the hearings testified that the petroleum industry had an efficiency of 84 percent by this measure. But the FPC granted only part of the gas volume requested, noting among other reasons for the decision that the true measure of the efficiency of the process is the minimum work theoretically needed to refine the oil. By this measure, which is the same as the second-law efficiency, the fuel efficiency of the petroleum industry is only about 9 percent. The FPC noted that "the petroleum refiners . . . do not outpace other industries in the overall efficiency of energy use." According to a report prepared for the Ford Foundation Energy Policy Project, the efficiency of other industries is comparable or higher (Table 2).

Table 2. The efficiency of fuel utilization in various industries. The measure of efficiency in each industry is the minimum amount of fuel theoretically needed to produce 1 ton of the product. The minimum fuel needed for the paper industry is very near zero because of the heating value of the waste products. [Source: E. P. Gyftopoulos, L. J. Lazaridis, T. F. Widmer, *Potential Fuel Effectiveness in Industry* (Ballinger, Cambridge, Mass., 1974)]

Industry	Second-law energy (%) efficiency
Petroleum	9
Steel	21
Aluminum	13
Cement	10
Paper	~0.3

One of the most promising suggestions for improved utilization of fuels by industry is the generation of electricity along with industrial heat or steam. Production of electricity at industrial plants was proved economically sound by several large paper companies during the 1920's, but was halted by the Justice Department [C. A. Berg, *Science* **184**, 264 (1974)]. Most industries would produce more electricity than they could use by cogeneration, at least during part of the year, and it is presently quite difficult for them to arrange for offsite sale of such electricity. But the technical capability is at hand, and the potential for energy saving is great. A study just being completed for the energy policy office of the National Science Foundation finds that as much as 700,000 barrels of oil per day could be saved by industrial cogeneration of electricity.

An alternative architecture for cogeneration of electricity and heat is a central power station redesigned so that its waste heat, which is now typically 100°F, can be used for domestic heating or industrial processes. Even though the amount of heat discharged in the cooling water of a power plant is large, the failure to use this water is not particularly wasteful because it typically contains only 1.5 percent of the available work represented by the fuel. To produce higher-temperature heat from a central power station requires modification of the design of the facility. The difficulties with a major project of this sort under way at Midland, Michigan, indicate that the institutional differences between power companies and potential industrial users are also serious problems. The Consumers Power Company is building a large nuclear facility in Midland to produce industrial steam at 360°F, in addition to electricity. However, the delays in starting this plant have apparently forced the largest potential customer, the Dow Chemical Company in Midland, to make other provisions. Dow has substantially reduced the amount of steam it was originally committed to purchase.

Combined systems can also be used to improve the efficiency of domestic and commercial energy usage. For instance, if a diesel motor is used to drive a generator, the efficiency is about that of a central station. But if much of the exhaust heat of the motor is recovered and used for space heating, significant amounts of fuel can be saved. According to a sample calculation in the APS report, in which a diesel generator provides the winter base-heating load for a sizable community and produces all the community's electricity plus more for sale, the overall second-law efficiency is 34 percent. This is so much higher than the typical efficiency of space and water heating that the fraction of the fuel saved by the combined system in the sample calculation was 31 percent. Another calculation, involving fuel cells with performance levels that should be available shortly, gave equal savings in energy without producing so much excess electricity.

For domestic and commercial energy needs, individual components such as heat pumps, fuel cells, and heat exchangers can also be greatly improved, according to the APS study. The efficiency of the heating system could also be greatly improved by plugging leaks and by using more sophisticated diagnostic instruments. The advances in infrared technology should make possible improved instruments for detecting heat losses in buildings, and the APS group noted that a small, easy-to-use heat flux meter, similar to a photographic light meter, would be very valuable.

Other sorts of badly needed instruments are gauges indicating energy consumption efficiency. One such meter could be a dial on the automobile instrument panel that would indicate the number of miles per gallon an automobile was getting over a short time interval, based on a comparison of the carburetor fuel flow and the speed. Empirical data could also be provided for the efficiency of home heating, with the use of the common predictor of energy consumption, the degree-day. Consequently, a meter that measures degree-days per gallon would be very useful.

