



## Update

# Disposable Equipment: A Mainstay in Bioprocessing

Richard Greene  
and Rita D'Aquino

For biotech plants, the time is ripe for the use of disposable plastic equipment as a replacement for stainless-steel tanks, mixers, reactors and piping. For instance, plastic tubing (typically platinum-cured silicone) can replace steel pipes and plumbing; expandable bags can substitute for stainless steel vessels; and pinch or side clamps can be swapped for valves. Increasingly, pharmaceutical manufacturers are looking at the whole process — upstream, downstream, and in the fill area, to close the gaps and replace capital-intensive unit processes with disposable systems. Meanwhile, equipment manufacturers are gearing up to meet the upward demand.\*

Stainless steel has long been the material of choice for pharmaceutical and biotech plants alike, and are typically used when automation is required. However, stainless processing lines require cleaning, sterilizing and validation every time a batch is changed. Disposables, on the other hand, arrive at the plant already sterile and can be assembled relatively quickly via a series of aseptic couplings. These systems rely on multi-use, plastic bags, as well as disposable filter systems ( housings and filter elements), and do not require an extensive validation process.

One such filter is Steadfast Equipment's (Mill Creek, WA; [www.steadfastequipment.com](http://www.steadfastequipment.com)) hand-sized, rotary-drum type, introduced about one year ago (Figure 1). Steadfast's technical manager, John Kossik, says that this unit handles 500–1,000 L of slurry when run for 4–8 h. "In a small production environment, centrifuges and batch filters can be expensive to purchase and involve high maintenance and costly manual cleaning. Our rotary filter can be run semi-

continuously, which allows it to be small compared to batch equipment that would handle the same amount of material. Once done, the filter is discarded."

Keith Wickert, European senior marketing manager at Pall Corp. (East Hills, NY; [www.pall.com](http://www.pall.com)) echoes Kossik's sentiments about disposables. "Regulations, labor costs and flexibility are the three major factors driving disposable manufacturing in biotech," he says.

Not only is this the opinion of the manufacturers of disposables, it is also that of consultants to biotech firms. Consultant Mark F. Wickert of BioPharmaceutical Operations (Chapel Hill, NC) agrees. "Disposables have an overall cost advantage. For many batch processes under 5,000 L, disposables are more reliable than stainless-steel systems. "It is much easier for a plant to use a bag that has been validated by its manufacturer, than to validate a tank built onsite. But the user still needs to validate the cycle in which the bags are used. Among my clients, I've found minimal resistance to using disposables," he says. But Wickert does offer one caution: "For fermenters and

bioreactors, the baffling and temperature control of bags can be difficult for large volumes. Tanks can sometimes offer better mixing."

### Cheaper, easier

The reason for using disposables is mainly economic. The costs of a biopharmaceutical system depend on whether it is bag-based, skid-mounted (portable) or fixed, as well as its size and number of batches produced per year, according to Craig Sandstrom, a senior process engineer with Fluor (Greenville, NC; [www.fluor.com](http://www.fluor.com)). "Bags have a low initial cost, but a high per-use cost," he says. As the size of a particular processing line increases, bags become more cost-effective, but there is a maximum size for many applications. "For instance, at the 20-L scale, a disposable-bag system costs about \$20,000/yr (per solution) vs. about \$40,000/yr for portable and fixed vessels," notes Sandstrom. "At the 200-L scale, a bag system costs almost the same, roughly \$21,000/yr, while portable and fixed systems run about \$62,000/yr and \$80,000/yr, respectively." Fluor is currently in the process of building a disposable-based production facility for one customer to produce hundreds of grams per year of a clinical drug. Bags are suitable for the process because of the small scale of product.

In addition to cost, flexibility is enticing companies, especially small-to-mid-sized firms and contract manufacturers, to turn to disposable equipment. "Manufacturers producing several products simultaneously cannot always afford the capital investment for separate process equipment for each product," according to Wickert. "Even firms that focus on a single product at a time or multiple batches of the same product throughout the year can save considerably by eliminating cleaning and cleaning validation of core equip-

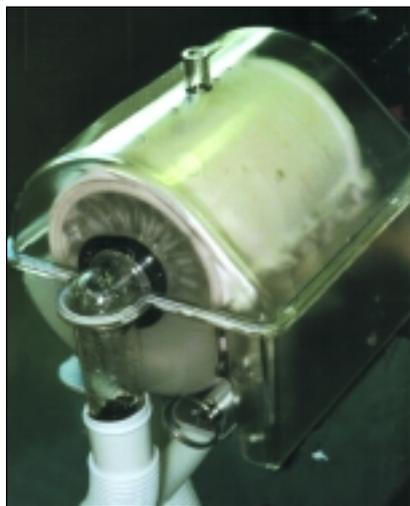


Figure 1. Steadfast Equipment, Inc.'s disposable drum filter rotates at 2–4 rpm, and is externally driven via a sealed connection.

