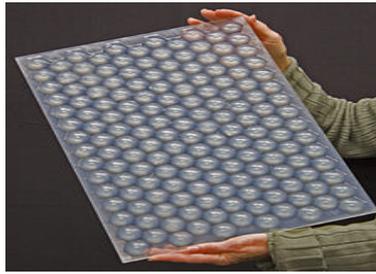


Energy



A Sharper Focus for Photovoltaics



SolFocus's second-generation solar panels cut costs by reducing the amount of photovoltaic material needed. They employ quarter-sized mirrors that focus sunlight on photovoltaic "dots" just 1mm².

The strategy of focusing sunlight on a solar cell to increase drastically the amount of energy generated is one of the hottest trends in alternative energy. SolFocus, a California startup which has secured \$25 million in venture capital financing to accelerate development of its concentrator photovoltaics, employs mirrors to focus sunlight 500-fold onto high-efficiency solar cells. Concentrator technology to increase the output of solar power is not new. But thanks to high-efficiency photovoltaics and novel manufacturing techniques photovoltaics systems are delivering more power at lower cost. At the same time, double-digit growth in demand for solar power systems is outstripping the ability of manufacturers to keep pace, given a tight supply of silicon for conventional solar cells and the high cost of the equipment needed to produce them.

The technology has the potential to lower costs because it uses a fraction of the semiconducting materials that convert light into power in photovoltaics. Most of the cost is in the lenses or mirrors to focus the light and tracking equipment to keep the device pointed at the sun -- elements that are more susceptible to economies of scale than silicon production. SolFocus' design, for example, uses 1/1000 as much semiconductor material per watt produced as a conventional silicon photovoltaic cell. The technology uses compound photovoltaics such as germanium and gallium arsenide which can capture up to 40 % of the solar energy hitting them -- more than double the efficiency of high-end silicon cells. But the bulk of the materials reduction comes from the concentrator, which Conley, SolFocus CEO, says resembles a car headlight: a primary mirror focuses sunlight onto a smaller mirror perched above, which, in turn, focuses the light on the solar cell.

SolFocus' current, first-generation design molds an array of 635 - 1 cm² primary mirrors into a glass plate. Secondary mirrors attached above them reflect light through holes in the plate onto 1 cm² high-efficiency cells below. A second-generation design squeezes the process into a single glass block: light beaming through the top of the block reflects off primary mirrors shaped into the bottom face, up to secondary mirrors shaped into the top face, and back to 1 mm² photovoltaic cells popped into the center of the primary mirrors.

Whereas silicon solar panels today cost close to \$3 per watt to produce, Conley says SolFocus will start manufacturing solar systems at \$2 per watt to go down for gigawatt-scale production to 50 cents. The second generation should cut costs further to as low as 32 cents per watt.

SolFocus's toughest competition could come from the world's largest photovoltaic manufacturer, Sharp, which has developed a concentrator using Fresnel lenses. Sharp's system employs an array of such lenses in a single block of relatively cheap injection-molded plastic.

The most critical test for concentrators will be durability. Previous attempts for concentrator have failed because sulfur in the air eroded the mirrors, hail and wind to smashed delicate lenses, dust jammed the tracking devices needed to keep the systems targeted on the sun. And in the worst cases damaged systems posed serious fire hazards. SolFocus' self-contained devices should be less susceptible to damage and safer than their predecessors.

Life Sciences

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Cancer: Caught in time

The detection of cancer at an early stage in its development can be life-saving. With research efforts under way to find better methods to detect minuscule tumours, how near some of these cancer 'biomarkers' are to the clinic?

In 2005, the US National Cancer Institute (NCI) spent around 8% of its research budget on detection and diagnosis, compared with 22% on treatment. Britain's National Cancer Research Institute, a collaboration of the country's major cancer-research funders, spent 9% of its 2004 budget on early detection, diagnosis and prognosis, versus 19% on treatment. Nevertheless, the technology needed to detect cancers at the very earliest stages is within sight.

As a first step, scientists are hunting for effective 'biomarkers' — DNA or proteins that act as indicators of normal or pathological biological processes that could be used to screen for the presence of a cancer. But a big challenge facing biomarker hunters is that blood is a complex soup of molecules: as well as posing a challenge for molecule-detection technologies, this makes it even harder for biologists to pick out which proteins are relevant.

