P012-E942

A Collection

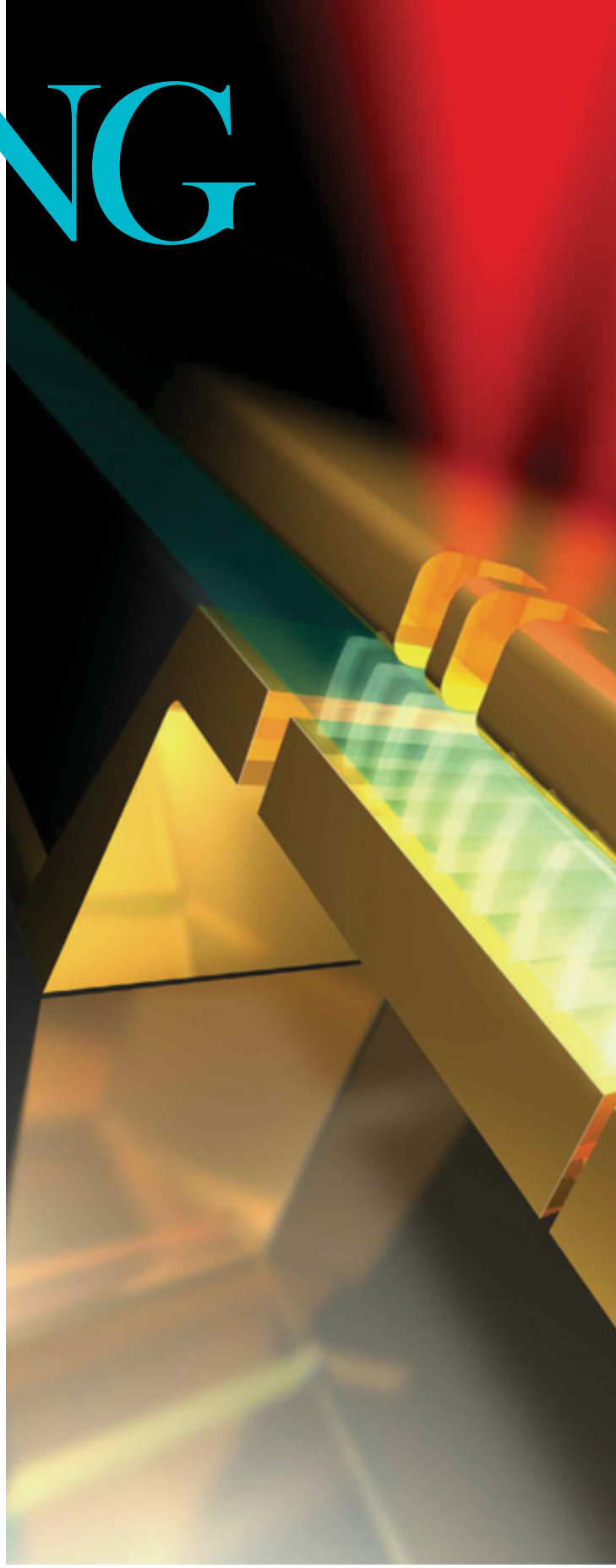
from nature and SHIMADZU

05

SHIMADZU npg nature asia-pacific

This collection was produced by NPG Nature Asia-Pacific on behalf of SHIMADZU CORPORATION.

SURFING THE WAVE



Light manipulation: surface plasmons could be generated (above) to help direct light using nanoantennas in devices such as solar cells (right).

Small oscillations of surface electrons that manipulate light on the nanoscale could be the route to applications as disparate as faster computer chips and cures for cancer. Joerg Heber reports.

Nature Vol.461 (720-722) / 8 October 2009

Toss a rock into a quiet pond, and watch the ripples spread out across its surface. This is pretty much what happens when a photon hits the surface of a metal — except that in this case, the 'ripples' consist of electrons oscillating en masse and have wavelengths measured in nanometres. Once they are set in motion, these 'surface plasmons', as the oscillations are known, can pick up more light and carry it along the metal surface for comparatively vast distances. "A river of light" is how Satoshi Kawata, a physicist at Osaka University in Japan, describes the phenomenon to his students.

Plasmons can also focus light into the tiniest of spots, direct it along complex circuits or manipulate it many other ways. And they can do all of this at the nanoscale — several orders of magnitude smaller than the light's own wavelength, and therefore far below the resolution limits of conventional optics.

The result is that plasmonics has become one of the hottest fields in photonics today, with researchers exploring potential applications in solar cells, biochemical sensing, optical computing and even cancer treatments (see 'Plasmons at work').

Their efforts, in turn, have benefited greatly from the flowering of

R. VAN LOON / A. POLMAN

H. ATWATER / A. POLMAN

nanotechnology in general over the past decade, which brought with it a proliferation of techniques for fabricating structures at the nanoscale — exactly what plasmonics needed to progress from laboratory curiosity to practical applications. "The late 1990s was kind of the turning point" for plasmonics, says Harry Atwater, a physicist at the California Institute of Technology in Pasadena.

One suprising example of the light-carrying phenomenon was witnessed in 1989 by Norwegian–born physical chemist Thomas Ebbesen, now at the Louis Pasteur University in Strasbourg, France. As he held to the light a thin film of metal containing millions of nanometre-sized holes, he found that it was more transparent than he expected. The holes were much smaller than the wavelength of visible light, which should have made it almost impossible for the light to get through at all. "I first thought, 'Here was some kind of mistake'," says Ebbesen.

But it wasn't a mistake, although it took Ebbesen and his colleagues the better part of a decade to work out what was happening. When the incoming photons struck the metal film, they excited surface plasmons, which picked up the photons' electromagnetic energy and carried it through the holes, re-radiating it on the other side and giving the film its transparency [1].