\*A feature article on the design of disposable equipment will appear in *CEP*'s January 2003 issue.

ment.” Wickert adds that, even though cleaning and validation are compulsory, companies sometimes find it difficult to allocate manpower for these activities, resulting in production delays, another factor favoring single-use systems.

### Suppliers’ alliances

Several suppliers have formed alliances to offer users more-complete systems. This past April, Pall teamed up with Stedim, Inc. (Concord, CA, with headquarters in Aubagne, France; [www.stedim.com](http://www.stedim.com)), manufacturers of single-use sterile, plastic bag systems. Together, these two companies offer a scaleable, fully disposable single-use processing system that incorporates capsule filters. The system uses Pall’s T-style Kleenpak Nova filter capsules and Stedim’s 3-D Flexel bag system. Flexel is made in capacities ranging from 100 L to 2,500 L. The system is suitable for a range of biopharmaceutical fluids, such as media, buffers, reagents, cell-harvesting fluid and final products. Custom-made bags are available up to a 3,000-L capacity, says Greg Ja, product marketing manager for Stedim.

Stedim also makes smaller 2-D bags, named Flexboy, which range in size from 5 to 50 L. The Flexboy 2-D bags are not only smaller, but flatter than their Flexel cousins, accounting for the 2-D designation. Flexboy can be used to make up solutions from powders. The bag is placed on a tray of a Wave Bioreactor, made by Wave Biotech, Inc. (Bridgewater, NJ; [www.wavebiotech.com](http://www.wavebiotech.com)), that mixes and aerates the bag by rocking it (up to) 40 times/min. The bag and mixer are placed inside of an incubator or the Wave Bioreactor can be equipped with a heater.

The HyNetics, LLC ([www.hynetics.com](http://www.hynetics.com)) alliance was launched in November 2001 to explore new areas of disposable manufacturing. A 50:50 joint venture between Kinetics Group, Inc. (Santa Clara, CA), which provides turnkey biopharmaceutical systems, and HyClone Laboratories, Inc. (Logan, UT),

which supplies culture media and disposable containers, HyNetics has developed a disposable hydration system for reconstituting large volumes of media and buffers at their point of use (Figure 2). The system is fully automated and skid-mounted, with disposable, presterilized components for process contact. The unit will enable onsite reconstitution of up to 10,000 L of cell culture medium or process fluid per batch.

HyNetics’ product is based on single-use disposable bioprocess containers from HyClone that have an agitation system directly in the bags. According to Spencer Parkinson, HyNetics vice president of business development, the agitation system uses an external electric motor that drives a shaft. The shaft, which screws into a fitting on the outside of the bag, moves up and down in an external tunnel and does not contact the inside of the bag. Within the bag is a disc-like structure that contains chambers and valves, much like a human heart. The up-and-down motion sucks in liquid and pushes it out, while opening and closing the appropriate valves to provide mixing. So-called “hard” tanks are used to support and align the bags. After use, all materials that come into contact with the product are thrown away.

HyNetics first installed such a system at HyClone’s facility in Utah. The system can produce anywhere from 1,000-L to 10,000-L batches. HyClone uses the system to make products, and it serves as a showcase unit, as well. “We already have several interested prospects,” notes Parkinson.

“The impetus behind the development of this agitated-bag system is an escalating worldwide demand for cell-culture media and process liquids, which already exceeds one million liters per year worldwide,” says Chris Julien, marketing manager at HyClone. “Obviously, the larger batches cannot be delivered as liquids. Customers need to consider powder media, which are easier to ship and store and can be hydrated at the point of use.”



Figure 2. HyNetics, Inc.’s multi-layer, sterile bags are available in 3,000 L (shown) and higher.

HyNetics therefore sees an opportunity in the increased demand for water-for-injection (WFI) and buffers. Also, there is a general lack of time and resources by users to construct systems to produce these essential components. Says Julien, “For every liter of medium used in a process, you need between five and ten times that volume in WFI downstream. With the industry moving quickly into large-scale cell-culture systems, as big as 20,000 L, it will be impossible to deliver these volumes of media in liquid form. Companies that are operating on scales that large — there are 15–20 such projects worldwide — need to consider hydrating powders onsite.”