In the past few years, the technology for identifying potential biomarkers has advanced quickly, and many have been added to the list. For example, modern mass spectrometers provide high enough resolution that mass spectra of small proteins can now be obtained and matched against sequence databases for identification. Another method, called high-throughput proteomic profiling, relies on large arrays of different antibodies that specifically bind to proteins found in the blood. These can detect new proteins and changes in the levels of existing proteins that correlate with the development of cancer.

Sam Hanash's group at Fred Hutchinson has been using proteomic profiling to identify markers for early-stage lung cancer, using two strategies. The first is to look for proteins that have been shed by the tumour and are circulating in the bloodstream; the second is to search for an immune response to the tumour. The host immune system may not be able to destroy the tumour cells, but it probably recognizes them as problem cells, and Hanash wants to harness that raised antibody response as a diagnostic tool. "We're finding that some circulating proteins are inducing an immune response," he says. "We're also finding antibodies to circulating proteins." Hanash's biomarkers are just some of many that scientists have identified. Underpinning all this work is the understanding that using a single biomarker to diagnose a cancer is unlikely to suffice. "We're all agreed now that to rely on one marker to make a diagnosis is not going to work," says Hanash. No single biomarker can detect a given cancer with 100% sensitivity (meaning that all diseased subjects would test positive) and 100% specificity (with all healthy subjects testing negative). Panels of biomarkers with different individual sensitivities and specificities are therefore needed.

A team led by David Sidransky at Johns Hopkins University is trying to find ways of improving the accuracy of the blood tests used to detect a protein called prostate-specific antigen, or PSA. PSA is produced by prostate cancers, but can also result from benign prostate enlargement or inflammation. Sidransky's team has identified an alteration to a gene called GSTP1 that is unique to prostate cancer cells. The hope is that men with high levels of PSA in their blood could be referred for a biopsy to test for this genetic alteration, to reduce the number of false positives that result from relying on PSA levels alone². To become fully cancerous, cells go through a complex, stepwise progression from normal cells to diseased ones. Scientists argue that, for optimal early detection, researchers need to find biomarkers targeted to a stage in this progression where changes can be detected with the highest sensitivity and specificity. That may be a 'pre-malignant' phase, when cells begin to behave abnormally, but have not yet developed all the characteristics of tumour cells.

One example of where this approach is being applied is in research on the common and sometimes crippling gynaecological condition endometriosis, where tissue that normally lines the womb appears on other pelvic organs. Women with endometriosis have a higher risk of developing a particular type of ovarian cancer and last year, Daniela Dinulescu, at Harvard Medical School, discovered genetic pathways underlying the progression from endometriosis to cancer in mice. This raises the possibility that a test could one day pinpoint early genetic changes in women. In separate work, Dinulescu is collaborating with Hanash to validate around 20 biomarkers for early ovarian cancer.

As researchers rush to assemble biomarker panels, the limiting factor to early detection is becoming the ability to detect these biomarkers in ever smaller quantities. Last year, Bert Vogelstein of Johns Hopkins University and the Howard Hughes Medical Institute showed for the first time that it is possible to detect trace amounts of mutated DNA against a noisy background of unmutated DNA, in a simple blood sample. He adapted a technique called the polymerase chain reaction, or PCR, to detect fragments of a mutated gene called adenomatous polyposis coli (APC) in the blood of patients with advanced colorectal cancer. PCR allows researchers to selectively amplify a particular stretch of DNA using an enzyme, which can start work on very small quantities of DNA. Vogelstein's team also detected mutant APC molecules in more than 60% of patients with early, curable colorectal cancer; these were circulating in the patients' blood in extremely low quantities.

