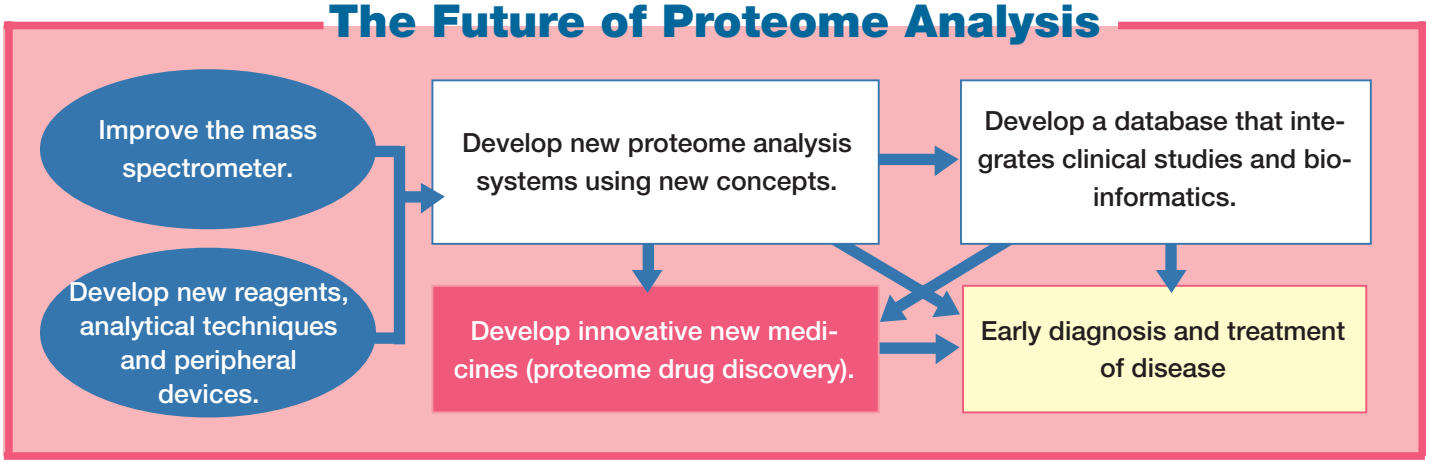
These achievements show that Shimadzu is more than just an instrument manufacturer. Shimadzu provides integrated systems that combine the newest analytical techniques and equipment that the company has to offer. And now Shimadzu is looking to take these systems to the next level by entering the diagnostic and drug discovery support markets.

Dr. Nishimura stresses that "protein analysis will be elevated to the level of a diagnostic business in the next five years."

A protein database must first be created to establish a diagnostic business, a database that begins with mapping. Mapping is used to determine what differences there are in the proteins that are found in healthy people versus those in people who are not healthy, and how proteins interact in a healthy body. The mapping process will identify proteins specific to an illness. If these proteins can be accurately cataloged in a database, diseases can be diagnosed early or the progress of the disease can be monitored, and a definitive treatment can be determined simply by analyzing the proteins in blood drawn from patients. This would be welcome news for healthcare services.

Mr. Tanimizu states unequivocally that "Protein analysis is still in its infancy. It is where biochemistry was some 20 to 30 years ago. New products were being developed then while researchers groped about in the dark. Life science is at that point today. Right now, Shimadzu is committed to developing new 'needs and seeds' products and technologies." At Shimadzu, obviously the life science business is getting a lot of attention these days.

The Future of Proteome Analysis



Koichi Tanaka Mass Spectrometry Research Laboratory

Paving the Way for Mass Spectrometry Research with Keen Intellect and Hard Work

The mass spectrometer is an integral part of today's life science research. The Mass Spectrometry Research Laboratory aims at producing world-leading technology by developing innovative mass spectrometry methods and instruments. Shimadzu Fellow Koichi Tanaka leads the Laboratory as its General Manager, while keeping an eye on the future of the mass spectrometer in his role as an engineer.

While the purposes of the Mass Spectrometry Research Laboratory are manifold, one of the most important is to conduct fundamental mass spectrometry research. The Laboratory primarily develops mass spectrometers, instruments that ionize samples with a laser beam, weigh the ions, and determine how many of each molecule is present. The capabilities of these instruments are now being expanded to include structural analysis of molecules as well.

