SCIENCE

19 July 1974

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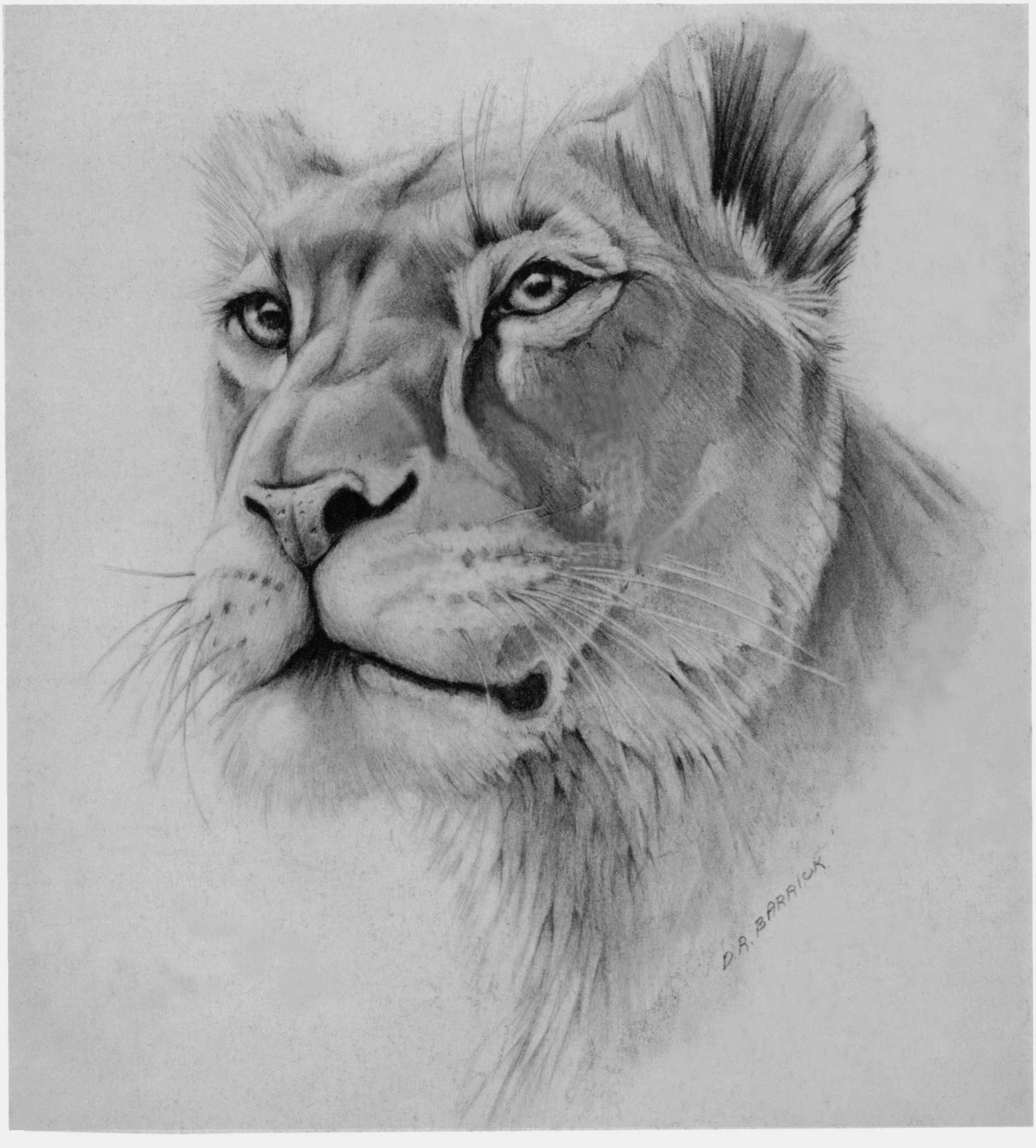
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



25 years in nuclear analysis

Over 25 years ago LKB was designing and building instruments for nuclear research. In fact, one of the earliest instruments developed for advanced work in the nuclear field was LKB's 200 million electron-volt synchrocyclotron, installed at Uppsala University in 1947.

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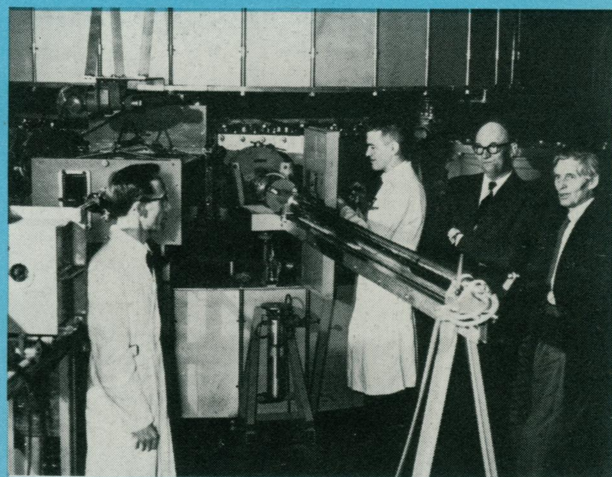

1947: LKB's 200MeV synchrocyclotron being installed at Uppsala University, Sweden.