But despite all the effort going into biomarker discovery, very few have so far been turned into diagnostic tests because validating them is a slow process. Sudhir Srivastava, who heads the NCI's Cancer Biomarkers Research Group, says another factor delaying test development is that for the past 30 years, biomarker discovery has been driven largely by scientists doing basic research; such researchers may be less aware of which markers are likely to be most useful clinically. To try to change that, the NCI has brought together dozens of cancer-research institutions into an Early Detection Research Network (EDRN), which already funds a lot of research on detection. Bringing biomarkers to clinical application is one of the EDRN's main objectives. The speed with which early-detection tests reach the clinic will also depend partly on how much of their development is taken up by pharmaceutical companies. Drug companies are acutely aware of the potential in this area. They are also keen to find ways of targeting their treatments more effectively. "There is no cancer drug that works for everybody, so drug companies will look more and more for biomarkers to select the populations that will benefit from a given drug,"

As promising as early detection sounds, it does have its problems. For one thing, simply being able to detect the presence of a tumour may not give doctors enough information to treat a patient appropriately. "Early detection must be able to distinguish incidental from dangerous cancers — a much more difficult job." And healthcare providers will still have to be convinced that early-detection tests are worthwhile at the population level. It involves calculating the cost-effectiveness of the screening test, which in turn requires detailed information on the cost of screening, the long-term costs of cancer care, the sensitivity and specificity of the screening test and its impact on survival.

Emory scientists develop new map of genetic variation in human genome

Genome insertions and deletions (INDELs) provide expanded view of human genetic differences. Emory University scientists have identified and created a map of more than 400,000 insertions and deletions (INDELs) in the human genome that signal a little-explored type of genetic difference among individuals. INDELs are an alternative form of natural genetic variation that differs from the much-studied single nucleotide polymorphisms (SNPs). Both types of variation are likely to have a major impact on humans, including their health and susceptibility to disease.

The human genome sequence in our DNA contains three billion base pairs of four chemical building blocks: adenine, thymine, cytosine, and guanine (A, T, C, G), strung together in different combinations in long chains within 23 pairs of chromosomes. When the first human genome was being sequenced, it became apparent that additional human genomes would have to be sequenced to identify the places in the genetic code that account for human variation. Scientists now know that humans share about 97-99 % of the genetic code, and the remaining 1-3 % dictates individual differences. These naturally occurring differences, called polymorphisms, help explain differences in appearance, susceptibility to diseases, and responses to the environment.

SNPs are differences in single chemical bases in the genome sequence, and INDELs result from the insertion and deletion of small pieces of DNA of varying sizes and types. If the human genome is viewed as a genetic instruction book, then SNPs are analogous to single letter changes in the book, whereas INDELs are equivalent to inserting and deleting words or paragraphs.

Most polymorphism discovery projects have focused on SNPs, resulting in the International HapMap Project -a catalog and map of more than 10 million SNPs derived from diverse individuals throughout the globe. Dr. Devine and his team focused instead on INDELs, using a computational approach to examine DNA re-sequences that originally were generated for SNP discovery projects. Thus far they have identified and mapped 415,436 unique INDELs, but they expect to expand the map to between 1 and 2 million by continuing their efforts with additional human sequences. Dr. Devine says INDELs can be grouped into five major categories, depending on their effect on the genome: (1) insertions or deletions of single base pairs; (2) expansions by only one base pair (monomeric base pair expansions); (3) multi-base pair expansions of 2 to 15 repeats; (4) transposon insertions (insertions of mobile elements); (5) and random DNA sequence insertions or deletions. INDELs already are known to cause human diseases. For example, cystic fibrosis is frequently caused by a three-base-pair deletion in the CFTR gene, and DNA insertions called triplet repeat expansions are implicated in fragile X syndrome and Huntington's disease. Transposon insertions have been identified in hemophilia, muscular dystrophy and cancer.

"We're entering an exciting new era of predictive health where an individual personal genetic code will provide guidance on healthcare decisions says Dr. Devine "Our maps of insertions and deletions will be used together with SNP maps to create one big unified map of variation that can identify specific patterns of genetic variation to help us predict the future health of an individual. The next phase of this work is to figure out which changes correspond to changes in human health and develop personalized health treatments. This could include specific drugs tailored to each individual, given their specific genetic code. Ultimately, each person's genome could be re-sequenced in a doctor's office and his or her genetic code analyzed to make predictions about their future health. Dr. Devine believes the technology holds the promise of predicting whether a person will develop diabetes, mental disorders, cancer, heart disease and a range of other conditions.