To meet customer demand to hydrate smaller batches of powders, Millipore Corp. (Bedford, MA; [www.millipore.com](http://www.millipore.com)) has licensed a disposable, liquid-filling technology, called Acerta, from Filvek, LLC (Springfield, VT; [www.filvek.com](http://www.filvek.com)), “Acerta features pre-assembled and pre-sterilized tubing, filling needles and reservoirs, for safety and ease of use,” explains Millipore’s product manager Joyce Bellefeuille.

Will all-disposable bioprocessing lines materialize in the near future? In small-scale systems (less than 1,000 L), the likelihood increases, especially since so many components are becoming disposable, such as sterilizing-grade filters, chromatography devices and viral-clearance products. Large-volume applications, however, will be late bloomers. CEP

## ChE ENROLLMENT DROPS — IS BIOTECH TO BLAME?

The Engineering Workforce Commission (EWC; Washington, DC; [www.aaes.org](http://www.aaes.org)) has issued a report entitled, "Engineering & Technology Enrollments, Fall 2001," which includes data on enrollments for engineering and engineering technology programs at more than 500 U.S. ABET-accredited colleges and universities. Alarming, the report indicates that enrollment in chemical engineering (ChE) curricula, at 4,342 in 2001, is down 12.1% from 2000 (see table).

"The disconcerting drop in chemical engineering enrollment may be due to a perception among students entering engineering curricula that the traditional chemical and petrochemical industry is staid and limited in the opportunities it offers," says Ron Darby, ChE professor at Texas A&M (College Station; [www.tamu.edu](http://www.tamu.edu)). A tighter job market in the chemical and oil industries may be another cause of the waning ChE enrollment. But by and large, the growth of bioengineering and biomedical engineering — and the lure of studying these "exotic" disciplines has taken the greatest toll on ChE enrollment. At the Univ. of Michigan (Ann Arbor; [www.umich.edu](http://www.umich.edu)), for instance, sophomore enrollment dropped from 125 (in 2001) to 115 this year, notes Ron Larson, ChE department chair.

"This drop is more common in schools that have a separate biomedical or bioengineering curricula," says Ignacio Grossmann, head of the ChE dept. at Carnegie Mellon Univ. (Pittsburgh, PA; [www.cmu.edu](http://www.cmu.edu)). "The phenomenon is similar to that which occurred when civil engineering added environmental engineering to the roster. Many of us expect that the trend will be reversed in few years when the bioengineering grads find that there aren't enough jobs for them."

"An education in chemical engineering is a fantastic springboard for launching careers in other disciplines, and it appears that students are catching on to this concept," says Lou

### Full-time Freshman enrollment: 2000–2001.

Discipline	2001 Enrollments	One Year Change, %
General	11,577	+81.6
Aerospace	3,204	+3.0
Bioengineering	2,297	+37.7
Chemical	4,342	-12.1
Civil	7,101	+4.0
Computer	22,576	+16.9
Electrical	12,808	-0.6
Industrial	1,452	+0.6
Mechanical	13,450	+5.0

Source: Engineering Workforce Commission.

Theodore, ChE professor at Manhattan College (Riverdale, NY; [www.manhattan.edu](http://www.manhattan.edu)), where ChE undergraduate enrollment actually increased from 2001 to 2002, following a decrease the year before. "An increasing number of graduates over the last few years have landed sales and marketing positions at pharmaceutical and chemical firms."

"We must work harder to convince students that a degree in chemical engineering vs. bioengineering will open more doors," says John Vohs, Chair, chemical and biomolecular engineering, Univ. of Pennsylvania (Philadelphia). But students are *not* convinced. "To at least partially address this issue, we have added the term 'biomolecular' to our department name."

To provide more flexibility for those who are interested in concentrating on topics outside of mainline chemical engineering, while maintaining the fundamental core of this discipline. The California Institute of

Technology (Pasadena; [www.caltech.edu](http://www.caltech.edu)) is in the process of revamping its traditional ChE curricula to offer students the flexibility to "tune" their degrees. "As early as next fall, undergraduate ChE students will have the freedom to 'branch out' into materials, environmental engineering and bioengineering," explains Mark Davis, executive officer of Caltech's ChE program.

"If it's any consolation, enrollments in chemical engineering are down everywhere, not just in the U.S.," says Darby. "The situation is the same, if not worse, at the Technical Univ. of Denmark. It is also true in Australia, England and Europe," he concludes.

Meanwhile, total freshman enrollments in all engineering disciplines are up 5.0% from 2000, master's enrollments are up 5.4%, and doctoral enrollments are up 8.3%. The enrollment level of foreign national students rose 18.6% at the freshmen level and 14.7% at the graduate level.