A verbal montage of the state of science in the 70's

"Science is a constantly changing series of approximations," a scientist-philosopher pointed out.

Thus, each of the 36 interviews between scientists and journalists is a snapshot of a particular science at a particular time. But, summed up, these interviews offer a verbal montage of the state of science in the early seventies: progress in genetics, the difficulties of finding technological answers to natural disasters such as earthquakes, volcanoes, and hurricanes; the pulsating need to explore the worlds beyond—Mars, cosmic puzzles such as pulsars, the oceans. We continue to probe ourselves—the basis of our violent behavior, our evolution, the nurturing of our young . . .

Each of these interviews—like fragments of a jigsaw puzzle—tells little. Assembled, they give a panorama of science that is revealing of its depth, its breadth, and its dynamic state.

Speaking of Science

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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

COVER

Lioness. See page 284. [Dean Barrick, Seattle, Washington]

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Targets

The targeting of research has always been with us, but it has lately become a more insistent theme. This stems, in part, from the demands of an increasingly informed public which looks to science for the prompt solution of an array of troublesome problems. As the fraction of the federal budget assigned to research and development in health, ecology, energy, space, and many other areas of science has increased, the taxpaying citizen has properly exhibited increasing interest in the selection of specific areas in which research is to be pursued. The taxpayer pays the piper and with some justification demands, if not to call the tune, at least to contribute to the cacophony.

The word "target" is one of a number of terms derived from the military which have been adopted by science, perhaps as a consequence of the shotgun marriage between scientist and soldier which took place during World War II. Other military words and phrases now somewhat incongruously but firmly fixed in the scientist's jargon are "strategy" and "task force."

A target, we may take it, is a special kind of a goal. It is well defined and clearly visualized, falling within the direct line of sight of the eye or, at the very least, of the mind's eye of the observer. He knows beforehand what the target looks like and has ways of ascertaining whether a hit has been scored. He need only muster his task force, assemble his ammunition, determine his strategy, and bang away.

Yet, targets are sometimes deceptive. Occasionally they may prove to be mirages. Not infrequently the map is inaccurate or is misread. The judgment of target size and distance may be erroneous, the estimate of munition needs may be faulty. As in war, so in science one of the most difficult judgments the investigator is called upon to make is the selection of a target towara the conquest of which he will dedicate his resources.

From the pages of history comes an anecdote that may prove illustrative. During the War of 1812, an arm of the British Royal Navy was cruising in Chesapeake Bay. At dusk on the evening of 10 August 1813, the ships approached the harbor of the modest fishing village of St. Michaels, on the Eastern Shore of Maryland. The British command, sensing that it had found a vulnerable target, neglected to send a spy ashore to case the joint. It therefore did not learn that the villagers, aware of their peril, had all agreed to extinguish every light in the village and hang all available lanterns on the branches of trees in a nearby forest. The ruse worked magnificently, and all night long the British ships lobbed cannonballs, most of which fell harmlessly among the trees. St. Michaels is known to this day as "The town that fooled the British."

The morals of this tale are self-evident.

1) The identification of the proper target may be more difficult than is generally supposed.

2) Aiming at the wrong target can be enormously costly in terms of ammunition and other resources.

3) In selecting a target, one should secure and study the latest and most sophisticated available information. This conclusion is equally true whether the target be military or scientific.—DEWITT STETTEN, JR., *Deputy Director for Science, National Institutes of Health, Bethesda, Maryland 20014*

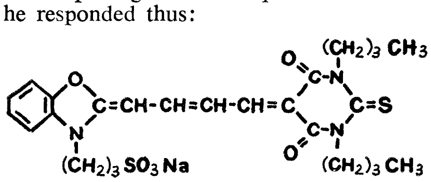
A membrane potential spike becomes a light flash with Kodak's Merocyanine 540

This dye can now be ordered as EASTMAN 14014.* A report in *Nature New Biology 241:* 159 (1973) tells how a group at Yale stained giant axon from squid with it, illuminated at 540 nm, and recorded fluorescence redward of 590 nm in response to electrical stimuli. The fluorescence lagged the action potential by less than 50 μsec. With good linearity found between the fluorescence intensity and the potential as measured with an internal electrode in the axon, optimism is expressed that electrodes may no longer be needed to pick up membrane potential spikes. We hope this is no flash in the pan.

