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# SCIENCE

	This Week in Science	1246
LETTERS	NIH Budget Growth: J. D. Ebert and M. A. Stoto; B. J. Culliton; Cost of Superconducting Super Collider: R. I. Louttit; M. Crawford	1260
EDITORIAL	World Supplies of Natural Gas	1263
ARTICLES	Tunable Coherent X-rays: D. Attwood, K. Halbach, KJ. Kim	1265
	Structure, Dynamics, and Reactivity in Hemoglobin: J. M. Friedman	1273
	The Mechanism of Irreversible Enzyme Inactivation at 100°C: T. J. Ahern and A. M. Klibanov	1280
	Biochemical Modeling of an Autonomously Oscillatory Circadian Clock in <i>Euglena: K. Goto, D. L. Laval-Martin, L. N. Edmunds, Jr.</i>	1284
NEWS AND COMMENT	Tax Plan Would Have Impact on R&D	1289
	Chemical Giants Push for Patents on Plants	1290
	DOD Program Proves Attractive	1291
	AAAS Meeting: Scientific Fraud Probed at AAAS Meeting; Scientific Secrecy; Nuclear Proliferation; TV Scientists; Biotechnology; High Energy Physics: Future AAAS Meetings	1292
	Biotech Policy Draws Flood of Comments	1296
RESEARCH NEWS	Solving Linear Systems Faster	1297
	Something Strange from Cygnus X-3	1298
	Why Are Male Hawks So Small?	1299

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#### AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

BOOK REVIEWS	<ul> <li>The Education of a College President, reviewed by L. Galambos; Beyond Velikovsky, J. W. Patterson; Genetic Variability in Responses to Chemical Exposure, G. J. Brewer; Late Quaternary Environments of the Soviet Union, G. H. Miller; Books Received</li> </ul>	1304
REPORTS	Free Radicals in the Stratosphere: A New Observational Technique: J. G. Anderson et al.	1309
	The Fajada Butte Solar Marker: A Reevaluation: M. Zeilik	1311
	Microinjected c-myc as a Competence Factor: L. Kaczmarek et al	1313
	Filamentous Fusion Phage: Novel Expression Vectors That Display Cloned Antigens on the Virion Surface: G. P. Smith	1315
	Phosphate Release and Force Generation in Skeletal Muscle Fibers:         M. G. Hibberd et al.	1317
	Defect in Vitamin B <sub>12</sub> Release from Lysosomes: Newly Described Inborn Error of Vitamin B <sub>12</sub> Metabolism: D. S. Rosenblatt et al.	1319

Correlated Measurements of DNA, RNA, and Protein in Individual Cells by Flow Cytometry: H. A. Crissman et al.	1321
Angiogenesis Induced by Degradation Products of Hyaluronic Acid: D. C. West et al	1324
Dragonfly Flight: Novel Uses of Unsteady Separated Flows: C. Somps and M. Luttges	1326
Monitoring the Time Course of Cerebral Deoxyglucose Metabolism by <sup>31</sup> P Nuclear Magnetic Resonance Spectroscopy: R. K. Deuel et al.	1329
Sonar Tracking of Horizontally Moving Targets by the Big Brown Bat <i>Eptesicus</i> fuscus: W. M. Masters, A. J. M. Moffat, J. A. Simmons	1331
Coral Community Reproductive Patterns: Red Sea Versus the Great Barrier Reef: Y. Shlesinger and Y. Loya	1333

PRODUCTS AND MATERIALS

Exonuclease; Microbiology Computer System; Automated Sample Processing; Laboratory Ovens; Benchtop Fermentor; Replaceable Junction pH Electrodes; Liquid Scintillation Analyzer; Heatable Plastic Beakers; Fluorescence Microscope; Peptide Synthesizer; Cloning and Expression System; Centrifuges; DNA Synthesizer; Gas Chromatograph; Literature Literature ..... 1336