Although the number of women enrolled in engineering continues to climb, the percentage of females enrolled in engineering programs fell from 18.9% (2000) to 18.3% (2001). "But figures are increasing both in number and percentage for women at the graduate level (from 10.0% to 10.3% at the master's level and from 6.2% to 6.6% at the doctoral level)," notes Matt Doster, director of EWC.

— Rita D'Aquino

## ENVIRONMENTAL

### WEB-BASED TOOL TELLS CHEMICAL TOXICITY

The Environmental Protection Agency's (EPA; Washington, DC) has launched a new online tool ([www.epa.gov/oppt/pbtpProfiler](http://www.epa.gov/oppt/pbtpProfiler)) for assessing the persistence, bioaccumulation potential and toxicity (PBT) of DDT, polychlorinated biphenyls (PCBs), dioxins and other toxic chemicals to determine their impact on health and the environment. Called the PBT Profiler, the tool is intended for use by chemical manufacturers to assess new chemicals, and by consumer-product companies for screening potential product ingredients and comparing alternative formulations. EPA hopes that the tool will encourage companies to use safer alternatives to these toxic chemicals. The PBT Profiler cannot provide definitive assessments of either chemical hazard or safety, and is more suitable for flagging chemicals that require further examination.

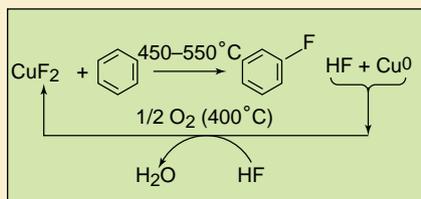


## TECHNOLOGY

### A "GREENER" ROUTE TO FLUOROAROMATICS

Existing commercial processes for making fluorinated aromatic compounds (FACs) yield large amounts of waste. Now, scientists at DuPont Central Research and Development, Experimental Station (Wilmington, DE; [www.dupont.com](http://www.dupont.com)) have discovered a new route to FACs that produces water as its only byproduct (*Science*, 279, p. 1665 (2002)). The process has been demonstrated in the lab for the preparation of fluorobenzene — a starting material for the manufacture of many fungicides and drugs — using benzene, HF and oxygen. It is estimated to cost significantly less than conventional route.

In the classical synthetic route to fluorobenzene (known as the Balz-Schiemann reaction), an aromatic amine is diazotized in the presence of tetrafluoroboric acid, yielding large quantities of  $\text{NaBF}_4$  and  $\text{NaCl}$  as waste. "Key to the success of the new process is finding a metal fluoride that is capable of oxidizing a C-H bond and being regenerated to the appropriate oxidized metal fluoride with oxygen and HF," says Mas Subramanian, senior research scientist. "Copper (II) fluoride,  $\text{CuF}_2$ ,



New reaction scheme for producing fluorinated aromatics using copper (II) fluoride.

which has the right reduction-oxidation potential, provides an excellent platform for this chemistry," he adds.

In a typical experiment, a reactor tube made from Inconel alloy (1.25 cm dia.) is charged with 5 g of copper oxide and heated to  $400^\circ\text{C}$  in a flow of HF to generate  $\text{CuF}_2$ . A stream of vaporized benzene with  $\text{N}_2$  as the carrier gas is passed over the  $\text{CuF}_2$  to yield fluorobenzene with 95% selectivity. Conversion of benzene is temperature dependent. At  $450^\circ\text{C}$ ,

5% of benzene is converted to fluorobenzene, and at  $550^\circ\text{C}$ , conversion peaks. X-ray powder diffraction studies show that  $\text{CuF}_2$  is reduced to copper metal after exposure to benzene vapor at  $500^\circ\text{C}$ , and the conversion is nearly stoichiometric, notes Subramanian. When the conversion drops, the benzene feed is switched off, and a stream of HF and  $\text{O}_2$  (2:1) is passed over the catalyst at

$350\text{--}400^\circ\text{C}$  to regenerate the  $\text{CuF}_2$ , while producing water. "The cycle can be repeated without loss of activity during the fluorination step," says Subramanian. This process can also be used to make other FACs, such as fluorotoluenes and difluorobenzenes.

According to Subramanian, the economics have not been fully worked out, but he estimates that the new process will cut costs by at least by 40% due to the use of inexpensive raw materials along with potentially no waste-disposal issues attached to the process.