What happened

Contact was initiated by L. B. Cohen, Department of Physiology, Yale University School of Medicine. He had heard that at the Kodak Research Laboratories new dye molecules are constantly being designed and constructed. According to the tales one hears, we have been putting together a few new dyes each working day for the past 50 years. Suspecting that such tales are not altogether apocryphal, Cohen told the Kodak Research Laboratories what he wanted a dye to do and asked that it be provided to him. Just like that.

Inexplicably, a warm, cordial letter informing Doctor Cohen that the Laboratories do not operate that way failed to go out. Instead, our D. W. Heseltine, a leading molecular architect, found himself contemplating Cohen's request. To which he responded thus:



Just like that. Zap. Call it Merocyanine 540. After a decent interval, dark crystals of Merocyanine 540 arrived in New Haven, where Cohen in company with H. V. Davila, B. M. Salzberg, and A. S. Waggoner got it into their seawater at a final dye concentration of 0.05 mg/ml, with 1% ethanol and 0.025% surfactant polyol.

There is reason to brag. The spike of intensity increase above resting fluorescence is five times larger than the authors had seen with any of over 150 dyes before Merocyanine 540. There is also reason to be modest: that great spike represents a change in resting fluorescence of about one part in 10^3. Perhaps if Heseltine had worked harder, that 10^{-3} might have been 10^{-2}, or 5% or even 20%. The thought nags.

Perhaps a better fluorochrome than Merocyanine 540 might turn up in a large paper bag of hundreds of little vials of dye samples from Heseltine's shelves. Reasons why a business executive, accountant, or lawyer might turn down a neurophysiologist's request for such a bag would not be well understood by the neurophysiologist. For screening at the seashore by the great axon of *Loligo pealii,* Cohen *et al* want many more dyes than the mere 15 Heseltine sent after Merocyanine 540. None of them was as good. Like Merocyanine 540, they had been designed for another purpose. Now the purposes of the neurophysiological laboratory interest Heseltine.

*From a lab supply house, or at $38.50 for 1 g from Kodak, Organic Chemical Sales, Rochester, N. Y. 14650. Price subject to change without notice.

Kodak

Since long before molecular biology turned on the light of fluorescence to see by, we have been marketing biological stains. With changes in the textile-dye industry, we have had to start making many a dye that we formerly were able to buy and have certified for laboratory use. As a result, quality is up. We do seek opportunity to put our competence with dyes at the service of the life scientist. Inquiries should impart nothing confidential, should be directed to G. S. Grau, Dept. 742B, Kodak, Rochester, N. Y. 14650 *(not to the Kodak Research Laboratories!),* and might say something like, "Your EASTMAN XXXXX is fine as far as it goes, but what I and my buddies really want to buy for money is [ ]."

For starters, here is a list of EASTMAN Organic Chemicals believed to shine forth in some useful way as fluorescent probes or fluorescent stains for proteins:

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10296	8-Anilino-1-naphthalenesulfonic Acid
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10990	8-Anilino-1-naphthalenesulfonic Acid Magnesium Salt
11512	8-Anilino-1-naphthalenesulfonic Acid Ammonium Salt
11128	N-[p-(2-Benzoxazolyl)phenyl]maleimide
11502	4-Chloro-7-nitrobenzo-2-oxa-1,3-diazole
11514	4-Dimethylamino-4′-isothiocyanatostilbene
11313	4-Dimethylamino-4′-maleimidostilbene
9090	5-Dimethylamino-1-naphthalenesulfonyl Chloride
11218	5-Dimethylamino-1-naphthalenesulfonic Acid
11808	N,N′-Dioctadecyloxacarbocyanine p-Toluenesulfonate
C10868	5-Fluorescein Isothiocyanate (Cert.)
P7281	8-Hydroxy-1,3,6-pyrenetrisulfonic Acid Trisodium Salt (Pract.)
11615	9-Isothiocyanatoacridine
11970	3-Isothiocyano-1,5-naphthalenedisulfonic Acid Disodium Salt
11886	Lissamine Rhodamine B Sulfonyl Chloride
14014	Merocyanine 540
11829	7-(p-Methoxybenzylamino)-4-nitrobenz-2-oxa-1,3-diazole
6566	1-Pyrenebutyric Acid
11439	5(6)-Rhodamine B Isothiocyanate
C2245	Rose Bengal (Cert.)
10613	6-p-Toluidino-2-naphthalenesulfonic Acid
10591	8-p-Toluidino-1-naphthalenesulfonic Acid
11002	6-p-Toluidino-1-naphthalenesulfonyl Chloride