American Association for the Advancement of Science

# SCIENCE

18 April 1986 $2.50
Vol. 232 ■ Pages 297–428


# Big News for the TL-100 Benchtop Ultracentrifuge

The Beckman TL-100 Ultracentrifuge—with a choice of fixed angle, swinging bucket and vertical tube rotors—has become the preferred way to separate small sample volumes, typically taking only one-fifth the time required by floor-model ultracentrifuges.

Now a new rotor, the TLA-100.3, brings even more capabilities to benchtop ultracentrifugation.

## Larger Capacity

The rotor spins six open-top tubes that hold 3 mL each, triple the volume of any other TL-100 open-top tube. The fixed angle rotor also can run six 3.5-mL Quick-Seal® tubes for a maximum capacity of 21 mL.

## Higher Performance

At a top speed of 100,000 rpm, the TLA-100.3 generates forces of 541,000 *g* (vs. a previous high of 436,000 *g*) and has a *k* factor of 16.5 for fast, efficient runs.

## Microcentrifuge Tubes

With adapters, the new rotor also can spin 1.5-mL conical-bottom microcentrifuge tubes at speeds to 50,000 rpm—ideal for pelleting subcellular fractions and DNA or protein precipitates. You'll find the 30°-angle titanium rotor useful for plasmid preps, protein binding studies and mRNA studies too.

Big NEWS! For the complete story on the TL-100 benchtop ultracentrifuge, its rotors, tubes, accessories and applications, write Beckman Instruments, Inc., Spinco Division, 1050 Page Mill Road, Palo Alto, CA 94304. Offices worldwide.

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For cells in culture

# Discover the Power of the ACAS™ 470

**Controlled Laser Illumination** with the ACAS 470 (Anchored Cell Analysis and Sorting) brings new light to discovery in cell biology. Focus the laser beam where you want it for

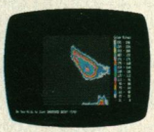
- fluorescence excitation
- photobleaching
- photoactivation
- cell surgery
- cell ablation

without disturbing the extracellular environment and attachment of cells.

Now you can use fluorescence to quantitatively measure

- orientation and localization of cellular components
- cell-cell interactions
- fluorescence redistribution after photobleaching (FRAP)
- cell subpopulations

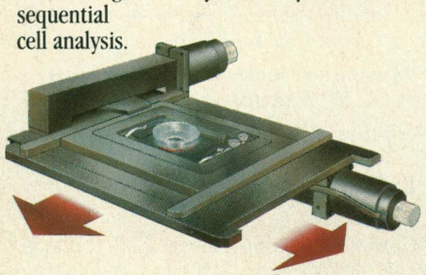
and much more.



Isolate cells for propagation or analysis

**Convenient Software** that is easy to learn and to use is the heart of the ACAS 470. Experimental parameters are set, data are accessed and the stage is controlled through an alphanumeric keyboard or hand-held mouse. The CRT screen displays collected data, results, menus and prompts for greater user interaction.

**Computer-Controlled Stage Movement** allows precise and automatic targeting of the laser beam. Stage speed provides for rapid sorting of cell monolayers in culture. Stage coordinates can be used for repositioning with the high accuracy necessary for automated sequential cell analysis.



By integrating computer-controlled laser illumination and stage movement, the ACAS 470 lets you explore new frontiers in cell research. Now you can automatically isolate

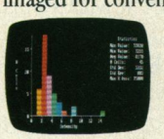
- subpopulations of cells
- mutant cells
- transfected cells

for propagation or analysis.

**Cell Sorting** of anchorage-dependent cells is now possible with the ACAS 470. Selective sorting is achieved by destroying unwanted cells via the laser beam, or by physical separation through a unique cookie-cutter selection method. In this way, homogeneous cell progeny can be obtained from a heterogeneous cell population.

Study cell-cell interactions

**Quantitative Fluorescence Analysis** is optimized with the ACAS 470. Cells are imaged for convenient manual or automated interaction. For fluorescence analysis, the ACAS 470 sequentially exposes only small areas of a cell to brief laser pulses. The resulting fluorescence represents emitted light from targeted fluorescent molecules, giving three-dimensional information.