E. SAWYER A E. WIDNALL	LINDA S	WILSON	WILLIAM T. GOLDEN Treasurer		WILLIAM D. CAREY Executive Officer		
OGY AND GEOGRAF 1 H. Matthews III M. McCammon	PHY (E)	BIOLOGICAL SCIENC Betty M. Twarog Judith P. Grassle	ES (G)	ANTH Albert Priscil	ROPOLOGY (H) C. Spaulding la Reining	COVER	
CAL SCIENCES (N) P. Fishman Ian E. Rhoads		AGRICULTURE (O) Roy G. Creech Raiph J. McCracken		INDU: Rober Rober	STRIAL SCIENCE (P) t H. Pry t L. Stern	Shadowgraph of a dragonfly, Aeschna palmata. The slender body and intri-	
STICS (U) art Hunter d J. Wegman		ATMOSPHERIC AND I F. Kenneth Hare Bernice Ackerman	HYDROSPHERIC (W)	GENE Harok Rodne	RAL (X) d P. Green ay W. Nichols	reflect millions of years of evolutionary pressures. Such structures support re-	
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#### This Week in Science

#### Sampling the stratosphere

A "reel-down" device invented by Anderson et al. has been used to measure the concentration of atomic oxygen high in the stratosphere (page 1309). The device, tethered to a helium balloon, rose 40 kilometers above Earth. The monitor was then lowered 12 kilometers on a filament 1.5 millimeters in diameter, and a stratospheric sample flowed through the detector. In the stratosphere, ultraviolet radiation from the sun and oxygen react to form ozone. The ozone layer at the top of the stratosphere prevents damaging ultraviolet radiation from reaching Earth's surface; close to Earth, ozone is a pollutant. A complex series of chemical reactions maintains the balance between oxygen and ozone in the stratosphere. Atomic oxygen was the first component measured with this device because it is an important reactant in most of these catalytic chemical cycles. On future balloon flights other free radicals of chlorine, nitrogen, and hydrogen will be measured in part-pertrillion amounts.

#### Vitamin B<sub>12</sub>

A step in the processing of vitamin B<sub>12</sub> has been inferred from studies of cells obtained from an infant with an unusual metabolic deficiency disease (page 1319). Vitamin B<sub>12</sub> is not made by humans or other animals and must be absorbed from food. In the body it forms a complex with a carrier protein. The complex interacts with a receptor at cell surfaces, moves into the cell, and is taken into lysosomes filled with digestive enzymes which release the vitamin from its carrier. Subsequently, the vitamin appears in the cytoplasm of the cell. Rosenblatt et al., in studies of cells from a child with delayed development and laboratory signs of vitamin  $B_{12}$  deficiency, found that the free vitamin accumulated in the lysosomes and did not enter the cytoplasm. They propose that healthy cells have a transport system for exporting vitamin B12 from lysosomes and that the transport system is defective in the child.

#### **Angiogenesis factors**

Sugar compounds can induce angiogenesis, or new blood vessel formation. Capillaries form in the body during normal development, during the repair of tissues damaged by wounds, disease, inflammation, and immune responses, and during tumor growth. West *et al.* show that one inhibitor of this process is hyaluronic acid, the gel-like substance that is an integral part of connective tissue and skin (page 1324). When hyaluronic acid is partially degraded, many smaller sugar fragments are produced that have strong angiogenic effects in a test system. Intact hyaluronic acid and its breakdown products may be crucial controlling factors in capillary formation and maintenance in normal and pathologic circumstances.

#### NMR for studying brain metabolism

A metabolic process making energy available for use in the brain can be measured through time in conscious animals by a noninvasive technique, nuclear magnetic resonance (NMR). Deuel et al. measured the metabolism of a sugar molecule traditionally used as an indicator of brain metabolism (page 1329). The first step in the metabolism of this molecule is phosphorylation, the incorporation of a phosphorus component into its structure. The phosphorylated sugar is detected by the NMR receiver because its atomic nucleus can absorb energy at the characteristic radio frequency for phosphorus. Rats received an injection of the unphosphorylated sugar, and a monitor over their heads measured phosphorylation and subsequent dephosphorylation at a later stage of metabolism. NMR will make possible studies of metabolic changes that occur in the active brain under normal and pathologic conditions.

#### **Bats**

The bat, an echo-locator, emits ultrasonic sounds and continually receives updates on the whereabouts of moving prey from returning echoes. Masters *et al.* trained two bats to sit on a platform and track a small ball moving in front of them (page 1331). Measurements of the head movements of the bats in relation to the positions of the targets suggested that the bats use a "nonpredictive" strategy for locating objects in the experimental setting. About 20 times per second a broad beam of sound was emitted and a bat aimed its head toward the target's last known position. There was no indication that the bat used information on past positions, velocities, or accelerations to predict the target's path.