Other parts of the three-part APS summer study dealt with windows and combustion, areas of interest to commercial and industrial designers that seem particularly well suited for physical modeling. The window study arrived at an important conclusion for the proper use of solar energy. While many inventors and scientists are trying to perfect collectors to attach to house roofs, the APS study found that windows themselves are excellent solar collectors which can provide a substantial amount of heating if properly designed.

Knowing that most scientists consider thermodynamics and fluid dynamics to be boring, "classical" subjects, the authors of the APS report urged fellow scientists to reconsider their importance. The overall second-law efficiency for consumption of U.S. energy resources is now only 10 or 15 percent.—WILLIAM D. METZ

Lasers in Biomedicine: Analyzing and Sorting Cells

At this time no one can say just how useful lasers will be for biomedical research. One area in which progress is already substantial, however, is the development of automated flow systems. These instruments, which are now becoming available commercially, use laser light to analyze cell characteristics; some can even sort or separate cells on the basis of differences in their characteristics. Flow systems promise to be powerful tools for studying basic cell biology. Moreover, they have potential clinical applications such as rapid screening of cell preparations for the presence of abnormal or cancerous cells.

Flow systems have several advantages over other techniques that may produce similar information. They examine individual cells with great rapidity. Some scan—and sort—cells at the rate of several thousand per second. Consequently, they can pick out cells that may be present as only a small minority in the population. The more advanced flow systems are de-

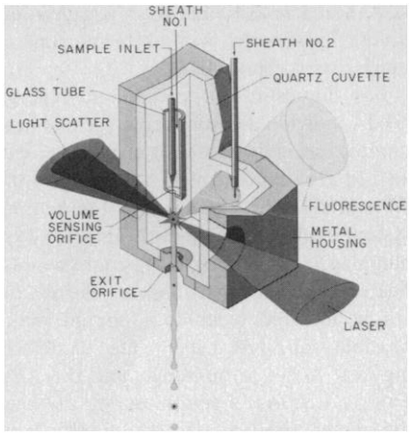

Fig. 1. Section of a multiparameter cell separator system showing sample and sheath fluid inlet tubes, cell stream, cell volume sensing orifice, laser illumination, and liquid jet from the exit orifice. The fluid introduced through sheath No. 1 flows coaxially around the inlet tube for the cell suspension and serves to center the cells as the two streams flow through the cell volume sensing orifice. Fluid introduced through sheath No. 2 ensures that the cell stream aligns properly with the exit orifice. [Source: Paul Mullaney, Los Alamos Scientific Laboratory]

signed to measure two or more cell properties simultaneously; this allows greater discrimination between cells of different classes than can be obtained by measuring only one characteristic. Finally, some cell properties can be measured without treating the cells with a fixative, a process that kills them, and they may either be left unstained or dyed with a vital stain that does not cause cell death. This minimizes the introduction of artifacts and means that living cells can be sorted for further study.

Investigators in several laboratories have contributed to the development of flow systems. Among them are Leonard Herzenberg and Richard Sweet of Stanford University School of Medicine; Louis Kamentsky, now at Bio/Physics Systems, Inc. (Mahopac, New York); Paul Mullaney of Los Alamos Scientific Laboratory; and Marvin Van Dilla of Lawrence Livermore Laboratory.

Although the design and capabilities of the instruments from the different laboratories vary, the principles on which they operate are basically similar. Suspended cells are made to flow in single file across a beam of light (Fig. 1). The light sources most frequently used are the argon ion laser and the helium-neon laser. As each cell passes through the beam, measurements are taken of the light absorbed or scattered by it, or of fluorescence from it (if the cells have been labeled with a fluorescent dye), or of a combination of these parameters.

Lasers are used in flow systems as the source of light because laser light is intense, monochromatic, and highly collimated (the waves are essentially parallel to one another). Because of these properties a narrow beam, usually 1 to 2 millimeters in diameter, can be focused to deliver a great deal of energy to a small area—with a diameter near to or slightly larger than that of the cell. The collimation of the beam permits the measurement of light scattered at small angles from the incident beam.