Perform quantitative fluorescence analysis on large numbers of cells

Analyze fluorescent images

**Are you considering instrumentation for CELL SORTING? FLUORESCENCE ANALYSIS?**

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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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■ The American Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objects are to further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, to improve the effectiveness of science in the promotion of human welfare, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.


COVER Image of comet P/Giacobini-Zinner taken 22 August 1985, 0934 U.T., using the Catalina 154-cm telescope of the University of Arizona Observatories. It is taken with a Charge Coupled Device (CCD) electronic camera using a visual (V) filter (center wavelength 5500 angstroms). The exposure time was 1 minute and the field of view of the picture is roughly 8 minutes of arc. See page 353. [Uwe Fink, Al Schultz, and Mike DiSanti, Lunar and Planetary Laboratory, University of Arizona, Tucson, AZ 85721]

# BIOSYSTEMS UPDATE

## Finally, high quality DNA/RNA can be automatically extracted from tissues, cells, plasmids and viruses.

## Introducing the first Nucleic Acid Extractor.*

**SPECTROPHOTOMETRIC PRODUCT PURITY ANALYSES**

| SOURCE MATERIALS | PHENOL+ PROTEIN ($A_{230}/A_{260}$) | PROTEIN ($A_{260}/A_{280}$) |
|---|---|---|
| Human fibroblasts, cell culture | 0.52 | 1.83 |
| Human lymphocytes, purified | 0.45 | 1.87 |
| Human lymphocytes/granulocytes, crude | 0.43 | 1.83 |
| Rat liver nuclei, crude | 0.47 | 1.85 |
| Rat liver, whole homogenate | 0.58 | 1.85 |
| E. Coli, JM 101, log phase | 0.45 | 1.88 |
| M13, mp8, PEG pellet | 0.50 | 1.77 |
| Phage Lambda DNA | 0.46 | 1.83 |

The new Model 340A Nucleic Acid Extractor* automatically extracts and purifies DNA or RNA from tissues, cells, plasmids and viruses. It ensures the consistent quality of your extracted product and eliminates tedious manual procedures. This instrument-reagent system is based on an extensive investigation of nucleic acid extraction. Three advantages of the Model 340A system are:

- The composition of the Applied Biosystems Lysis Buffer provides rapid digestion of proteins by Proteinase K and quick phase separation;
- A high purity, pre-mixed phenol-chloroform reagent that attaches directly to the instrument eliminates handling of this toxic corrosive liquid; and
- A choice of final purification by either ethanol precipitation or dialysis.

### Proven, Quality Product

DNA isolated with the Model 340A standard protocols has been assayed by UV absorption which confirms the absence of phenol and protein in the final product. In addition, gel electrophoresis confirms that the DNA can be cut by restriction endonucleases.

Genomic DNA in the range of 160 kb can be routinely isolated. To eliminate cross-contamination between samples, the system is automatically purged with hot 6N nitric acid.

### Easy to Operate and Program

Users can select standard methods which are included with the 340A to process such source materials as blood, liver and plasmids. For other materials, users can easily develop their own methods using the Extractor's easy-to-follow software.

### Multiple Sample Capability

The Model 340A can extract DNA or RNA from eight samples simultaneously. The time required varies from 1½ hours for plasmids to three hours for liver. Final purification by ethanol precipitation requires only 30 minutes. Dialysis can be completed overnight with the Applied Biosystems Model 345A Dialyzer which automates previously time-consuming buffer changes.

### For More Information...

Contact your local Applied Biosystems representative, the nearest office listed below or indicate reader service number 404.

*Patents pending

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## Limiting space-based military systems

An arms-control agreement that limits antisatellite systems, both space-based and ground-based, could be effective because compliance with the terms of the agreement could be verified (page 336). Military space systems, including satellites, ground stations, and electronic links, vary in their vulnerability to attack depending on the height of the satellite orbits, the "hardness" of materials and design, and the susceptibility of sensors to jamming and of the electronics to damage or false signals. If target satellites are hardened, effective laser antisatellite systems would have to be quite large and distinctive, and thus their testing and deployment would be verifiable. Other antisatellite threats could be alleviated by "rules of the road" that would govern space use. May recommends combining arms-control treaties (banning both ground-based and space-based antisatellite weaponry) and passive countermeasures (hardening existing satellites, developing rules of the road) for safeguarding space-based systems.