#### **Reproduction in coral reefs**

Coral communities in two tropical seas are replenished through different reproductive strategies. Shlesinger and Loya found that in the Red Sea at Israel the corals reproduce at different times but in a regular sequence (page 1333). At the Great Barrier Reef off Australia, the corals reproduce simultaneously, with most species spawning essentially on a single night. Following a freeswimming stage, larvae of most species settle on the reef, where they remain fixed. The reproduction pattern at the Red Sea may minimize competition for space on the reef among coral species as well as between coral and algae (the major noncoral competitors on the reef) since most of the corals are settling when the algae are at an annual low. At the Great Barrier Reef, the simultaneous reproduction of the corals may actually minimize overall losses of larvae by satiating predators. Local differences such as the length of the warm season may also have contributed to the development of these distinct reproductive patterns.



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<u>A new radar can map military targets with high resolution equal to that of infrared devices</u>, even in rain and other bad weather. The Advanced Synthetic Aperture Radar System (ASARS-2), designed to complement electro-optic sensors, is flown on a U.S. Air Force TR-1 reconnaissance aircraft and provides real-time radar imagery to a ground station. ASARS-2 operates in all weather at ranges far exceeding the capabilities of infrared and other electro-optic devices, thanks to new state-of-the-art signal processing and other advances. The Air Force gave the system an excellent rating after it underwent strict operational performance tests as part of a "fly-before-buy" program. Hughes Aircraft Company is producing the system under a development and production contract. Eventually ASARS-2 is expected to be adapted for tactical aircraft and mobile tactical stations.

Jam-resistant communications have been introduced into NATO by a new terminal for AWACS earlywarning aircraft. The Joint Tactical Information Distribution System (JTIDS) Class 1 terminal is designed to combat the formidable and growing electronic countermeasures threat to tactical communications. JTIDS uses principles of time division multiple access to provide secure, highcapacity communications for AWACS radar planes and ground stations. The system relays a wide variety of information, such as command and control, surveillance, intelligence, force status, target assignments, warnings and alerts, weather, and logistics. Software filtering lets each participant select data pertinent to his own needs. Hughes is producing the JTIDS terminal for use with NATO's Airborne Early Warning/Ground Environment Integration Segment (AEGIS).

Lasers soon will be inspecting solder joints of fighter aircraft radars, thanks to new manufacturing technology being set in place at Hughes. Solder joints will be examined by a computerized technique using lasers and fiber optics, the glass threads that carry laser light transmissions. The process will free manufacturing personnel from tedious and time-consuming inspections of more than 36 million solder joints created in a single year's production. The project is part of an Industrial Modernization Incentive Program (IMIP) awarded by the U.S. Navy and Air Force. IMIP is a share-the-savings concept that will reduce costs of the F-14, F-15, and F/A-18 radar programs by more than \$10 million, while improving the quality and reliability of the systems.

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Cellular Engineering® technology

No. 3 in a series of reports

**Scale-up production process** – in your facility or ours, the decision, and flexibility to change that decision, is yours.

# In Its Time, It Was A Reliable Way To Produce Antibody....

Now economics, purity, quantity, and quality requirements have rendered this system – "research grade", expensive and difficult to scale-up. The ACUSYST-P<sup>™</sup> mammalian cell culture system is now available. This automated technology will produce grams to kilograms of secreted substance with high purity, at low-cost, in your facility or in our new licensed GMP facility for diagnostic as well as therapeutic substances.

#### Efficient Production Of Biologicals – Grams To Kilograms

Secreted cell product such as monoclonal antibodies as well as interferons, growth hormones, tissue plasminogen activator, and other low molecular weight proteins can be efficiently produced. The



The optional research ACUSOFT<sup>™</sup> software package is the users interface to the media flowrates, fluidigas pressures, pH, etc., for bioprocess control development. Different process control algorithms and strategies can be programmed to optimize the secretion parameters of different mammalian cell lines.

ACUSYST-P system incorporates patent-pending, hollow fiber culture technology with sophisticated process control strategies to produce secreted biological substances – economically.



Bioreactor just after inoculation of cells



# ACUSYST-P<sup>™</sup> production system for secreted mammalian cell products



This cell line has been producing for 90 days with McCoys 5A medium. No serum has been added for 9 weeks. Unlike ascites methods, suspension culture, encapsulation technologies, support matricies, or stand alone hollow fiber cartridges, the ACUSYST-P system incorporates patent-pending technology to provide a high purity product. Glucose uptake, lactic acid production, and oxygen uptake show strong signs for all vital parameters.