Proteins consist of fairly large, complex molecules that are easily damaged. Twenty years ago it was quite an accomplishment to observe molecular weights on the order of several hundred. The mass spectrometer developed by Koichi Tanaka et al successfully bombards proteins with a molecular weight of several tens of thousands with a high-energy laser beam that ionizes particles with absolutely no damage to the protein structure. This was a huge advance in protein analysis.

Shimadzu is currently developing fundamental device technologies and is conducting closely coordinated application research that includes the Life Science Laboratory, Technology Research Laboratory, and other divisions inside Shimadzu and elsewhere. The aim of this effort is to simplify, speed up, and improve the operation of mass spectrometry instruments.

Mr. Tanaka describes it this way, "When a pretreatment reagent is developed, for example, the reagent is evaluated and the results are fed back to further improve the reagent. This generates a lot of positive results that are then used to enhance software and hardware products. The relationship between the Mass Spectrometry Research Laboratory and the Life Science Laboratory is particularly close since over 50% of mass spectrometer usage is devoted to life science projects."

Pictured from left are Shinichi Iwamoto Asst. Manager , Sadanori Sekiya Asst. Manager , Koichi Tanaka General Manager , and Yuko Fukuyama Asst. Manager .

Future-Oriented Research Also Proceeds

Mr. Tanaka explains, "We are trying to develop a mass spectrometer where you simply press a button to identify a disease and can check a person's health condition from a single drop of blood. The first step must be where we determine the specifications that are required. Then we can upgrade the hardware accordingly. However, this goal cannot be achieved by simply developing new hardware. The cause-and-effect relationship between proteins and diseases must also be understood in order to diagnose a disease. This is a problem that researchers around the world are working on today."

Many issues, including specifications, remain to be worked out. The mass spectrometer must be simple enough that novice and expert alike can operate it and achieve the same results. It must also be completely redesigned, to make it small enough to fit on a desk.

Light at the End of the Tunnel

Mr. Tanaka continues, "A number of ideas have come from people inside Shimadzu and from elsewhere. The common thread running through all those ideas has provided a very hopeful clue that should allow us to announce some achievements within a year."

The Mass Spectrometry Research Laboratory was established well over two years ago, and the size of the staff has grown as the Laboratory has matured. Today the staff, mainly in their twenties and thirties, has a youthful enthusiasm that has helped produce no less than ten significant papers this past year alone.

Mr. Tanaka states "I appreciate it when staff members take their own initiative rather than having to be told what to do. After all, there's a lot more work that lies ahead."

Mr. Tanaka often makes comments to junior staff members like "That's pretty interesting. Let me take the measurement." He sometimes volunteers to do the actual work. He goes on to say, "This might sound strange, but I simply want to do things that any engineer would be proud of doing."

This meticulous, step-by-step approach to research that earned Mr. Tanaka his Nobel Prize promises to bring forth innovation once again.

Environmental Solutions

Exploring New Frontiers

Looking Ahead to the Future of the Earth

Turning Soil Remediation and Carbon Dioxide Fixation Technologies into Business Opportunities

The field of environmental solutions is one of the three new business fields to which Shimadzu is committed. One of these business opportunities ready to be launched is an electro-kinetic soil remediation system that will have minimum impact on the environment.
Carbon dioxide fixation technology has also garnered quite a lot of attention since the Kyoto Protocol went into effect. Demonstration plant development has been completed and Shimadzu is already looking forward to the next phase.