Hole arrays are increasingly finding their way into applications, for example as selective filters for colour sensors. It turns out that the increased transmission through the sheet works only for light around the plasmons' natural oscillation frequency. But this frequency, which is typically in the visible or near-infrared part of the spectrum, can be adjusted by changing the geometry of the holes and their spacing. So hole arrays can be made into highly selective filters for sensors that depend on detecting specific colours, or for efficiently extracting monochromatic light from light-emitting diodes (LEDs) and lasers. Indeed, a number of commercial research labs, such as the Panasonic laboratory in Kyoto, Japan, and NEC in Tsukuba, Japan are working on prototypes of plasmon-enhanced devices for displays and telecommunications.

Hole arrays can also be used to channel light into optical devices. In imaging chips for digital cameras, for example, researchers are studying how hole arrays placed on top of individual pixels might help capture incoming light more efficiently, and thus reduce pixel noise and improve camera sensitivity.

Another plasmonic technique for channelling light into a device is to sprinkle its surface with nanoscale particles made of a metal such as gold. These nanoparticles function like an array of tiny antennas: incoming light is taken up by plasmons and then redirected into the device's interior.

Slimming down

From a commercial perspective, perhaps the most promising application of such nanoantennas — or indeed, of hole arrays — is in the improvement of solar cells. Present-day solar cells are made from semiconductors such as silicon. But to catch as much light as possible from the broadest range of wavelengths, particularly in the red and infrared part of the spectrum, the semiconductor layer has to be relatively thick. "Right now a silicon solar cell is up to 300 micrometres thick," says Albert Polman, a photonics researcher who directs the AMOLF institute in Amsterdam, where he works on improving solar-cell designs. And when cells are being deployed in arrays that cover a rooftop or more, he says, that adds up to a lot of expensive silicon. The price would come down a long way if the silicon was only 1 micrometre thick. "But then you don't catch the

red light because it goes straight through the chip," he says, thus wasting much of the sunlight's available energy. Other solar-cell materials have the same problem.

With plasmonics, however, the problem goes away. In one approach that researchers are exploring, gold nanoparticles on the surface would act as reflectors that focus light into the semiconductor, where absorption efficiency increases with the light concentration. In another scheme, tiny gold nanoantennas could redirect sunlight by 90°, so that it propagates along the semiconductor rather than passing straight through. Either way, the cell could get by with a much thinner semiconductor layer.

Even as plasmonic techniques are decreasing the cost of the cells, they could also greatly improve the cells' efficiency at extracting the available energy from sunlight — in a field in which even a few percentage points in efficiency improvement are celebrated. Overall, the use of plasmonics could increase the absorption two to five times, says Atwater, who has co-founded Alta Devices in Santa Clara, California, to commercialize such solar cells. For cells made from amorphous silicon, which today have efficiencies of around 10–12%, the predicted enhancements could translate into efficiencies of about 17%. For crystalline silicon cells, which currently have efficiencies around 20%, the new figure could approach the theoretical maximum of 29%. For commercial applications, the remaining challenges include developing workable device designs and fabrication techniques for mass production.

Guiding light

Plasmonics researchers are also grappling with a longer-term challenge: the integration of optics and electronics on a single microchip. The decades-old idea is that, just as a fibre-optic cable can carry much more information than a copper wire, a light beam could, in principle, relay information through the chip on more channels and at a higher speed than conventional integrated circuitry can handle. But the experimental optical devices produced to date have been too large, and have showed rather high losses in the optical signal strength.

"You want to bring the optics closer in size to the transistor," says Polman. And that's the beauty of plasmonics, which can offer optical pathways on virtually the same scale as the silicon structures found in advanced microchips. "Metals can be well integrated with the chip design," says Polman, "so you may be able to distribute light over an integrated circuit by plasmons." Indeed, structures such as silver nanowires[2] or grooves etched into metal surfaces[3] can provide pathways that guide light across a chip in whatever direction the designers might need.

But there is a trade-off as the structures get smaller. If the plasmons are forced to travel through a channel that's too narrow, they start to leak out from the sides and get lost, says Sergey Bozhevolnyi from the University of Southern Denmark in Odense, who is leading a European research project into integrated plasmonic circuits. Nevertheless, researchers can guide surface plasmons over distances of more than 100 μm, which is roughly a thousand times bigger than the features on a currentgeneration microchip. This is enough to open rich possibilities for plasmonic nanocircuits, in which light would carry information along complex paths and through many processing steps.

Plasmonic waveguides are particularly promising if the light source — typically a laser— can be incorporated on the chip as well. This has been done with comparatively large lasers, on the order of the

Although plasmonic effects have been known for more than a century, the history of plasmonbased applications began in the early 1970s, when Martin Fleischmann, a chemist at the University of Southampton, UK, and others began to study how light scatters from molecules stuck to a silver surface[7]. Richard Van Duyne, a chemist at Northwestern University in Evanston, Illinois, then discovered this scattering to be enhanced by a seemingly incredible six orders of magnitude[8].

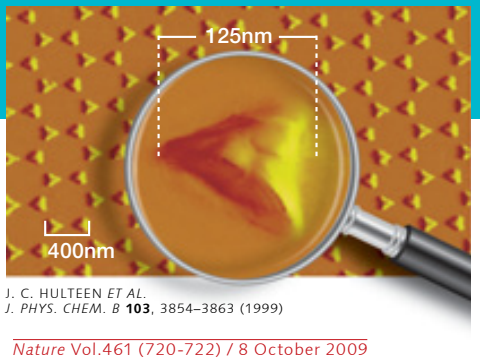
In today's optimized devices, this enhancement, known as surface-enhanced Raman spectroscopy (SERS), can be several orders of magnitude larger still — strong enough to detect a single molecule[9]. Moreover, SERS has proved very useful in the biochemical and materials sciences by providing information on the chemical composition of molecules at very small concentrations.