### Metalocene Catalyst Creates Resins With a Softer Touch

Equistar Chemicals LP (Houston, TX; [www.equistarchem.com](http://www.equistarchem.com)) and Procter & Gamble Co. (Cincinnati, OH; [www.pg.com](http://www.pg.com)) are working together to develop and commercialize a new metallocene catalyst technology that creates resins with elastomeric properties using only polypropylene as a feedstock. "Conventional systems for making elastomeric polymers require a multiplicity of monomers, such as ethylene, propylene and dienes, and multiple reactor sequences," explains Equistar's chief scientist, Mark Mack. "The new catalyst system uses a single monomer and cuts the number of reactors from many to one. This should have a positive impact on economics," he adds.

P&G has been developing the catalyst at the laboratory scale for three years. It features special organic ligands attached to a transition metal base, such as titanium. "But other tran-

sition metals may be used, depending on the desired polymer attributes," says Mack. The number, structure and arrangement of ligands are key factors in controlling how the monomer approaches the transition metal, and how the catalyst incorporates the monomer into a polymer. In contrast, a conventional elastomeric polymerization process uses an inorganic catalyst system in which chloride ligands are attached to titanium supported on magnesium chloride or silica.

Equistar is currently piloting the new catalyst system in gas-phase, solution-phase and slurry-phase polymerization processes and will scale-up the routes that are most viable for producing polymers with the properties of interest. P&G is providing direction for catalyst optimization to achieve the desired characteristics in final products — namely a "softer touch" and more resiliency for applications such as packaging, shampoo bottles and non-woven fibers. Mack would not com-

ment on which process is being favored, but says that during scaleup, catalyst activity will play a critical role. Commercialization of the technology is anticipated within 2–3 years.

### Novel Fuel Processor Targets Fuel-Cell Commercialization

IdaTech LLC (Bend, OR; [www.idatech.com](http://www.idatech.com)) has launched what it is said to be the first fuel-processor module designed for fuel cell applications that incorporates a steam reformer and a two-stage hydrogen purification process into a compact unit. Measuring  $31\text{ cm} \times 37\text{ cm} \times 47\text{ cm}$ , this module, called FPM 20, is the first commercial product introduction for IdaTech and the first of a family of fuel processors to be commercialized.

During operation, a feedstream containing 67% methanol and 33% water is superheated to  $350^\circ\text{C}$ . The energy required for vaporization is initially provided by burning a small  
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amount of the methanol-water feedstock, and is subsequently generated by burning the waste gas from the hydrogen-purification process. The feed is reformed over a pelletized, heterogenous non-precious-metal catalyst into hydrogen (70%), carbon dioxide (25%) and carbon monoxide (5%), with trace quantities of water and unconverted methanol. The reformat passes through a module containing a stack

of several nonporous, foil palladium-alloy membranes through which 99.9%-pure hydrogen permeates via solution diffusion at a flux of approximately 100 ft<sup>3</sup>/h-ft<sup>2</sup>. "Before exiting the module, the permeates passes over a polishing catalyst that removes all but less than 1 part per million (ppm) CO and less than 5 ppm CO<sub>2</sub>, and is sent to the fuel cell," says David Edlund, IdaTech's chief technical officer.

The processor is now being inte-

grated into IdaTech's family of fuel cell systems, including the FCS 1200 portable fuel-cell system, which is expected to be released in the near future, and has reportedly piqued the interest of several fuel cell companies. "For feedrates of 0.6–2.0 L/h, the FPM 20 produces 7–25 L/min of hydrogen — enough to power fuel cell modules with outputs of up to 2.5 kW. Furthermore, the membrane has shown a lifetime of 27,000 h," explains Edlund. "In

## NOVA CHEMICALS INVENTS VOC-FREE ROUTE TO EXPANDED POLYSTYRENE

**N**OVA Chemicals, Inc. (Pittsburgh, PA; www.novachem.com) has developed a way to make expandable polystyrene (EPS) beads that replaces pentane as a blowing agent with water and air/CO<sub>2</sub>, eliminating many of the hazards associated with the conventional process, including pentane flammability (which requires special equipment); volatility, which requires special packaging for the polystyrene beads to prevent pentane from escaping; and limited shelf life (6 months), due to pentane loss. In the existing process for making EPS beads, a 50/50 reactor feed of styrene and water is mixed, and styrene droplets of about 0.5 mm are formed. The suspension is heated to about 90°C and peroxide initiators are added to start the polymerization, which is carried out at that temperature to more than 80% conversion. The polystyrene suspension is dosed with pentane to effect a 4–6% weight in the polymer, which is heated to 100–130°C to reduce the residual styrene to 0.1% or less. The suspension is cooled, centrifuged and sieved to separate the beads into different fractions ranging from 0.5–2.0 mm in dia. These beads are then coated and packed in pentane-tight containers and shipped to the customer.