The INDEL research, led by Scott Devine, at Emory University School of Medicine, will be published in the September issue of the journal *Genome Research*.

New Tools for Minimally Invasive Surgery

Combining imaging technologies with tracking systems for surgical instruments will allow clinicians to navigate the body.

Philips Research is developing an image-guidance workstation that would generate more information than current systems and help surgeons navigate better during minimally invasive procedures. The technology brings together images from computed tomography (CT) scans and ultrasound, and uses an electromagnetic tracking system to pinpoint the position of surgical instruments within the body.

Guy Shechter, of Philips Research, with Brad Wood, at the National Institutes of Health, have focused on a minimally invasive procedure called radio-frequency ablation (RFA) as a treatment for tumors. During this procedure, cancerous tissue is heated with electricity until it dies. The procedure has become a popular alternative for treating certain cancers without full-blown surgery. But delivering the current to the right location is crucial. A patient undergoing a radio-frequency ablation procedure would typically undergo several CT scans, first to locate the tumor, then multiple scans to ensure that the ablation probe is inserted in the right place. CT scans provide the clearest picture of the body's anatomy, but because of the radiation dose, they cannot be performed while a clinician is present. The Philips workstation eliminates the need for multiple scans by bringing together CT and ultrasound imaging, along with tools that track the position of the surgical instruments. The patient is first scanned using CT to create a three-dimensional image. Then an electromagnetic tracking system locates the position of the ablation needles in the body (much like a GPS navigation system locating an object in space). This information is then calibrated to information from the CT. "You can now see where your needle is relative to your CT image," Shechter says.

During the procedure, the patient's progress is monitored in real time with ultrasound. The position of the ultrasound probe is also tracked electromagnetically and matched to the relevant slice of the pre-acquired CT image. And both images are brought together on one monitor, and can be viewed side-by-side or overlaid. In the past, other groups have introduced techniques for creating a model of the patient's anatomy taken from CT scans before the surgery, which is then used to help guide the operation. This technique works well in surgeries of the head, neck, and knees, where the structures are rigid. But these techniques fail when looking at soft tissue, such as the liver, intestines, breast, or prostate, where the anatomy can easily move or change. "The dynamic nature of ultrasound, when married to CT, would address that huge limitation."

Philips worked with the NIH team to complete a small pilot study of 20 patients testing the technology for radiofrequency ablation of soft tissue biopsies in the liver, kidney, lungs, and spine. They are now continuing to improve it in preparation for larger trials. Helen Routh, vice president of Philips Research, says that the workstation is still a few years away from the market.



A workstation for minimally invasive surgeries brings together images from CT and ultrasound to give a better view of a patient's anatomy, while tracking the position of surgical instruments in the body.

Magnetic imaging

Researchers at Dundee University are investigating a technique that magnetises diseased body tissue to improve the effectiveness of keyhole surgery. By giving the tissue magnetic properties, they hope to allow better imaging before and during an operation, as well as improving methods for checking its spread.

Surgeons are constantly looking for ways of imaging, holding, cutting and repairing diseased tissue while lowering the chance of injury to the patient. The development of minimally invasive keyhole surgery has done much to reduce post-operative pain, scarring, and the risk of infection. However, surgeons are limited in what they can see and feel, as well as in the range of instruments they can pass through the keyhole.

'If the tissue can be magnetised in a biocompatible fashion, this opens up therapeutic avenues in dealing with disorders such as small cancers,'

The researchers aim to find ways of creating magnetic tissue, as well as measuring the strength of achievable magnetisation. They believe tissue can be magnetised in one of three ways. The first involves creating surface treatments that are applied to the tissue by mixing a magnetic material with an existing surgical glue. The second involves injecting biologically safe magnetic material directly into the tissue. A final method would use ultrasound or electric fields to force magnetic nanoparticles into the tissue's cells.

The results of this 1-year project could aid drug delivery and would allow the creation of a new generation of instruments for endoscopic or keyhole surgery that would enable surgeons to dissect tissues and move them aside without damage. If robots are used to assist surgery, it is also easier to create small electromagnetic robotic components than their mechanical counterparts.