SERS is a plasmonic effect: silver nanoparticles act as antennas that take the incoming laser light and, through their surface plasmons, concentrate it. The concentrated light is then scattered by nearby molecules and amplified again by the silver nanoparticles on the way back out. This dual amplification results in a huge overall signal enhancement.

Some applications have reached the market. For example, in specifically prepared colloids of gold nanoparticles, a clustering of these nanoparticles is triggered by the presence of pregnancy hormones. This leads to a colour change induced by plasmonic effects that has been widely commercialized in pregnancy tests.

The commercialization of SERS has been hampered in many areas by difficulties in achieving highly accurate control over the surface nanostructures. For this reason, researchers are also looking at other sensing techniques such as localized surface plasmon resonance (LSPR). The idea is that, when a surface is covered with nanostructures in the shape of rods or triangles, their plasmonic properties depend strongly on

Plasmons at work



J. C. HULTEEN *ET AL.*
J. PHYS. CHEM. B **103**, 3854–3863 (1999)

Nature Vol.461 (720-722) / 8 October 2009

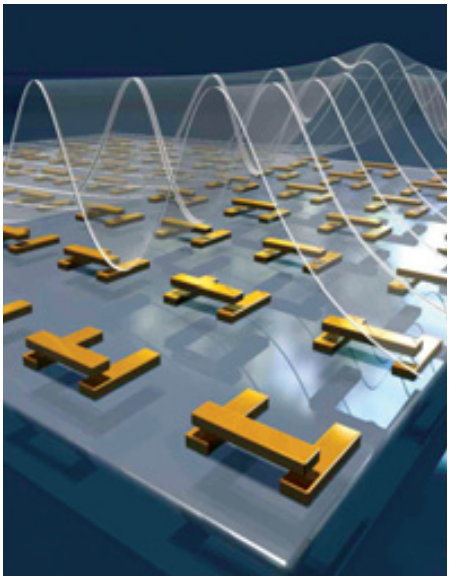
the properties of medium that surrounds them. For example, a solution containing a certain type of molecule has a refractive index that varies with the concentration of those molecules[10]. "These changes to the refractive index lead to measurable changes to the surface plasmon resonance wavelength, which can be observed experimentally," says Stefan Maier from Imperial College London, who studies plasmonic nanostructures and their applications. "The effects can be dramatic." Devices based on LSPR are becoming so sensitive that Van Duyne thinks that they, too, are about to reach the limit of single-molecule detection.

And at Rice University in Houston, Texas, biomedical engineer Naomi Halas is pursuing an optical technique to destroy cancer cells. She hopes to inject cancer patients with gold nanoparticles that will be guided to the tumour by antibodies bound to the particles' surface. Once the nanoparticles are in place, she can illuminate the area with a low dose of infrared laser light that leaves healthy tissue undamaged, but gets absorbed to create plasmons in the gold. The energy heats up the nanoparticles and kills the cancer cells[11].

So far, Halas's cancer therapy has been successful in trials with mice, where she achieved seemingly complete elimination of the tumours. The technology is now in human clinical trials with patients who have head and neck cancers. Halas says the results have been very encouraging so far. "There is no reason one would expect complications from something like this in humans relative to animal trials, because you are using physical mechanisms, heat and light, to induce cell death." Halas is also optimistic that the treatment will be approved for use more quickly than a drug, which can involve difficult and expensive trials and many years to reach the clinic. She says the technique is being considered as a 'device' by the US Food and Drug Administration rather than a drug, which could also accelerate the approval process. **J.H.**

> "Plasmonics has given photonics the ability to go to the nanoscale."
> — Harry Atwater

Naomi Halas (centre, below) wants to use plasmons to fight cancer; others use them as sensors (inset) to detect single molecules.



S. HEIN/H. GIESSEN

Plasmon resonance could be used to make very sensitive biochemical sensors (yellow bars). The waves here represent absorption spectra.

wavelength of the laser light. But plasmonics now offers the possibility of doing so at the nanoscale, at lengths much shorter than the wavelength. Rather than amplifying light in a conventional laser cavity, a plasmonic 'spaser' would amplify it with the help of plasmons — the first experimental evidence for such plasmon-based lasing was published in August[4,5]. To fully integrate these plasmon lasers into standard microcircuitry, however, researchers will need to find a way to trigger the spasers using standard electrical currents.

In addition to creating light and guiding it across a chip, optical computing will require a way to turn the flow of plasmons on and off at high speeds, so that the flow becomes a series of bits in a digital data stream. Many people have been working on such devices, and a plasmonic modulator based on silicon technology has been realized by Atwater's group. Like a conventional transistor, in which an electric voltage controls a tiny electrical current, the group's device is based on the use of an electric field to control the propagation of surface plasmons through the device[6]. Apart from their small size, compared with conventional optical counterparts, the operation frequency of plasmonic modulators can easily reach tens of terahertz, well above the gigahertz regime of modern computers.

Many roadblocks still remain to the commercialization of such technologies— ranging from the integration with silicon to device issues. "The key thing that keeps coming back are losses in the metals," says Mark Brongersma, a materials scientist at Stanford University in California. However, he adds, smart design of the plasmonic structures could, in principle, reduce losses to acceptable levels.