## Translocation and translation uncoupled

Protein translocation (movement through cellular membranes) is a process that, in higher eukaryote systems, is normally tightly linked spatially and temporally to protein translation (the construction of a protein from information in the cell's genetic material) (page 348). Perara *et al.* uncoupled translocation from translation for two proteins, one that is normally secreted and one that is normally integrated into cell membranes. The proteins were engineered so that they could attach to the membranes and be transported, could not grow longer because inhibitors of elongation were used, and could not be released from the ribosomes (the engines of protein synthesis) because termination sequences that signal release under normal circumstances were deleted. Translocation depended on continuous association of the protein chain with the membrane system and was a process that required energy. It appears to be driven by proteinaceous machinery in the membrane system of the cell. The ribosomes were found to be important structures for maintaining the translocation-competent state. Additional details of the translocation process, such as whether proteins are pushed or pulled through membranes, can now be studied.

## Carcinogenesis in epithelial cells

Eighty percent of human cancers are thought to arise from epithelial cells; thus, an epithelial cell culture system is a crucial tool for studying the genetic and cellular changes that take place in cells during malignant transformation and the ways in which carcinogens and oncogenes induce the process (page 385). Rhim *et al.* describe the establishment of an epithelial cell line first immortalized by exposure to DNA tumor viruses and then transformed by exposure to carcinogens. Growth and morphologic characteristics of the cells resembled those of malignant cells after exposure to the virus-carcinogen combination. Within a month of being injected into mice, the transformed cells induced tumors in the animals; these carcinomas contained cells of human origin. This system will be useful in evaluating the carcinogenic potential of environmental chemicals and for studying what genes are activated and suppressed in the multistep process leading to malignancy.

## Comet Giacobini-Zinner encounters ICE

September 11, 1985 was a historic day for comet studies: it was the day of the first encounter between a spacecraft and a comet (pages 353–385). Comet Giacobini-Zinner (cover), known since 1900 and orbiting with a 6.5-year period, was moving at 38.3 kilometers per second when the International Cometary Explorer (ICE) flew through its tail. ICE was launched in 1978 as a joint venture of the European Space Agency and NASA to study the interaction between the solar wind and Earth's magnetosphere. Its encounter with Giacobini-Zinner was not in the original plan; this clever afterthought (icing on the cake) took the spacecraft 50 times as far from Earth as it had been designed to go. Some of its 13 instruments collected and transmitted data that are helping in the characterization of the interactions between the solar wind and the comet, including identification and velocity measurements of ions and other particles in the tail and measurements of the strength and orientation of magnetic fields associated with the tail. ICE has just observed Comet Halley, although not at such close range, and some comparisons of features of the two comets will now be possible.

## Senescence factor

Old cells contain messenger RNA molecules that are associated with their diminished capacity to proliferate (page 393). Comparable RNA molecules are not detected in healthy young cells, but are detected (though in much lower abundance than in the old cells) in quiescent young cells deprived of growth factors. Lumpkin *et al.* show that, when the senescence-associated RNA is microinjected into healthy young cells, cell division is inhibited. The RNA may promote cellular senescence by directing synthesis of a protein that inhibits DNA synthesis and cell division. Tumors, in contrast, may be immortalized if the RNA, its protein, or its gene is somehow altered. With the RNA in hand, screening for the gene is now feasible. Characterization of the senescence-associated molecules and an understanding of their regulation may provide an explanation for the range of proliferative behaviors possible for cells: inhibited proliferation in aging cells, regulated proliferation in normal cells, and unchecked proliferation in tumor cells.

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# Survival Politics: Science and the Budget Dilemma

At the 11th AAAS Research and Development Colloquium (26 and 27 March) in Washington, D.C., the hearts and minds of the 400 participants were riveted on the wondrous workings of Gramm-Rudman-Hollings, a.k.a. the Deficit Reduction Act of 1986. No government speaker could predict the outcomes of the standoff between Congress and the Administration, much less the extent of the damage likely to befall funding for research and development. The good news was that the worst has already happened for the 1986 budget; the bad news was that under some scenarios the blow in 1987 could be much more damaging.