Subsequently, during pre-expansion of the beads, the customer injects saturated steam at 100°C into the polymer, which causes the pentane to evaporate, and the polymer to soften and expand, thereby reducing the density of the beads from 600 kg/m<sup>3</sup> to 12–20 kg/m<sup>3</sup>. After 12–24 h of stabilization, these pre-foamed beads are molded into a foamed article with a desired shape.

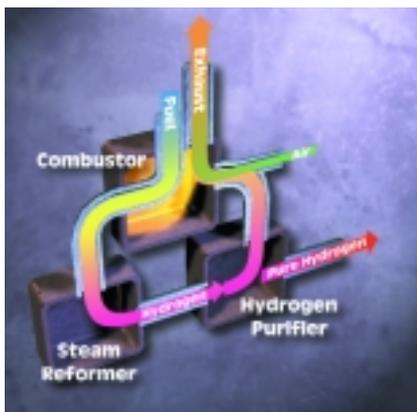
The foam product contains an array of closed cells with 30–150 µm dia. "The cell pattern in the foamed beads impacts the properties of the finished products," says Kees Bleijenbergh, NOVA Chemicals' vice president of styrenics technology. "Small cells give packaging foams a better appearance and provide better cushioning properties. However, inconsistencies can occur in cell formation and expansion when the unexpanded beads are exposed to different temperatures. This may happen in the

current process when the customer, who is not always aware of the time- and temperature- history of the raw material, is taking care of cell formation in the pre-expansion step. A key novelty of the new method is that cell formation is controlled in the polymerization process. "All the customer needs to do is to grow the cell nuclei to obtain the desired low density," Bleijenbergh notes.

In the new process, 5–10% water is incorporated as fine droplets in a pre-polymer phase (20–50% polymerized styrene) to serve as the cell nuclei that grow as polystyrene expands. There are two ways to form this pre-polymer phase. In the inverse emulsion process, water and surfactants are added to the pre-polymer, resulting in an even distribution of approximately 10-µm water droplets. Alternatively, a water absorber, such as finely ground starch, is dosed before adding water, resulting in small pockets of absorbed water in pre-polymer. The pre-polymer is either pumped in equal volume to a vessel containing water, (or an equal volume of water may be added to the pre-polymer mix) and finishing of the polymerization process is carried out conventionally.

When water is used as the sole blowing agent, the PS can only be expanded to 50 kg/m<sup>3</sup>. To reduce the density to 20 kg/m<sup>3</sup>, NOVA Chemicals recommends injecting up to 25 bars of air and/or CO<sub>2</sub> into the cell nuclei at the customer's site. "We are optimizing the pressurization and expansion process to avoid having the customer purchase costly high-pressure equipment," says Bleijenbergh.

"One may think that the pentane process is cheaper to use because the new process requires additional ingredients such as emulsifiers or water absorbers. However, production cost per pound of polymer will probably be similar to the conventional process (when using existing production hardware) because in the absence of pentane, the polymerization process can be a few hours faster, as pentane is a chain-transfer agent in free-radical polymerizations," clarifies Bleijenbergh. NOVA Chemicals is now piloting the process in 100–500-L reactors, and has built a prototype of the pressurizing and pre-expansion equipment together with a partner. This prototype will be installed in the NOVA Chemicals labs by the end of 2002.



IdaTach's fuel-processor reforms a methanol solution, then purifies the reformat to yield 99.9%-pure H<sub>2</sub>.

contrast to costly bottled hydrogen, FPM 20 offers a payback as short as one year," he adds. Idatech's next step is to develop processors with a higher hydrogen output and the ability to process other feedstocks, such as propane and natural gas.

## MATERIALS & CHEMISTRY MAKING MEMBRANES FOR HOT PROCESSES

Celanese AG (Kronberg, Germany; [www.celanese.com](http://www.celanese.com)), through its Celanese Ventures subsidiary, has opened up the first pilot plant at Frankfurt-Höchst industrial park for manufacturing its high-temperature membrane electrode assemblies (MEAs) for use with polymer electrolyte membrane (PEM) fuel cells. The pilot plant will enable Celanese to further develop its fuel cell technology, optimize the production process and meet the growing market demand for MEAs for fuel cells.

The MEA, which consists of catalysts, gas-diffusion layers, and a high-temperature-membrane made of polybenzimidazole (PBI), is the core of the PEM fuel cell. "This PBI membrane is produced solely by Celanese under the tradename Celtec, and enables the fuel cell to operate at temperatures of up to 200°C, versus 80–100°C, which is typical of currently available membranes made of fluoropolymers," says Ernst Schadow, chief technology officer of Celanese AG.