Plasmonics research has made remarkable progress in the past decade, and researchers are working on pushing our knowledge of plasmons even further, for example to understand the physics very close to the metal surface. Nonetheless, says Atwater, "what has happened in the past seven or eight years is that plasmonics has given to photonics the ability to go to the nanoscale and properly take its place among the nanosciences."

Joerg Heber is a senior editor at *Nature Materials*.

1. Ebbesen, T. W., Lezec, H. J., Ghaemi, H. F., Thio, T. &Wolff, P. A. *Nature* **391**, 667–669 (1998).
2. Verhagen, E., Spasenović, M., Polman, A. & Kuipers, *L. Phys. Rev. Lett.* **102**, 203904 (2009).
3. Bozhevolnyi, S. I., Volkov, V. S., Devaux, E., Laluet, J.-Y. &Ebbesen, T. W. *Nature* **440**, 508–511 (2006).
4. Noginov, M. A. *et al. Nature* **460**, 1110–1112 (2009).
5. Oulton, R. F. *et al. Nature* **461**, 629–632 (2009).
6. Dionne, J. A., Diest, K., Sweatlock, L. A. & Atwater, H. A. *Nano Lett.* **9**, 897–902 (2009).
7. Fleischmann, M., Hendra, P. J., McQuillan, A. J. *Chem. Phys. Lett.* **26**, 163–166 (1974).
8. Jeanmaire, D. L. & Van Duyne, R. P. *J. Electroanal. Chem.* **84**, 1–20 (1977).
9. Nie, S. & Emory, S. R. *Science* **275**, 1102–1106 (1997).
10. Anker, J. N. *et al. Nature Mater.* **7**, 442–453 (2008).
11. Hirsch, L. R. *et al. Proc. Natl Acad. Sci. USA* **100**, 13549–13554 (2003).

BIOMARKERS FOR IDENTIFICATION

Shimadzu protein instruments open new avenues to speed biomarkers to the clinic

Is a patient really sick? What medicine is necessary? In what dosage? Is the patient responding to it? Doctors customarily answer these questions based on a variety of symptoms. But many of the symptoms used today, because of their subjective description and uncertain relationship to the disease state, are misleading.

Scientists are rushing to find new 'biomarkers' — biological molecules and physiological characteristics — that are more closely linked to the underlying causes of health or disease. Their discoveries are set to transform the practice of medicine by giving doctors a more objective and quantifiable basis for clinical decision-making. The proteins found in various tissues, the structure or concentration of which varies with disease progression, offer the most promising leads.

The discovery of such biomarkers, however, which must be plucked from tens of thousands of proteins that fill our cells, presents a challenge. If not identified with precision and validated in large patient groups, they could do more harm than good. New technology is needed. Fortunately it is here. Biomedical scientists, like the three introduced below, are using this new technology to address the challenge and fulfill the promise of biomarkers. Their instruments of choice come from Kyoto-based Shimadzu Corporation, a multibillion dollar enterprise with manufacturing bases in six countries.

Separating the bad from the good

Daniel W. Chan

Professor of Pathology, Oncology, Radiology & Urology
Director, Clinical Chemistry Division & Center for Biomarker Discovery
Johns Hopkins Medical Institutions

In September 2009, the US Food and Drug Administration (FDA) gave the nod to Vermillion's ovarian cancer diagnostic test, OVA 1. It was the first blood test the agency cleared for estimating the risk of ovarian cancer. Based on five biomarkers (transthyretin, apolipoprotein A-1, beta2-microglobulin, transferrin, and cancer antigen 125), the test uses an algorithm to produce a numerical score indicating the likelihood of malignancy. It was the first of its kind — a protein-based *in vitro* diagnostic multivariant index assay — approved by the FDA.

The test had a long history. The tight link between the five biomarkers and disease was first demonstrated by the research group of Daniel W. Chan, a professor of pathology, oncology, radiology and urology at Johns Hopkins Medical Institutions[1]. In 2004, after the technology had been licensed from the university, a clinical trial with 600 patients found that it greatly improved sensitivity compared to the previous test, which assayed only cancer antigen 125. Further successful clinical work led to FDA clearance. "It is a great example of what we want to do — find biomarkers, validate them and then translate them to the clinic," says Chan.

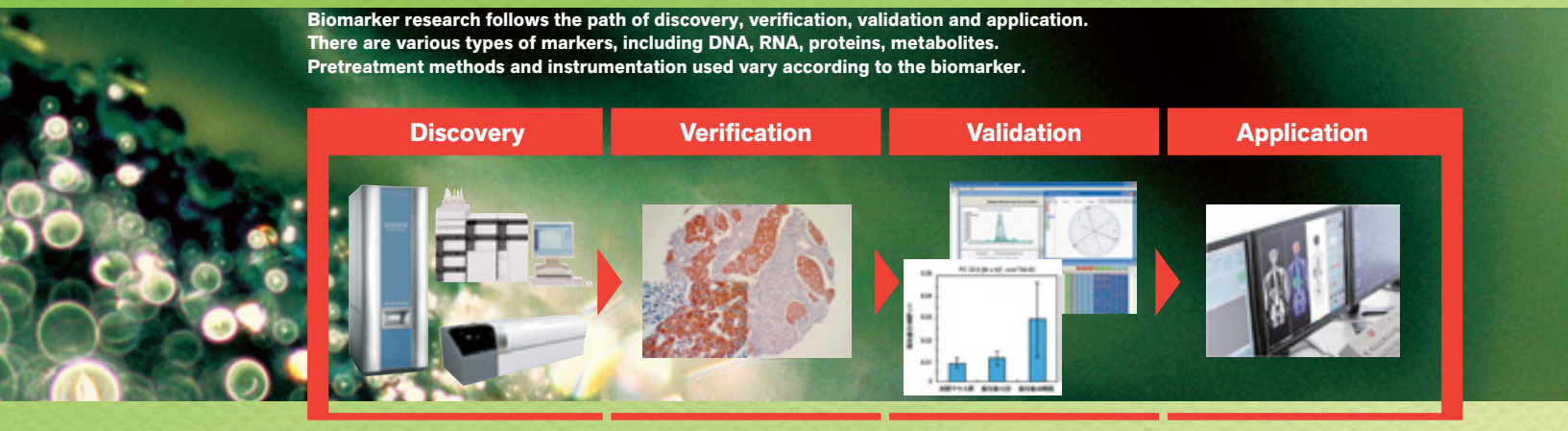
As the potential of biomarkers comes to be further understood and appreciated, more such success is sure to come. Chan directs the Center for Biomarker Discovery at the university hospital. There he has assembled a team that includes specialists in cancer biology, mass spectroscopy technology and clinical diagnosis, as well as an electrical engineer who develops statistical bioinformatics tools.