Not for the first time, the audience at the colloquium was advised to practice up on the martial arts, to climb into the ring and fight for their scientific lives, interests, and projects. The complaint is that legislators rarely hear from the scientists, who forget that reminders of their voting power are efficacious in inspiring legislators to do the right thing. There is a point to this, in that members of Congress are seldom visited by their scientific constituents during the long recesses when fence-mending and opinion-sounding are practiced. On the other hand, there is no lack of evidence that some universities have discovered the value of professional lobbying in persuading legislators to tuck money for special research facilities into appropriations bills. But the question is whether, in the long run, much semblance of balance and scientific merit in the conduct of research could survive the close and inelegant combat that pressure politics sooner or later becomes. It is one thing to systematically inform legislators about the consequences of allowing our scientific and engineering assets to depreciate with the concomitant danger to U.S. technological leadership, but quite another to employ the muscular tactics of the organized voting bloc. Perhaps a middle ground is to learn to thank legislators when they do stand up for science.

All this said, it is apparent that the overwhelming consensus for public investment in R&D is insufficient to avert damage to what Frank Press called the "ecology" of the research system in his remarks at the colloquium. In much of the ensuing discussion participants struggled with the question of the research community's ability to agree internally on strategies to preserve the core strengths of the system, as support dwindles. Here the issues pile up quickly: the upthrust of funding for defense-applied R&D while support for the nondefense sector rapidly ebbs; allocations to university-based special research centers as opposed to project support; the inevitable consequences of terminating support for student education; the displacement implications of costly megaprojects relative to general purpose research; and the fading chance to put a floor under the existing reinvestment deficit in the tools and facilities for research. Answers to these complex and confusing issues and to science's ability to find answers were not visible. But there was a strong sense that unless science produces some answers soon, government will produce them under the forcing pressures of its fiscal problems and its mainstream priorities.

Lost and unnoticed in the blizzard of the budget numbers is a significant data point. By the fifth year of the deficit-reduction plan now engraved in law, the discretionary region of federal expenditures—the area in which civil R&D reside—is programmed to fall to only 7 percent of total spending. The sleeper is that nondefense R&D will then occupy a startling fourth of the small discretionary pie. Here lies trouble, because such a conspicuous share of the controllable fraction of the budget is bound to draw heavy fire from every interest group that is feeling hunger pains.

At risk is the broad national consensus, supported by this Administration and all others since World War II, that strong financial support for basic research is not only critical to national strength but the almost exclusive responsibility of the federal government. If this can be reaffirmed by the President and Congress amid the confusion surrounding Gramm-Rudman-Hollings, the financial basis for the consensus can be stabilized. It is urgent for the scientific community to remind our political leaders of this and assist in the process of setting priorities. The clock is running.—WILLIAM D. CAREY and J. THOMAS RATCHFORD

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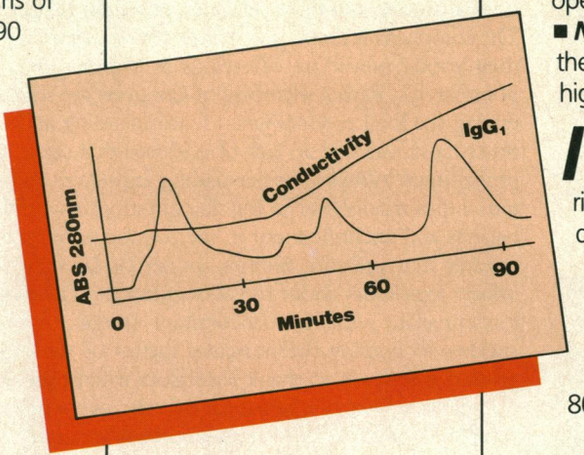