## FROM NATURAL GAS TO A GASOLINE SOURCE

Converting natural gas to a liquid fuel via the Fischer-Tropsch process has always depended upon economies of scale — typically more than 100 million ft<sup>3</sup>/d — to be profitable. Texas A&M Univ. (College Station; [www.tamu.edu](http://www.tamu.edu)) and Synfuels International, Inc. (Dallas; [www.synfuels.com](http://www.synfuels.com)) have co-developed a new gas-to-liquid (GTL) technology that is said to be economical at 3 million ft<sup>3</sup>/d of inlet gas. "This Synfuels process differs from the conventional Fischer-Tropsch GTL process because it bypasses the formation of syngas and cracks the natural gas into acetylene, which is ultimately transformed into a clean-burning, stable liquid fuel," explains Kenneth Hall, head of the chemical engineering dept. at Texas A&M. "This fuel can be easily transported by pipeline or tanker at a cost of about \$17/bbl, versus \$25–30/bbl for fuels made using Fischer-Tropsch technology," he adds. Synfuels International has built a 100,000-ft<sup>3</sup>/d pilot plant demonstrating the process and has hired S&B Engineers and Constructors (Houston) to scale it up and begin construction of a commercial plant in Houston in the first quarter of 2003.

In the pilot-plant process, about 2,000 ft<sup>3</sup>/d of natural gas plus hydrogen recycle is piped into a cylindrical furnace (about 1 ft dia. and 3–4 ft long) and combusted at about 3,400°F. The reaction proceeds for about 1–5 ms before being quenched with water, which helps keep coke formation below 5% from start to finish. "Conversion of methane to acetylene is 20–50%, if the feed is essentially all methane and 10–20%, if the feed is an associated gas," says Hall. This stream, which also contains carbon dioxide, carbon monoxide, steam, hydrogen and unreacted methane is cooled to ambient temperature, compressed to 300 psig, and hydrogenated in a packed-bed reactor over a precious-metal-zeolite catalyst at 200–500°F to convert acetylene into ethylene.

The gas, still at about 280 psig, diffuses through a tubular polymeric membrane in which about 95% of the hydrogen and steam is recovered and rerouted to the first reactor for use as fuel. The hydrocarbon-rich stream enters a second reactor packed with a non-precious-metal zeolite catalyst, operating at about 700°F and 280 psig, in which the non-permeate compounds are combined into hydrocarbons ranging from C<sub>5</sub>–C<sub>12</sub>. "The average chain length of the stabilized liquid is C<sub>8</sub> and depending on how we run the reactor, we can make the distribution broader or narrower," Hall points out.

The product is cooled and enters a three-phase separator where the vapors are recycled and the liquefied hydrocarbons are recovered. The vapor stream (mainly methane, propane and butane) is sent back to the initial reactor at a ratio of roughly 2:1 to the inlet gas. "Depending on how the reactor is operated, the liquid product can contain 20–50% aromatics, about 60% isoalkanes and about 40% cycloalkanes." This fuel is converted to gasoline or other fuel products at the customer's site.

There are other advantages of the Celtec membrane. "Small differences between the operating temperature and the environment temperature require larger cooler surfaces to get rid of the heat. When the fuel cell operates at 200°C, you need only half of the cooling surface of a conventional fuel cell," notes Schadow. The membrane can also tolerate up to 1% carbon monoxide in the hydrogen gas, with a performance decrease of only a few percent. "The

performance of a conventional MEA deteriorates significantly at carbon monoxide concentrations of more than 0.05%," notes Schadow.

### Getting Metal Atoms to Behave

Metals deposited in a vacuum on metal oxides, such as alumina normally grow as three-dimensional clusters because atom-atom interactions are stronger than atom-substrate interactions. This tendency hinders the ability

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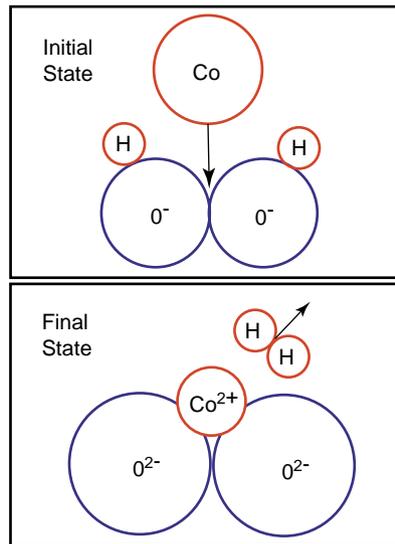
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to form interfaces of ultrathin laminar metals on oxides for use in microelectronics and other technologies where nanostructural control is desired. A team of scientists from Pacific Northwest National Laboratory (Richland, WA; [www.pnl.gov](http://www.pnl.gov)) and Sandia National Laboratories (Albuquerque, NM; [www.sandia.gov](http://www.sandia.gov)) have discovered that exposing the metal oxide to low-pressure (about 1 torr) water vapor before metal deposition changes its surface energy, mitigating the formation of metal clusters.