Light scattered from cells at small angles—less than 2 degrees out of the path of the incident beam—is a measure of cell size; light scattering at greater angles can be used to derive information about internal structures. In addition, the instruments may determine cell volume the way the Coulter counter does; that is, cells suspended in electrically conducting salt solution flow through a tiny aperture and the change in electrical resistance of the fluid in the aperture is measured as each cell or other insulating particle passes through it.

A number of common biological dyes, including acriflavine, acridine orange, mithramycin, ethidium bromide, propidium iodide, and the fluorescein dyes have absorption maxima within the range of wavelengths—from 457 to 514 nanometers—emitted by the argon ion laser. The laser light is sufficiently intense to excite measurable fluorescence in a dye in a single cell, even if its wavelength does not exactly coincide with the absorption maximum of the dye.

As long as a particular fluorescent dye binds quantitatively to only one cell constituent, the fluorescence stimulated by the laser beam will be proportional to the content of that component in the cell. In theory, flow systems are capable of quantitative measurements of any constituent for which there is an appropriate fluorescent label. In practice, the most common analyses are those of DNA content because stains specific for DNA are available.

There are also dyes that bind to cell proteins. Some instruments have the capacity to measure fluorescence at two wavelengths at the same time and can thus determine both the DNA and protein contents of a cell that has been doubly labeled. Several investigators point out, however, that the experiments that can be performed are now more restricted by lack of suitable techniques for preparing cells than they are by the limitations of the instruments.

The cell-sorting systems can select from the mainstream those cells that meet the

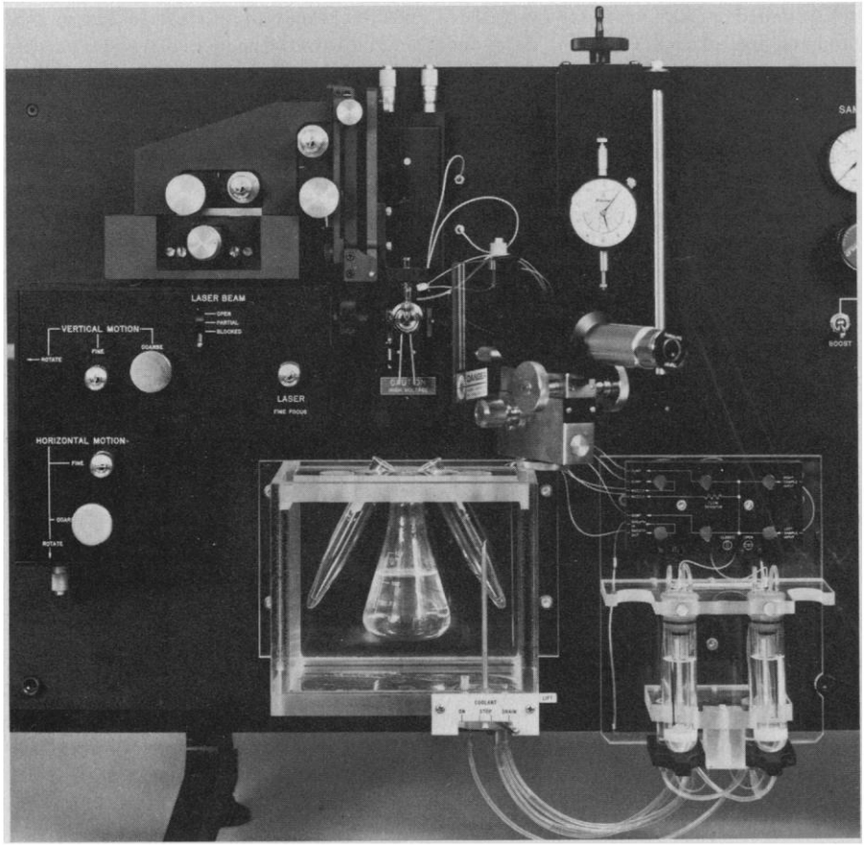

Fig. 2. View of a portion of the FACS. Two different populations of cells may be deflected from the main stream of droplets and collected separately in the test tubes. Undeflected droplets are caught in the flask. [Source: Leonard Herzenberg, Stanford University School of Medicine]

separation criteria established by the investigator and collect them for further study, including visual examination. This is important because the properties analyzed by flow systems are not the same as those observed by the human eye. It is the latter that have served as the basis of cytological classifications. Thus the researcher who wants to apply flow techniques clinically must verify that the cell categories detected by the system correspond to those that interest the clinician.