The major targets of the group's studies are glycan modifications — the addition or removal of sugar molecules — to proteins. 'Glycosylation' is often up-regulated or down-regulated in cancer, so the amount of glycoproteins is a good indication of the presence of a tumor. But quantity alone is not enough to tell whether that tumor is benign or

DISEASE

Biomarker Research Flow

**Biomarker research follows the path of discovery, verification, validation and application.
There are various types of markers, including DNA, RNA, proteins, metabolites.
Pretreatment methods and instrumentation used vary according to the biomarker.**



malignant. For that, other characteristics of the glycoproteins must be studied. For example, glycoproteins rich in sialic acid are known to help cancerous cells enter the blood stream and spread cancer, offering a potentially more accurate diagnostic tool that could enhance early detection of deadly cancers and at the same time reduce unnecessary surgeries. "It's a good marker of cancerous growth," says Chan.

Mass spectrometers are used to analyze the proteins in bodily samples. But conventional mass spectrometers often cannot distinguish proteins that share certain characteristics but differ in others that are crucial to understanding their function. To get that kind of resolution, a two-stage test is needed. Chan found success with the Shimadzu AXIMA QIT, a mass spectrometer that combines a quadrupole ion trap (QIT) and high-performance reflectron time-of-flight analyzer.

The Shimadzu AXIMA QIT "provides high mass accuracy and resolution in the peaks," says Chan. In addition to high precision and reliability, it enables a sample to be analyzed sequentially, with each fragment providing more minute detail, whether that be glycan modifications, sialic acid content or other characteristics. "It's a unique capability of this Shimadzu instrument. For complicated things with small differences in structure, it is the best," says Chan.

This hair-splitting precision will be important for detecting other kinds of cancer, says Chan. For example, tests for prostate specific antigen (PSA) could reveal not only the presence and amount of glycoproteins but also differentiate them into specific types. The Shimadzu AXIMA QIT technology could potentially improve the effectiveness of diagnostic tests such as the OVA1 test, says Chan.

With an improved version of the Shimadzu AXIMA QIT, the Resonance, on the way to his laboratory, Chan is excited. "The better the tests we come up with, the more we can help patients," he says.

Structural integrity

Samir M. Hanash
Program Head
Molecular Diagnostics
Fred Hutchinson Cancer Research Center

Samir M. Hanash of the Fred Hutchinson Cancer Research Center has perhaps the largest set of plasma proteins around — nearly 8,000. "That covers about one-third of the human genome," he says. "It's a phenomenal set of data adding up to many terabytes." Armed with this resource, he will be taking on some of the most common and lethal disorders known to humans: heart, lung, colon, pancreas, breast and ovarian cancer, as well as heart disease and stroke.

This huge collection promises great benefits but it also poses a huge challenge in terms of analyzing the structure of the different proteins. "Quantity is not enough. We need to go deeper," he says.

Hanash also relies on cutting-edge mass spectrometry-based analyses of glycan modifications. He says that one shortcoming of conventional mass spectrometry is that it usually requires cleavage of

Samir M. Hanash with the Shimadzu AXIMA Performance mass spectrometer at the Fred Hutchinson Cancer Research Center

Shimadzu's Product Line for Support of Biomarker Research

Metabolomics

Gas Chromatograph-Mass Spectrometer

Liquid Chromatograph Ion-trap Time-of-flight Mass Spectrometer

fNIRS Imaging System

Small Animal PET System

PET/CT System

MS/Molecular Imaging

the glycan followed by separate analyses of the glycan and the deglycosylated protein. It is therefore impossible to see the critical glycan structure as it is in a mixture of proteins.

Hanash has been tackling this problem with Shimadzu's next-generation mass spectrometer, the Shimadzu MALDI Digital Ion Trap (DIT). Hanash says his respect for Shimadzu has grown, especially because of the work of Nobel laureate Koichi Tanaka. "We appreciate what he has done, the resolution of the instruments, the ability to fly large proteins into the instrument, and the software for analysis."

Intact proteins are labeled with isotopes, fractionated with high-performance liquid chromatography, and then analyzed using the MALDI DIT. With its wide mass range, the MALDI DIT can analyze both the peptide and oligosaccharide components simultaneously. The instrument uses a square-wave electronic signal — the resemblance of which to a 0 or 1 digital signal gives the device its name — to trap the ion used to measure the molecule's mass-to-charge ratio.

Through this multi-stage process, Hanash can tell not only which proteins are increasing or decreasing in concentration, he can also get precise information about their structures. "The first screen tells us which type of receptor is in circulation. But then we want to determine the exact structure of that type. With the Shimadzu device, we can zoom in on specific structures of the proteins," he says.