#### Endotronics Offers The "Flexible Alternative" When Choosing A Method For Production

The pharmaceutical and biotechnology industry is at a crossroads. A production process for secreted substances from mammalian cells must be put in place in order to compete in the marketplace. <u>Economics</u>, flexibility, and the ability to deliver are key factors in choosing the process.

**Economics** – cost per gram in the ACUSYST-P production system is lower than any other production system. Our low-cost Cell Line Characterization Program will prove to you and your management that this system is the most economical way to produce your secreted substance. When the program is completed you will receive a Research Report, Cost Analysis and harvested product on your particular cell line. Flexibility – Endotronics offers Contract Production Services in our new FDA approved GMP production facility, or you can place the ACU-SYST-P systems in your facility for research and production purposes.



Anchorage — dependent cell lines do very well in the ACUSYST-P production system.

Sophisticated process development software allows further optimization of production processes for further reductions in cost per gram. Endotronics offers maximum flexibility for your production needs. Produce your product on contract with us in our licensed manufacturing facility for clinical trials or first production runs with the flexibility to transfer the production technology to your facility at any time. No other company can offer the flexibility of ACUSYST-P instrumentation as well as contract production services.

**Delivery** – ACUSYST-P systems are now in place in the U.S., Canada, and Japan. More systems are producing substance in our GMP Contract Production Facility and Cell Line Characterization Laboratory. Response to our "flexible alternative" has been gratifying as we are forming mutually beneficial business relationships that can help solve production problems in biotechnology.



The ACUSYST-P<sup>™</sup> production system for secreted mammalian cell products can be utilized for anchorage-dependent or independent cell lines.

#### **Share With Us Your Needs**

Your needs in cell culture are seen as opportunities by Endotronics. We would like to discuss with you, your cell culture research and production questions, and offer some answers, and share with you our technological advances over other production methods.



#### Get more information.

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# LKB offers you a choice of two

# This one combines fi

If it's genuine versatility you're looking for, then you need look no further than the LKB Vertical Electrophoresis System. With a dual gel capacity that allows you to run up to 40 samples at a time, its design ensures that all gels are always run under uniform conditions, thereby guaranteeing superior reproducibility. And now we have further enhanced the already impressive versatility of this system by adding a 30 cm gel capability for even higher resolution, a tube gel kit for greater 2-D flexibility, and the new LKB Transphor Electroblotting Unit for improved visualization.

This fine 2-D gel shows the use of the LKB Gel Dryer in preparing gels for storage, scanning or autoradiography  $\blacksquare$ 



#### THE LKB SYSTEMS APPROACH

At LKB we believe that we should be able to give you professional training, advice and support in the use and application of our products. And we should certainly be able to supply you with everything you need to perform your experiments, so you never have to worry about where each item comes from, how good it is, whether it will work properly with all the other pieces of apparatus, and who to turn to when you have problems. That is why we offer complete integrated systems, not merely a range of individual units. LKB systems contain all the instruments, kits, chemicals, accessories and supplies you will need in your laboratory. Every component of the system is designed to work together with and enhance the high performance of all the other components. Every item carries our name, and we take full responsibility for it.

LKB - the electrophoresis experts

#### No grease, no leaks, no mess

One clear benefit of using the LKB Vertical Electrophoresis System is the simplicity it brings to the job of gel casting. The basic system includes everything you need to cast and run perfect gels first time, every time. The gels are cast between glass plates, avoiding both the use of grease and the probability of leaks and turning gel casting into a clean and pleasant activity.

The Tube Gel Kit allows the LKB system to perform both the first and second dimensions in 2-D applications  $\triangleright$ 

#### **PAGE and gradient PAGE techniques**

Conventional PAGE and SDS/PAGE techniques, using either continuous or discontinuous buffers, are fully catered for by the basic LKB system. The addition of our Gradient Gel Kit provides a quick and convenient method of casting both linear and exponential gradient polyacrylamide gels. Due to their relatively small pore size, these gels effectively limit diffusion. Linear gradients counteract band broadening effects, while exponential gradients are useful for resolving components with widely differing molecular weights.