In order to achieve cell sorting, the stream of fluid containing the cells in single file is broken into tiny, uniform droplets after it passes through the light beam. This is done by vibrating the orifice from which the stream emerges at ultrasonic rates; 40,000 hertz is typical. The idea is that no droplet should contain more than one cell, although most contain none.

Meanwhile the detector signals meeting the separation criteria are converted to electrical pulses that are processed in such a way that they charge the droplet containing the cell from which the signals originated. Actually two or more consecutive drops may be charged to ensure that the right one is included. The droplets then pass through an electric field that deflects the charged droplets into containers (Fig. 2). The system is set up in such a way that the droplets will not be charged if the desired cell is so close to others that separation can not be assured.

The potential of these instruments is just beginning to be explored, but already a wide range of applications can be visualized. One of them is cell-cycle analysis, that is, the determination of the percentages of cells in the four stages of the cell cycle. The four stages are M (mitosis), G_1 (the growth period following division), S (the period of DNA synthesis), and G_2, which is followed by another round of mitosis. During S, the DNA content increases so that cells in G_2 and M have twice the DNA content of those in G_1.

The Los Alamos group is among those performing cell-cycle analysis by what they call flow microfluorometry. When fluorescence measurements are not involved, the process is called flow microphotometry. Others designate the same processes as flow cytofluorometry and flow cytophotometry, respectively. To count the number of cells in each stage of the cell cycle, the Los Alamos investigators stain the cells with acriflavine or mithramycin, both of which bind specifically to DNA, and determine the DNA content of each cell in the population with the flow microfluorometer. The result is a histogram of the number of cells with each DNA content (Fig. 3). The fraction of cells under the three major portions of the curve can be obtained by computer analysis of the data.

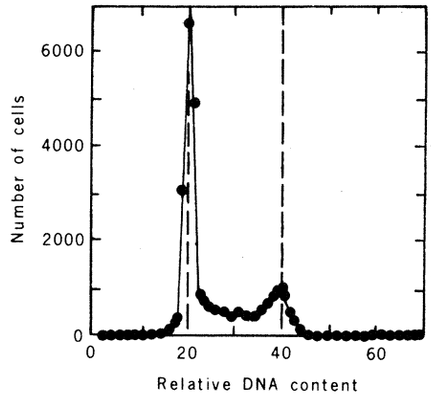

Fig. 3. DNA distribution pattern of exponentially growing Chinese hamster ovary cells. The first peak represents cells in G_1; the second represents cells in G_2 or M that have twice the DNA content as those in G_1. Cells in S phase with varying degrees of completion of DNA replication are distributed between the two peaks. [Adapted from data of Robert Tobey and Harry Crissman, Los Alamos Scientific Laboratory]

Flow systems provide an easy way to study the mechanisms by which agents perturb or alter the cell cycle. These agents include drugs used for cancer chemotherapy, radiation, and substances thought to play a role in the normal regulation of cell activities. Clinicians who want to devise more effective chemotherapeutic treatments for cancer need this kind of basic information. Drugs that act at different stages of the cell cycle, for example, may inhibit tumor growth more effectively in combination than they do alone.

Other medical applications of automated flow systems are screening for abnormal or cancer cells—as in the Pap test—and counting the different kinds of white blood cells in human blood. The latter test is the differential white count.

In most flow systems, the excitation and measuring apertures are larger than the cells of interest. This permits examination of large numbers of cells in a short time, but Leon Wheeless of the University of Rochester Medical Center says that the techniques give too little cell detail for the purpose of screening for cancer cells. Systems having apertures much smaller than cell size provide a lot of information about cell structure, but are too slow to examine large numbers of cells. Wheeless has compromised by using a slit aperture that permits adequate resolution of cell detail plus a reasonable speed of analysis for examining cells from the female genital tract.