As an illustration of the power of this new method, Hanash's team analyzed a set of glycoproteins in the plasma that are known to differ in concentration between normal individuals and lung cancer patients. They examined 41 protein groups, including CPI, C4BPB, DNAH3 and UBR1. The study allowed Hanash's group to note how the concentration of the proteins and how their glycan structure changed with physiological changes resulting from the disease. The result is a group of well-characterized and promising biomarkers. Hanash says there are three factors involved: the type of chemistry used to label the protein, the type of hardware, and the type of software used to interrogate data. "You need all three and Shimadzu has them. We can do it all with Shimadzu."

Proteins, individuals and families

Fred E. Regnier
J.H. Law Distinguished Professor
Department of Chemistry
Purdue University

Fred E. Regnier is fighting a similar battle to sort through nature's complicated mixtures of proteins. His weapon is liquid chromatography (LC). Unfortunately, conventional LC only works with mixtures of 100 to 200 proteins. "When more than a thousand proteins are involved, which is often the case, you can't resolve them," says Regnier, the J. H. Law Distinguished Professor in Purdue University's chemistry department.

But if you take each of a 100 peaks and then separate those into 100 components in a 'second dimension', a process known as orthogonal analysis, then individual proteins can be singled out from a mixture of thousands. "This is the kind of resolution the scientific world needs now," says Regnier. Shimadzu's two-dimensional (2D) LC instrument is uniquely capable of fulfilling that need.

In Regnier's study on breast cancer, the first dimension is an affinity test that selects for molecules with lectin, a possible indication of cancer. With that, he narrowed 30,000 proteins down to 30. Shimadzu's 2D-LC instrument further homes in on the culprits using another property,

From basic research to clinical applications and drug discovery

Chemical Printer

MALDI-QIT-TOF
Mass Spectrometer

^{13}CNBS® Stable Isotope Labeling Kit-N

2D-LC

MALDI
Spotting System

MALDI TOF/TOF
Mass Spectrometer

Proteomics

such as size. Using this 2D analysis, Regnier's group found 15 proteins that are strongly associated with metastisis in breast cancer.

Regnier says the technique helps place blame where blame is due. In one dimension, you might find a family of proteins at fault. In two dimensions, you find that only one member of that group is linked to the disease. "All the members might have a similar feature and therefore be grouped together. But it's like members of a family — just because they have the same last name doesn't mean they are all the same. It would be like punishing a whole family for something that one individual did wrong," says Regnier.

The success could transform the way proteins are studied, beginning with the evaluation of antibodies. Antibodies might be assumed to bind a certain protein, but in actuality, they might be binding one or all of a family of similar proteins. If these proteins function differently, the distinction will become crucial. Regnier even used Shimadzu's 2D-LC device to discover some faulty antibodies. One such antibody was supposed to bind transferrin. It didn't. 2D-LC analysis showed why: the antibody was already saturated with transferrin. "You'd never know that with any other method except using the Shimadzu instrument." Regnier thinks regulatory authorities should start requiring people to use an instrument like Shimadzu's when validating antibodies.

Shimadzu's device has other advantages. Its automation makes possible experiments with picoliter amounts of sample that might, if transferred manually, dry up. "This is particularly important in clinical analysis," says Regnier. The Shimadzu instrument is also flexible. "You can assemble it in many ways. But when you get it together, it looks like it's made to be a single integrated unit. It's so compact," says Regnier.

Given the ease of use, it will bring biomarkers to the fore of medical care for a range of disorders. Regnier also hunts biomarkers for diabetes and heart disease. Such 'oxidative stress' diseases result from

The Shimadzu 2D-LC at Purdue University

a modification of a protein's carbonyl group. "We can single out those molecules that are oxidized and even tell in which organ the oxidative stress occurred," says Regnier. That specificity helps with diagnosis: oxidative stress in the substantia nigra suggests Parkinson's disease; in the cerebrum, Alzheimer's disease; in the arteries, atherosclerosis.

In a study of ten 'normal' volunteers, four already had elevated levels of oxidized proteins in their arteries. "We can see indications of heart disease 20 years before they will face the risk of a heart attack," says Regnier. He thinks such diagnostics could be ready for the clinic within five years.

In another common test for PSA, useful in diagnosing prostate cancer, antibodies for PSA are used. But it turns out PSA is actually comprised of more than 50 different molecules. Most likely only a small fraction of those are related to cancer. "The Shimadzu device will let you see only the form related to disease. It will be the new standard in clinical diagnostics," says Regnier.

[Reference] 1 Cancer Res 64, 5882 (2004)

Strong Tailwinds

With a presence in 16 countries in South and Southeast Asia, Shimadzu Asia Pacific (SAP) is well positioned to take advantage of the increasing interest in health and growing demand from emerging economies — a business supported by a commitment to adapting to the distinctive culture and customs of each country.

The Singapore office of Shimadzu (Asia Pacific) Pte Ltd (SAP) is the headquarters for marketing, after-sales service and logistics for the full Shimadzu product line in 16 Asian countries from Pakistan to the Philippines (excluding China). SAP has a Malaysian branch handling its medical equipment business, a subsidiary company in the Philippines, and two subsidiaries in India — a total workforce of 260.

SAP started out in 1981 as Shimadzu's Singapore office with two representatives. In 1989, SAP was established as a corporation in Singapore and relocated to Science Park. Celebrating its 20th anniversary in 2009, the company moved once again, this time within the Science Park. The new office was inaugurated by Shimadzu Chairman Shigehiko Hattori, and a number of events were held to mark Shimadzu's 20 years as a corporation in Singapore.