Shimadzu Management Principles in the Real World

The environment and related issues are top corporate concerns at Shimadzu. Shimadzu's corporate activities ever since have strived to realize our wishes for the "Well-being of Mankind and the Earth" as outlined in our management principle. By the fall of 2002, Shimadzu had brought its business interests in line with its management principle and had officially launched the Environmental Solution Development Department.
Mr. Junzo Ose, who is the first General Manager of the Environmental Solution Development Department*, put it this way, "It's only fitting these days that corporations invest in environmental protection. Environmental problems demand the use of analytical equipment at the input end to diagnose environmental conditions and again at the output end to verify the results of processing. Since this equipment is one of Shimadzu's core business areas, we should be developing decontamination and processing technologies across the entire spectrum, from input to output, in a more comprehensive approach to environmental issues." He goes on to say that, "We have to prevent our corporate philosophy and management principles from becoming merely catch phrases by making them vehicles for exploring new ideas and enhancing forward-looking business opportunities."
In the two and a half years since the Department's inception, Shimadzu has held over 300 free seminars for the general public, corporations, students and children as an environmental solution. At the same time, Shimadzu is developing technologies for new environmental projects.

Contaminated Soil under Buildings

One of the technologies Shimadzu is promoting is an electrokinetic remediation system that uses direct current to remove contaminants from polluted soil. Cathode and anode electrodes comprising part of a forced electrolytic solution system are inserted in soil contaminated with heavy metals and a DC current is applied. The heavy metals in the soil are ionized and migrate to one of the electrodes where the heavy metals are dissolved in an electrolytic solution to remove them.

Pictured from the right in a containerized plant used for soil remediation system research are Environmental Solution Development Department General Manager Junzo Ose, Manager Fumihiko Sato, and Manager Tatsuo Choso*

As of Oct. 2005, the Environmental Solution Development Department was re-named the Global Environmental Management Department. Here, Junzo Ose was appointed General Manager, while Fumihiko Sato and Tatsuo Choso were transferred to the newly created Environmental Remediation Business Promotion Group in the Corporate Strategy Planning Department.

With conventional soil remediation methods, the contaminated soil is excavated and removed for remediation elsewhere. This method cannot be used if a building is already standing on the contaminated site. Electroremediation is a far better method because it can be used to remediate soil on land below existing structures.

Hak Milieutechiek B.V. developed the system in its native Holland, which today is one of the leading countries on the environmental front. Looking to conclude a licensing agreement with Hak Milieutechiek B.V., Shimadzu ran the system through a battery of demonstration trials.

"Instead of using artificially polluted soil to collect data during the trials, Shimadzu chose instead to check the efficacy of the system at an actual site in Japan. The logical choice was the soil below Shimadzu's plating plant at Sanjo Works in Kyoto, and that is where an experimental plant was built to test the system," explained the test supervisor, Mr. Fumihiko Sato (Manager of the Environmental Solution Development Department*). As a result of trials conducted over a six-month period, the system proved to be highly effective in removing hexavalent chromium from the soil. This was proof enough for Shimadzu to conclude a formal licensing agreement with Hak Milieutechiek B.V. upon completion of the trials.

The overall effectiveness of decontamination depends on a variety of factors, such as the concentration and type of contaminants in the soil, however the system was able to decontaminate an area measuring approximately 100 x 100 x 5 meters deep. Shimadzu has already received a number of inquiries about the system and has introduced an advanced-level, fully operational version of the plant this spring. This will mark the start of the company's first soil remediation business venture.

The CO_2 fixation technology demonstration plant that produces reusable carbon nanofibers.

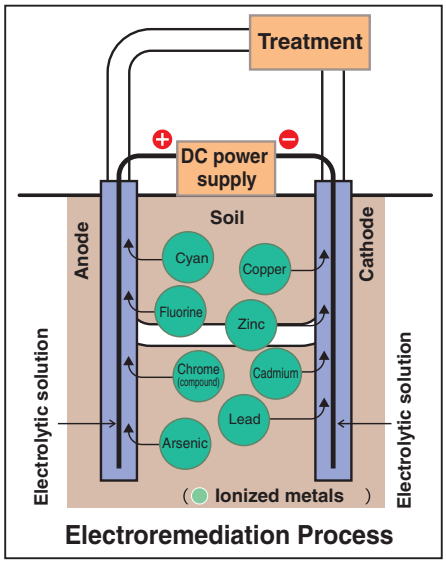
Future of Carbon Dioxide Fixation

Another area where Shimadzu has committed resources is in developing carbon dioxide fixation technology. The Kyoto Protocol designed to reduce carbon dioxide and other greenhouse gas emissions was adopted at the Third Session of the Conference of the Parties to the United Nations Framework Convention on Climate Change (COP3) held in Kyoto in 1997. Since 1997, Shimadzu has investigated carbon dioxide fixation in collaboration with the Research Institute of Innovative Technology for the Earth (RITE) .