The slit is 5 micrometers wide—much narrower than the average cell diameter. This permits the fluorescence of the cell, which has been stained with acridine orange, to be measured sequentially as it flows past the slit. The result is a graphic fluorescence contour of each cell; essentially this is a plot of the averaged fluorescence along the cell versus time. Computer analysis of the contours gives the cell and nuclear diameters plus the nuclear and cytoplasmic fluorescences.

In previous investigations, Wheeless established that this data would be adequate to distinguish the full range of cell types—from normal to precancerous abnormal to cancerous—found in cells from the female genital tract. He says that this method should be useful for rapid, automated prescreening of such cell preparations and, perhaps, of cells shed from other body parts, such as the bladder. Pathologists would still have to confirm any abnormal diagnosis by conventional methods, but automated prescreening would be a time-saving technique. Moreover, an analyzer with sorting capabilities could separate abnormal cells for further examination.

Other investigators think that multiparameter analysis with low resolution systems may provide adequate information for screening and for doing differential white counts. According to Mullaney, light-scatter patterns alone may be adequate for characterization of cells in heterogeneous populations. In one system using helium-neon laser light with scattering detected at only two angles, the Los Alamos workers separated human white blood cells into four of the five major classes.

With a more advanced system, they are now measuring light scattered at 32 different angles from the laser beam. Preliminary work showed that they could distinguish three distinct classes of cells in normal gynecological preparations and four in abnormal ones; the groups were not separated and identified, however. Light-scattering measurements have the advantage of not requiring staining or fixing of cells.

Investigators who want to study the functions of a specific cell type need pure—and living—preparations of that cell. Such separations can now be rapidly accomplished by cell sorters such as the one developed by the Stanford group. This instrument, called the fluorescence-activated cell sorter (FACS), separates according to the amount of fluorescent material bound to cells and according to cell volume. The instrument has the capacity to separate cells that vary only slightly. For example, Herzenberg, with Leonore Herzenberg, also of Stanford, isolated subclasses of peripheral T lymphocytes (the type of lymphocytes needed for cellular immunity and immune regulation) and of thymus cells. They used antibodies combined with a fluorescent dye to label cell surface antigens.

Not only may whole cells be character-

(*Continued on page 874*)

Microscope Slide Incubator

Incu-Stage is designed for use with 1- by 3-inch slides to maintain microorganisms at 37°C. The slide is placed at the bottom of a compartment in contact with the substage condenser. The top of the incubator is covered with a mica sheet with a hole in the center through which the objective projects into the incubating chamber. A soft rubber washer serves as a seal. Incu-Stage has integral heating elements and a bimetallic thermostat. Lab-Line Instruments, Incorporated. Circle 737.

Literature

Water Technology Manual covers 14 methods and has a reference section of hints on spectrophotometry. Bausch & Lomb Analytical Systems Division. Circle 742.

Metro Disc describes a water sampler for heavy metal analysis. Data sheet 18 lists capabilities and applications. Environmental Devices Corporation. Circle 743.

p*H Meters* features the model 103—a precise, reliable model with sensitivity to 0.01 unit. Brinkmann Instruments Incorporated. Circle 744.

Solution Calorimeters are covered in bulletin 1451 for the measurement of heat of reaction from 2 to 2000 calories with an accuracy of 1 percent. Parr Instrument Company. Circle 745.

Catalog 750 features thermometers, hygrometers, and accessories for measurement of heat in research applications. Brooklyn Thermometer Company Incorporated. Circle 749.

1975 Research Products Catalog lists radiochemicals, standards, liquid scintillation and gamma counting supplies and accessories. Amersham/Searle Corporation. Circle 747.

Laboratory Products Catalog 750 describes reagents and specialty chemicals. J. T. Baker Chemical Company. Circle 748.

Model AR-2 Recording Vacuum Balance includes description of stability, features, accessories, and design specifications. Perkin-Elmer Corporation, Instrument Division. Circle 751.

NMR Deuterated Chemicals and Shift Reagents lists an expanded product line for this mode of chemical analysis. Pfaltz & Bauer Incorporated. Circle 752.

Laboratory Products Catalog describes apparatus for cell harvesting, solution pumping, air filtration in vacuum systems, and other scientific applications. Spectroderm International. Circle 753.