The new office has a comfortable work space designed based on ideas put forth by the employees, but is most notable for its new Customer Support Center. Equipped with an analysis lab and seminar rooms, the center features enhanced facilities and services no other competitor can match. The center also provides a point of contact for requests, feedback to the manufacturing department, and leads for the development of new products, as well as acting as an intermediary for joint research with laboratories in the region.

Each country in the region covered by SAP has its own distinctive culture, and it's essential that business be carried out in way that fits into the local customs. "Not a few countries are politically unstable, and Chinese and Indians in particular are influential. So a network of connections is especially important. Trusting your local distributors and speedy decision-making for everything are key," says Tsuguo Kishida, managing director of SAP. Through its 40 distributors in the region, SAP stresses the importance of 'localization' and 'humanities', providing training to our business partners and working together to ensure a good fit with the local business culture.

SAP's major clients include research- and quality assurance-related departments in public research institutions, universities, hospitals and other private sector organizations. Among SAP's wide variety of offerings, the best-selling product is the UV-1800 general-use spectrophotometer, followed closely by the LC-2010CHT liquid-chromatography platform for quality control in pharmaceutical applications. The Prominence series of liquid chromatographs and the GC-2010 Plus high-performance gas chromatograph are also in demand. In the early 1980s, Shimadzu's UV-160 spectrophotometer became the reference standard for such instruments in the region following the widespread deployment of UV-160s to influential universities with the support of official development assistance funding and other programs. The system is still used by many research institutions, laying the foundation for Shimadzu's brand image.

In 2002, the LC-2010 series of liquid chromatographs was modified to meet requirements for the quality control of generic drugs in India, and through that process the method and perception of customer service changed considerably, triggering a strong advance by SAP in that country. The workforce in many Asia-Pacific countries is highly mobile, with workers regularly changing roles. The equipment they operate must therefore be easy to operate, convenient, robust and accurate. SAP's strong sales growth in the region can in many ways be attributed to its focus on meeting the needs of its customers through the initiatives of service representatives rather than simply supplying high-spec products.

SAP made strong year-on-year gains in the area of medical applications in 2009, with an increase in the popularity of X-ray systems being a notable feature of the period. Daniel Chow, manager of the Medical Systems Department, says, "In many hospitals, we find many Shimadzu X-ray systems supplied more than 15 years ago still in working condition. This impresses many customers, giving them confidence in Shimadzu's reputation for reliability." Shimadzu's mobile X-ray system, MobileArt, is also achieving high sales through its particular suitability for use in areas with poor medical infrastructure.

In many Asian countries, the public's interest in health is rising. "The popularity of medical tourism is remarkable. Every year, two million patients from the US, Japan, Europe and Arab nations visit Thailand, Singapore and Malaysia. There are also active needs to reduce healthcare costs, and so we expect sales increases in the medical systems in the future," says Chow.

Kishida highlights three future challenges for SAP: next-generation healthcare, safety and the environment, and nanotechnology. "The region has excellent market scale and growth potential. When you look at information technologies and pharmaceutical applications, India's level of technology is equal to that of industrialized nations. India is indeed a promising market. Indonesia and Vietnam have strong domestic demand, and Singapore is equally important as it is unrivalled in advanced technologies," explains Kishida.

Despite the global economic downturn and appreciation of the Japanese yen, SAP stepped up to the challenge in 2009 by launching intensive sales activities directed toward public institutions and tailoring solutions to local situations. SAP is now aiming for further expansion by responding to the needs specific to Asia, including measures for meeting environmental and safety regulations in Europe and the US, and the distinctive demands of emerging nations.

Tsuguo Kishida, Managing Director

Shimadzu Chairman Shigehiko Hattori with staff from the SAP office in Singapore

SHIMADZU (ASIA PACIFIC) PTE LTD.
SHIMADZU SINGAPORE PTE LTD.
79 Science Park Drive, #02-01/08 Cintech IV,
Singapore Science Park I, Singapore 118264 Singapore
Phone: 65 (6778) 6280 Fax: 65 (6779) 2935
Web: http://www.shimadzu.com.sg/

SAP Customer Support Center

Offering a complete range of equipment for feature-packed training

SAP's upgraded Customer Support Center in the company's new office in Singapore is fully equipped with over 60 instruments for demonstrations and training. The spacious center, with a floor area of 700 m^2, has a laboratory, two training rooms, an analysis room and biosample processing room, all located in consideration of the busy flows of attendees.

The comprehensive collection of analyzers, all properly configured for actual analyses, allows the center to meet the specific needs of Singapore, where life-science research is particularly strong. No other competitor has a customer demonstration center for the complete line of equipment like that offered by SAP. This is a key strength of the SAP Customer Support Center. "Receiving our customer's samples and carrying out analysis is good not only for the customer's achievement of goals and the solution of problems, but also for improvement of our analysis technology and expertise," explains Takako Tokura, manager of the Customer Support Center. SAP is already involved in extensive collaboration with research institutions and universities.

The Customer Support Center has 11 staff, including four with PhD degrees and three with master degrees, providing high-level support in Mandarin, Malay and Indonesian, not to mention English and Japanese.

SAP was active in providing customer training from the beginning. In recent years, SAP has conducted more than 100 training sessions each year for about 700 participants, and the numbers are expected to increase in the future. Moreover, about 100 companies visit SAP each year to evaluate equipment before purchase or to select equipment configurations to fulfill intended purposes. "We are always focused on dealing with our customers promptly to meet their needs precisely, and we explain the principle, equipment and the analysis procedure to make sure every one of our wide range of customers — from people who are handling the analyzer for the first time to those who have performed analysis for decades — fully understands not only the operational method but also the applications. We will also put our efforts into the development of new applications using various analyzers," says Tokura.