Researchers verified this theory by producing an atomically flat film of cobalt on hydroxylated aluminum oxide, but say the technique may also work for other metals, such as iron and nickel, which are used in magnetic tunnel junctions,\* and with ruthenium and rhodium, which have applications in catalysis. "The discovery could save material costs in the production of catalysts, because the reactive metal on an oxide support is only one atomic layer thick," says Scott Chambers, a chief scientist at PNNL.

In laboratory experiments,  $\text{Al}_2\text{O}_3$  is exposed to water vapor and retains a full layer of dissociated water. Then, cobalt is deposited onto the oxide layer in a vacuum chamber at room temperature at a rate of  $1 \times 10^{13}$  atoms/cm<sup>2</sup>-s. Photoelectron spectroscopy reveals that the hydroxyls on the surface of the oxide release a hydrogen atom in exchange for a metal cation during a strongly exothermic reaction. "These metal ions act as atomic anchors for the cobalt layer, binding other metal atoms to themselves just above the oxide surface," explains Chambers. Laminar growth is achieved because the density of anchors is sufficient to prevent 3D-island formation. Furthermore, adds Sandia, in the presence of hydroxyls, the higher-temperature cobalt atoms

\* In a magnetic tunnel junction, a 1-nm-thick layer of aluminum oxide or other insulating material is sandwiched between layers of a magnetic metal, such as cobalt. When current flows through the device, the magnetic orientation of the two metal layers can be switched, resulting in different values of the tunneling current. This creates an environment in which "bits" of computer memory can be stored.



Cobalt atoms cause the release of a hydrogen gas molecule and link up with newly available oxygen atoms. These metal atoms "anchor" to themselves and to each other, forming the flat crystalline surface.

would be able to bond to  $\text{Al}_2\text{O}_3$  in a tenth of a picosecond — long before they would begin clumping.

### A Not-So-Hard Way to Make Denser Ceramic Composites

A less expensive way to make complex-shaped ceramic composites incorporating some of the world's hardest materials, including boron-, zirconium-, and titanium carbide has been developed at Ohio State Univ. (Columbus, OH; [www.osu.edu](http://www.osu.edu)). The recently patented technique, called displacive compensation of porosity (DCP), uses a chemical reaction between a molten metal and a porous

ceramic to generate a new composite material, which can be 40% lighter than the pure metal. Such composites have applications in making high-quality machine tools, body armor and parts for the manufacturing industries. MetaMaterial Partners (Columbus, OH) is negotiating a license for the process to further develop it for commercial use.

In tests performed in a controlled-atmosphere furnace, engineers immerse a nozzle-shaped preform made of tungsten carbide (ceramic) powder into a molten zirconium-copper alloy at 1,200–1,300°C (*i.e.*, a few hundred degrees above its melting point). The pores in the preform become filled with molten liquid, which reacts with the tungsten carbide to form a zirconium carbide-tungsten (ZCT) composite. The composite retains the shape and external dimensions of the preform.

"The conventional process would involve applying high pressures to the powder within a die heated to 2,000°C, so as to consolidate the powder into pore-free part," explains Kenneth Sandhage, professor of materials science and engineering. Sandhage says the costs of making dense parts via DCP have not been enumerated, but should be "much lower" than with the conventional process, since a number of relatively expensive processing steps used in the latter (*e.g.*, the use of high temperatures and pressures and of slow diamond machining) are eliminated.

## BIOTECHNOLOGY

### DEFINING DNA SEQUENCES — THOUSANDS AT A TIME

**D**iversa Corp. (San Diego, CA; [www.diversa.com](http://www.diversa.com)) has just been granted a patent (U.S. #6,455,254) for a process, called sequence-based screening (SBS), that enables the discovery, decoding and analysis of the genomes of thousands of different microorganisms, simultaneously. Says Jay Short, Diversa's president, "The technology is being used to discover new biomolecules for digesting toxic wastes, manufacturing drugs and discovering new antibiotics. Scientists can compare the genomes of thousands of unknown organisms with genomes that have been "mapped" to find similar gene patterns and note differences in gene sequences that may account for a new product or reaction. "In doing so, new biomolecules can be discovered," says Short. The most recent example is the discovery of an organism that improves the efficiency of producing an intermediate used in the manufacture of the cholesterol-reducing drug, Lipitor.