Demineralized Pure Water is devoted to the Osmo system of reverse osmosis. Osmonics, Incorporated. Circle 750.

NEWS AND COMMENT

(Continued from page 818)

New Mexico desert, but that won't be ready until the early or mid-1980's.

In spite of these continuing difficulties, the prevailing view of nuclear engineers seems to be that no real technological barriers exist to the safe and economical disposal of nuclear waste. But the continuing muddle over what to do with spent fuel and what to do with the final radioactive dregs of nuclear power generation are doing nothing for the technology's image.

—ROBERT GILLETTE

RECENT DEATHS

Frederick B. Davis, 65; professor of education, University of Pennsylvania; 2 March.

Richard F. DeMar, 50; professor of mathematics, University of Cincinnati; 11 February.

Donald W. Denna, 44; associate professor of horticulture, Colorado State University; 15 January.

Alden H. Emery, 73; chemist and former executive secretary, American Chemical Society; 14 March.

Paul H. Margolf, 78; professor emeritus of poultry science, Pennsylvania State University; 13 February.

Bernard D. Tebbens, 65; professor of public health and engineering; University of California, Berkeley; 10 February.

C. Mildred Thompson, 93; dean emeritus, Vassar College; 16 February.

Adolph E. Waller, 82; professor emeritus of botany, Ohio State University; 28 January.

Edward H. Watson, 72; retired chairman, geology department, Bryn Mawr College; 21 February.

Arnold V. Wolf, 58; dean, Graduate College, University of Illinois Medical Center Campus; 27 February.

Nathan A. Womack, 73; first chairman, surgery department, University of North Carolina School of Medicine; 2 February.

George M. Worrilow, 70; former dean, College of Agriculture, University of Delaware; 27 February.

Bernice M. Wright, 66; former dean, College for Human Development. Syracuse University; 17 February.

Erratum: Excerpts of an address by Benno C. Schmidt (16 May, p. 716), chairman of the President's Cancer Panel, erroneously implied that the Cold Spring Harbor Laboratory is an officially designated "comprehensive cancer center." Although the laboratory receives support from the National Cancer Program, it is not a "comprehensive center."—B.J.C.

RESEARCH NEWS

(Continued from page 823)

ized and separated with flow systems, but the Livermore group is finding that chromosomes are also distinguishable. The investigators stained chromosomes isolated from cultured Chinese hamster cells with ethidium bromide. This dye combines specifically with DNA so that the chromosomes are separated on the basis of differences in their DNA content. The technique does not completely resolve the chromosomes but the resolution was sufficient to detect a chromosomal rearrangement in a mutant line of hamster cells.

Van Dilla thinks that the method is a highly promising approach to karyotyping and to purifying individual chromosomes for biochemical and biological characterization. The Livermore investigators are now attempting to apply the same procedures to human chromosomes. This will obviously be more difficult since humans have roughly twice the number of chromosomes as hamsters. In an early experiment, the investigators resolved chromosomes prepared from cultured cells from a human male (24 different chromosomes) into 7 groups. Again, karyotyping appears to be more limited by availability of suitable methods for preparing chromosomes than it is by the instrumentation.

Numerous additional applications of flow systems are being investigated. For example, the techniques provide a rapid, quantitative means of determining the amount of antigen or antibody on individual cells and thus for studying immune responses. Flow techniques should also prove valuable for studying lectin binding by cells. Lectins are widely used to probe the differences between normal and malignant cells.

The availability of commercial instruments will no doubt accelerate the applications of flow systems to biomedical research. Becton, Dickinson Electronics Laboratory (Mountain View, California) is now producing the FACS-1 after the prototype developed at Stanford. Bio/Physics Systems manufactures a series of systems with capabilities ranging from simple cell counting to multiparameter analysis with sorting. And Particle Technology, Inc. (Los Alamos) is also starting to produce flow instruments. Developments that will further stimulate research include incorporation into the instruments of lasers tunable over a wide range of wavelengths and of lasers emitting infrared or ultraviolet light. The potential impact of flow systems on biology, according to Mullaney, equals that of the electron microscope.—JEAN L. MARX