The Vertical Electrophoresis System, based on the LKB 2001 Electrophoresis Unit, also includes a power supply, thermostatic circulator and all the necessary accessories, kits and quality chemicals  $\checkmark$ 





# Vertical Electrophoresis Systems

# ve different techniques



#### Agarose gel techniques

For researchers who sometimes want to use agarose, there is a special kit to help you cast and run the 3 mm agarose gels on the LKB Vertical Electrophoresis System. The kit includes frosted glass plates to provide essential support for the gel.

#### **Two-dimensional techniques**

This is the only complete vertical electrophoresis system that can carry out both the first and second phases of 2-D electrophoresis in a single unit, and can offer the user a choice of either tube or slab gels for the first dimension. Our 2-D Kit includes a special cleaver for preparing slab gels, while tube gels are easily applied to the top of a standard slab gel by means of the trough built into the upper buffer chamber.

LKB's new Transphor Electroblotting Unit improves the sensitivity and resolution of detection procedures  $\blacktriangleright$ 

#### Autoradiography techniques

Another kit, containing all the accessories you need to cast accurate gels only 0.75 mm thick, makes it easy for you to use the LKB Vertical Electrophoresis System for high resolution autoradiography using thin gels. The LKB Slab Gel Dryer, which combines dry heat and reduced pressure to rapidly dry and affix the gel onto paper or film for later analysis and storage, is ideal for drying down thin gels onto disposable plastic sheets prior to detection.



The result of gradient gel electrophoresis of two crude extracts from Beneckea harveyi on the LKB system  $\blacksquare$ 

#### **Electroblotting techniques**

The new LKB Transphor uses the principles of electrophoresis to transfer proteins or nucleic acids from polyacrylamide or agarose gels onto nitrocellulose or other immobilizing matrices. In this way the electrophoresis bands are made easily accessible for faster and more sensitive visualization than on the original gel. The resulting patterns can be stored for months without deteriorating and multiple analyses can be performed using just the one pattern.

#### Want proof?

These may sound like extravagant claims, but just call us and we'll be happy to come and demonstrate the versatility of the LKB Vertical Electrophoresis System for you and your colleagues. At your convenience.





344

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## Hoefer has expanded the Mighty Small line

Hoefer's Mighty Small I has become the laboratory standard for doing electrophoresis in the small gel format. Now Hoefer is introducing Mighty Small II, and to complete the system, Mighty Small Transphor, Casting Stand, and Power Supplies.

• Mighty Small II is Cool and Fast: It can run two mini-gels, 8 x 10 cm, in 45 minutes. Two mini-gels are produced in two gel sandwiches, held back to back, in a



double-sided pod. The pod consists of two discretely separate upper buffer chambers and a serpentine coolant chamber between. Cooling is the key feature of the Mighty Small design. The back plate of each gel sandwich is in contact with the upper buffer and is made of sturdy alumina. Alumina is an excellent heat conductor, 40 times faster than a comparable thickness of glass. It rapidly conducts joule heat away from the gel sandwich into the buffer. A serpentine coolant chamber, permanently sealed between the two buffer chambers, assures further heat dissipation. This excellent cooling system means you can get flat, side by side sample lanes with no smile in 45 minutes.

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• The Mighty Small Multiple Gel Caster enables you to cast 10 gels at a time, 8 x 10 cm, gradient or native. You can pour batches of gels ahead of time,



probably a week's supply. Reader service card no. 335

• The Mighty Small Transphor can transfer proteins from four small gels (up to  $9 \times 10$  cm) at once, to either nylon membranes or nitrocellulose, *in as little as 30 minutes*. It comes complete with four



glass-filled polycarbonate cassettes. A serpentine cooling channel milled into the base and covered with alumina assures *excellent cooling*. Under standard transfer conditions the temperature variation will be less than 5°C. Platinum wire, 155 cm of it, strung in 14 opposing strands  $1\frac{1}{2}$  cm apart establishes a *uniform electrical field*. Because of its small size, it is possible to use a standard electrophoresis power supply—we recommend the Hoefer PS 500X. Mighty Small Transphor requires only a small amount of buffer, about one liter, another important cost-saving factor. *Reader service card no.* 336

• If you want to run small gels, 100 mm wide x 80 mm high, the **Mighty Small I** does the job fast and right. You can run a 10% gel at 200 constant volts in only 42 minutes. The gel sandwich is the core of the design. Its alumina back interfaces with the buffer pod to insure even heat distribution across the gel surface. The result: flat,



side-by-side bands.