Tetsuo Choso, who was temporarily stationed at RITE at the time, subsequently became involved in Technology Research Laboratory projects and worked on developing catalysts that later became pivotal technologies.

He described the situation this way, "In the beginning, we reacted carbon dioxide with hydrogen to produce carbon and water. The problem was, unfortunately, that the commercial steam reforming process used to produce the hydrogen gas for the reaction generated more carbon dioxide than the process could fix. Then the idea of using methane as an alternative came to our attention."

Shimadzu tested hundreds of catalysts to see if they could make methane react with carbon dioxide and successfully developed new fundamental technologies in the process.



The diagram shows how heavy metals ionized by a DC current are drawn out. Nearly six months of demonstration testing proved the process to be a highly effective method of remediating soil.

Shimadzu moved quickly to start building a pilot-test plant as a step toward commercialization. Demonstration tests ended by spring 2004, completing the development phase.

Armed with this technology, Mr. Choso was then transferred to the Environmental Solution Development Department*. There he is currently working closely with the Technology Research Laboratory to develop other forward-looking technologies. One of these derived from carbon dioxide fixation technology: hydrogen production. Hydrogen gas has caught the eye of many as a next-generation clean energy source, and today it is of tremendous interest as fuel for fuel cells.

Mr. Choso stated "Shimadzu is planning to build a demonstration plant at one of its factories to test hydrogen produced by waste conversion. We hope that in the next couple of years, the factory forklifts will all be running on clean energy and that the amount of carbon dioxide emissions from the factory will be cut significantly."

There are countless ideas for environmental solutions and Shimadzu's program has now taken a giant leap forward.

Semiconductors and Flat Panel Displays

Technologies that Yield Core Industries

Taking on the Competition with Powerful New Ideas and an Array of Core Technologies

Exploring New Frontiers

With the IT revolution now in full swing, the semiconductor industry is one of the core industries of the 21st century. It was three years ago that Shimadzu launched its Semiconductor Equipment Division. Shimadzu has been involved with semiconductor production equipment for over 50 years and created this division to meet the needs of a semiconductor market that was expanding and changing at incredible speed.

Integrating Highly Developed Expertise

Shimadzu has developed a variety of products that are critical to the production and inspection of semiconductors and flat panel displays. This makes Shimadzu a power player in the semiconductor industry. The scope of Shimadzu's expertise is impressive, ranging from chamber vacuum pumps and equipment for manufacturing and finishing LCDs, to an array of devices used to inspect semiconductor elements. The Semiconductor Equipment Division in Shimadzu has only been in existence for about three years. Prior to that time, its technologies were spread over several separate divisions, including the Industrial Machinery Division and the Analytical Instruments Division.

Shimadzu has always enjoyed tremendous support from customers because of the high quality of its products. It was difficult, however, to come up with aggressive sales strategies because important technologies were spread over several departments. Meanwhile, semiconductor industry demands had intensified and there were stirrings from researchers and management teams alike that the time was right for Shimadzu to go full bore into the semiconductor business by establishing the Semiconductor Equipment Division.

Takashi Nishimura, who is deputy general manager of the Division, described it this way, "Many of our competitors were already in the semiconductor business, and we felt like latecomers. We had to work hard and create unprecedented added value for our products to have any hope of leading the industry."

A number of development directions became possible simply by consolidating technologies from several departments. The first step was to re-evaluate the situation.