Second Annual Singapore Society for Mass Spectrometry Seminar and Life Science Workshop

A seminar and workshop on the critical roles of mass spectrometry in life sciences research and chemical analysis with Nobel laureate Koichi Tanaka

The second annual symposium of the Singapore Society for Mass Spectrometry (SSMS) was held on 4 November 2009 at the Biopolis, the largest life-science research base in Singapore. The SSMS is an academic society for the promotion of research related to mass spectrometry in Singapore and the surrounding region. Prem Anand, deputy general manager of Shimadzu's Analytical Department, is the incumbent president of the society.

The keynote speaker for the seminar was Koichi Tanaka, a Nobel laureate in chemistry, general manager of the Koichi Tanaka Mass Spectrometry Research Laboratory and a fellow of Shimadzu Corporation. At the lecture, he spoke about the history of development of the matrix-assisted laser desorption / ionization (MALDI) system, and how the development of MALDI led to his award of the Nobel Prize in Chemistry. His talk was very inspirational to all — about never giving up and how mistakes are an essential part of great research and discovery. Attended by an audience of 400, the seminar also featured presentations on numerous research efforts concerning mass spectrometry, with research related to biomarkers a notable theme.

The seminar was followed by a day-long Life Science Workshop on the critical roles of mass spectrometry in life sciences research and chemical analysis. Held at SAP, the workshop included presentations on the methods of analyzing various molecules, as well as research results, and was attended by about 70 top researchers from around the region. Tanaka gave another presentation on the history of matrix development for the MALDI system. The information-packed seminar included presentations on six studies based on MALDI-time-of-flight (MALDI-TOF, MALDI-TOF/TOF) and MALDI-quadrupole-ion trap-TOF (MALDI-QIT-TOF), covering their advantages such as capacity to measure high-molecular-weight molecules and to take direct measurements of solid samples like tissue, which is useful for tissue MS imaging, microorganism identification and polymer analyses. The system's non-destructive measurement capability, useful when reanalysis is required, and ability to be coupled with liquid chromatography were also remarked upon. The workshop was concluded with a demonstration of mass spectrometry systems augmented by ultrafast liquid chromatography (UFLC-MS) and multidimensional gas chromatography (MDGC/GC-MS).

Prime Minister of the Netherlands Visits Shimadzu

Prime Minister Jan Peter Balkenende and government dignitaries from the Netherlands visited Japan in October 2009 to celebrate the 400th anniversary of business relations with Japan. In their official itinerary, the delegation visited Shimadzu Corporation as a representative high-technology company in Japan. Shimadzu President Akira Nakamoto talked about the company's business strategies and future direction, and Nobel laureate Koichi Tanaka, a fellow of Shimadzu, explained the company's methodology for creative research.

During the factory tour, the prime minister showed much interest in Shimadzu imaging technologies, especially Shimadzu's functional near-infrared spectroscopy (fNIRS) instrument, which allows activity in the human brain to be visualized in real time. In a telling demonstration, the prime minister shook hands with a demonstrator, producing a remarkable response in the demonstrator's brain activity that could be observed instantly using the fNIRS instrument.

The prime minister of the Netherlands listens with interest to an explanation of the latest medical imaging technologies

Swiss Vice President Visits Shimadzu

In association with the recent establishment of the Japan–Switzerland Free Trade and Economic Partnership Agreement, then vice president (now president) of Switzerland, Doris Leuthard, and a delegation of leaders from major Swiss enterprises visited Japan in October 2009 to strengthen the relationship between the economic leaders of the two countries. The delegation visited Shimadzu Corporation as one of the leading companies in Japan. Shimadzu President Akira Nakamoto introduced the company's approaches to analytical technology for securing food safety, advanced medical diagnostics and molecular imaging among other endeavors, attracting pointed interest from the delegation and sparking a lively question-and-answer session.

The Shimadzu President introduces the Medical Systems Showroom to the then vice president of Switzerland

Digital Radiographic Mobile X-Ray System now Features a Thinner, Lighter Large Field-of-View FPD and a Compact FPD

Shimadzu's large field-of-view flat panel detector (FPD) is now thinner and lighter, enhancing the ease-of-use of mobile X-ray systems for radiographers. Users can select systems with a large field-of-view FPD, a compact FPD, or a two-panel configuration combining large field-of-view and compact FPDs. The two-panel configuration enables radiographers to perform a wide range of applications using a single system, from adult chest X-rays to the imaging of infants in incubators.

EPMA-1720 Series Electron Probe Micro Analyzer with an Easy Analysis Mode that Allows even Novice Users to Perform Sophisticated Elemental Analyses

Electron probe microanalyzers (EPMAs) are used to observe the surfaces of metals, electronic materials, glass and ceramics, providing qualitative and quantitative analysis of constituent elements. EPMAs are also used to map concentration distributions. With the EPMA-1720, by automating the setting of analysis conditions, a process typically possible only by experienced users, the system is now even easier to operate. This means that even inexperienced users can perform sophisticated analyses.

RSNA 2009: The 95th Scientific Assembly and Annual Meeting of the Radiological Society of North America

Under the theme of 'The POWER OF Safire — Evolving the Science of Imaging', the Shimadzu booth at the 2009 RSNA meeting featured our line of X-ray diagnostic imaging systems equipped with direct-conversion flat panel detector and Safire technology. In addition to an exhibition of actual instruments, our team also created a 'Cutting-Edge Technology Zone' for exhibiting a wide range of clinical images and applications, dealing not only with diagnostics, but also with everything from preventive medicine to treatment. The new display was a resounding success and drew strong interest from those in attendance.

SHIMADZU
http://www.shimadzu.com
2310-02001-80AIT