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• Hoefer introduces a new line of transfer membranes for all blotting techniques: a pure grade of nitrocellulose to insure faithful replicas and minimal background staining, and high binding capacity Nylon 66 membranes. You have a wide choice of shapes and pore sizes.

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• The PS 250 power supply is a workhorse for the electrophoresis lab. It can produce 0-250V; 0-2.5A, adjustable in



both voltage and current. It has two digital panel meters and a 7 hour timer. You can run six Mighty Small II units at one time and monitor each separately. For transfer work the PS 250 provides ample current for several small or large transfer units. We recommend running transfers in constant current to eliminate overheating. Reader service card no. 339

• The PS 500X

is the standard power supply for small gel electrophoresis. It can produce 0-500V, 0-400mA; adjustable in voltage and current; automatic crossover from current to voltage. You can run two Mighty Small II units at one time or two Mighty Small Transphor units.



The PS 500X is portable (only 8 lbs.) and compact  $(4'' \times 8'' \times 12'')$ . Reader service card no. 340

• Hoefer Scientific Instruments, P.O. Box 77387, San Francisco, CA 94107 USA. In California: 415-282-2307. Outside California: 800-227-4750. Outside USA: Telex 470778.

For demonstration of the Mighty Small line, Reader service card no. 341 For complete catalog, Reader service card no. 342



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#### World Supplies of Natural Gas

Once regarded as a nuisance, natural gas is emerging as an important substitute for oil. During the past 10 years, proved reserves of natural gas have doubled, whereas those of petroleum have not grown. Worldwide, natural gas with a total energy content approaching that of oil has been found in about 50 countries, and as the search continues, world reserves of gas will probably surpass those of petroleum. Already some less-developed countries (LDC's) such as Thailand, once totally dependent on imported hydrocarbons, are using local natural gas. The pace at which petroleum will be displaced in developing countries will depend on arrangements for technical, financial, and managerial assistance. Such arrangements are not easy to achieve. Most LDC's are overburdened with debt, and their currencies are usually not freely convertible.

There are three major reasons for speculating that much more natural gas will be found. First, some petroleum companies that for decades were interested only in discovering oil are now more willing to look for gas. Second, geophysical prospecting methods continue to improve. The third reason relates to geochemistry. Natural gas is created and can survive in circumstances where oil either cannot be formed or is unstable. For example, source rocks for petroleum must contain what was originally lipidrich organic matter. Natural gas can be derived from all kinds of organic matter, including cellulose. It can be formed through a broader range of temperatures than those required for petroleum and is stable at temperatures at which other hydrocarbons are destroyed.

In most instances the proven reserves of natural gas are in countries where it was found in association with oil. In 1984, of a world total of about 100 trillion cubic meters, reserves, in these units, were Soviet Union, 39.6; Iran, 13.6; United States, 5.6; Qatar, 4.2; Algeria, 3.6; Saudi Arabia, 3.4; and Nigeria, 3.1. Natural gas has also been found in about 30 countries in which no petroleum has been discovered.

The proven reserves in the Soviet Union have nearly doubled in the last 10 years. The energy content of Soviet gas reserves is now substantially larger than that of the oil reserves of Saudi Arabia. In recent years, exports to Western Europe have increased. A new development is an agreement by Turkey to import gas from the Soviet Union.

In an era of cheap oil, many of the developing countries became dependent on it. Sooner or later, they must reduce this dependency by utilizing alternate lower cost and preferably domestic sources of energy. A World Bank study in ten LDC's has shown that they could save foreign exchange and obtain energy more cheaply by developing local resources of natural gas. Costs for them of clean, nonpolluting natural gas delivered at the city gate are estimated to be between \$0.61 to \$1.79 per million Btu's. Comparable costs for unrefined petroleum are about \$5.

A few of the LDC's will export some of their gas, but the major use will be internal. To explore for, develop, and create even a limited distribution system for it, a minimum of 5 years is usually required. In addition, frontend costs are large, though later expenditures are small. Thus foreign investors must have great confidence in the stability of agreements and on the chances of being repaid in hard currencies if they are to risk their capital. In this situation, the World Bank is playing an important role. It has increased its involvement in energy matters and has assembled a group expert in exploration and development of natural gas. Thus far it has assisted in efforts in about 20 countries, furnishing funds for feasibility studies, bringing the necessary parties to an investment together, and helping arrange terms that are fair to all concerned. As such efforts continue, the substitution of natural gas for petroleum will expand.

-PHILIP H. ABELSON

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163