Power and Flexibility in a Turbomolecular Pump

A direct result of that re-evaluation was the turbomolecular pump. Silicon wafers are where semiconductors begin and every process in the manufacture of silicon wafers must be isolat-

The above photograph shows a large-capacity TMP-3403LMTC turbomolecular pump being assembled in a clean room. On the right is Tatsuhiro Taguchi Asst. Manager of the Instrument Group in the Research & Development Department, and on the left is Shingo Tsutsui Asst. Manager of the Component Group.

ed from air. A vacuum pump is essential for creating an airless environment.
Shimadzu's newest high-flowrate turbomolecular pump, TMP-3403LMTC, is 2.1 times more powerful than Shimadzu's conventional products. It also ranks among the top in the world for exhaust speed. This turbomolecular pump is highly acclaimed by customers and can be used in the manufacture of even the largest silicon wafers.
Ongoing R&D is aimed at creating new turbomolecular pumps with additional functions, such as pressure levels that can be adjusted by the customer.
Shingo Tsutsui, Asst. Manager of the Component Group in the Research and Development Department, explains, "We asked our customers what they wanted and listened carefully to their answers. In some case they wanted us to produce a semiconductor using different pressures. Conventional products only operated at fixed pressures, however, with the new turbomolecular pumps that are currently being developed, the customer will be able to set the exhaust rate and operate at any pressure."
This will make it easier for device manufacturers to configure systems that are even more user friendly.

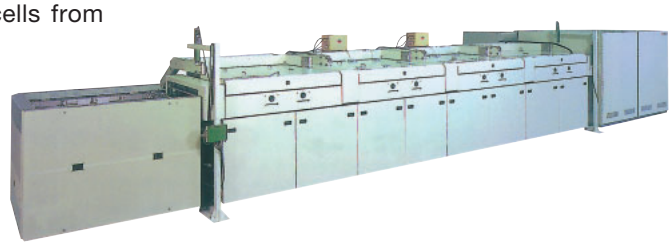
Protecting the Environment with New Solar Cells

The Semiconductor Equipment Division has another ace in the hole. It is the plasma CVD (Chemical Vapor Deposition) system that is used to manufacture solar cells. At first glance, semiconductors and solar cells seem to have nothing in common, but semiconductors are actually used as solar cell light receptors. Light excites the electrons in the semiconductor to generate a voltage. This is photovoltaic power generation.
The plasma CVD system is installed on production lines that are used to manufacture bulk polycrystalline silicon solar cells. The type of solar cell is determined by the materials and production methods that are used. Bulk polycrystalline silicon solar cells can be made from lower grade silicon to save costs, and they are ideal for commercial solar cells. The downside of these solar cells is that they are not as efficient as other solar cells. This inherent problem is caused when a portion of the generated electrons recombine with holes and are lost. Shimadzu's plasma CVD system takes care of that problem by applying an anti-reflective layer on the silicon substrate. As a result, less of the sunlight that strikes the silicon is reflected and more sunlight can be absorbed. At the same time, the silicon undergoes a structural change internally when the coating is applied. This prevents electrons from being lost so they can flow unimpeded to produce electricity. This system increases the efficiency of bulk polycrystalline silicon solar cells from 12% to 15% and has helped to commercialize solar cells.
Tatsuhiro Taguchi, Asst. Manager of the Instrument Group in the Research & Development Department told us that "With European demand now starting to rise, by the year 2010, the cost of solar cells will likely fall to 1/3 their present levels. Shimadzu will be part of the effort to lower costs and improve efficiency through the company's commitment to ongoing research."

Takashi Nishimura,
Deputy General Manager of the Semiconductor Equipment Division.

Aiming for Significant Advances

Vacuum pumps and solar cells are two success stories that have boosted the image of the Semiconductor Equipment Division, but there is much more. Another excellent example is the high-speed electron-beam TFT array inspection machine.
This machine is used to inspect transistors on a TFT-LCD substrate used in televisions and other products. It uses a high-precision electron gun to conduct inspections and can repair any defective transistors that it finds. The result is a higher yield and lower cost for LCDs. With the current exploding popularity of large-screen LCD televisions, Shimadzu is hoping to raise the bar by concentrating on developing new versions of this machine.
Shimadzu's corporate history stretches back some 130 years, but it is still a novice in the field of semiconductors. This means, however, that we are not restricted by worn out concepts, which is proving to be a driving force behind our fresh new ideas. Shimadzu is like a breath of fresh air in the semiconductor industry.



This shows the SLPC-series inline plasma CVD system for applying non-reflective coatings on solar cells.

This is the Pixel Scope high-speed electron-beam TFT array inspection machine.