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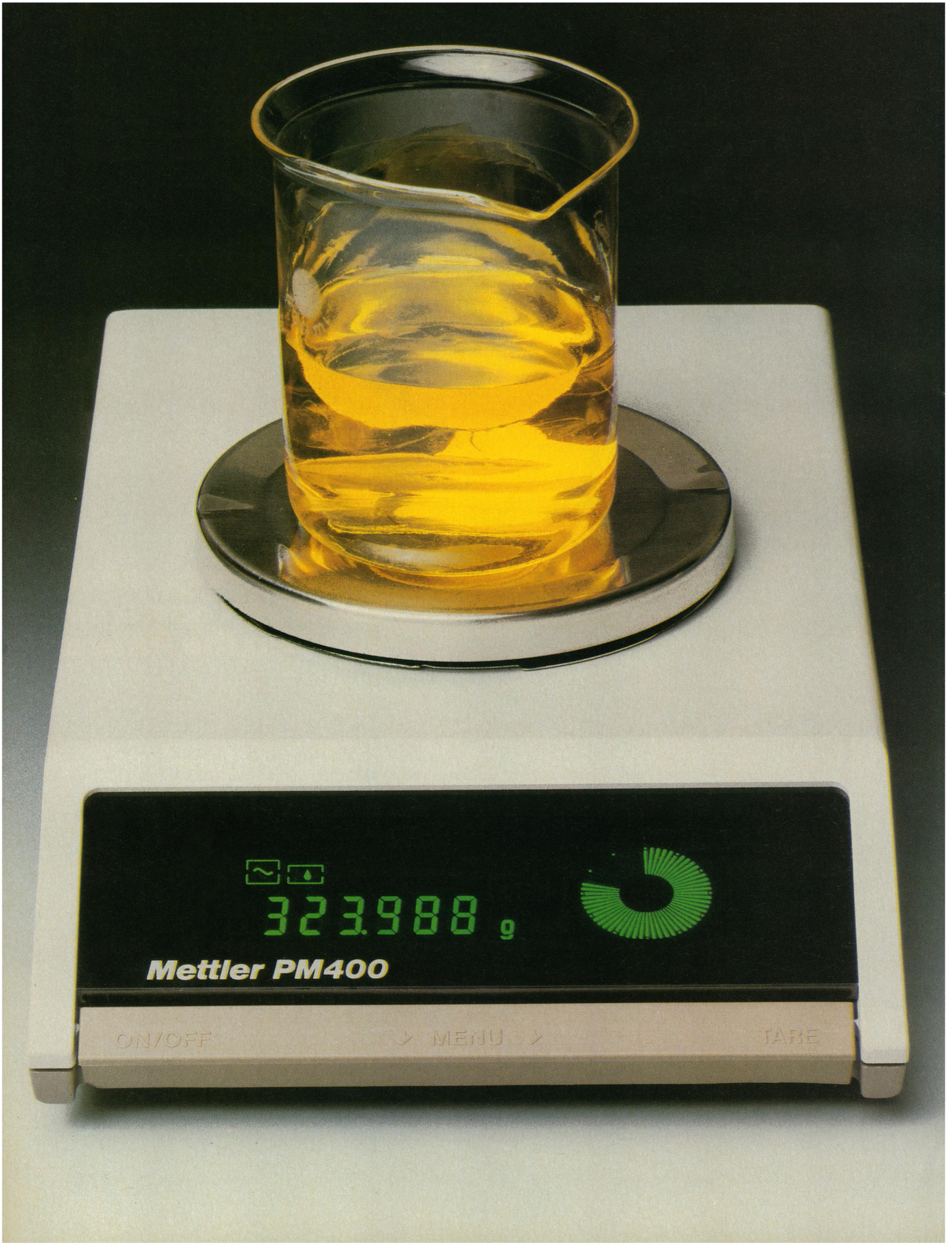
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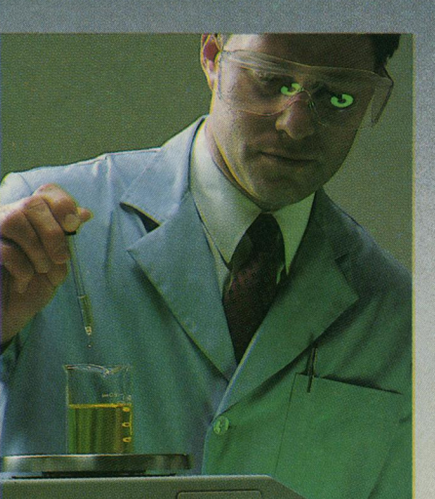

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