

7. J. F. Hamilton and P. C. Logel, *Photogr. Sci. Eng.* **18**, 507 (1974).
8. H. E. Roscoe and A. Schuster, *J. Chem. Soc.* **27**, 942 (1874); E. Wiedemann and G. C. Schmidt, *Ann. Phys. (Leipzig)* **57**, 447 (1896).
9. H. G. Smith, *Proc. R. Soc. London, Ser. A* **106**, 400 (1924).
10. K. P. Huber and G. Herzberg, *Constants of Diatomic Molecules* (Van Nostrand, New York, 1981).
11. J. A. Pople, R. Seeger, K. Raghavachari, *Int. J. Quantum Chem. Symp.* **11**, 149 (1977).
12. H. F. Schaeffer, Ed., *Modern Theoretical Chemistry* (Plenum, New York, 1977).
13. K. Sattler, J. Muhlbach, E. Recknagel, *Phys. Rev. Lett.* **45**, 821 (1980).
14. A. Herrmann, E. Schumacher, L. Woste, *J. Chem. Phys.* **68**, 2327 (1978).
15. J. L. Gole, G. J. Green, S. A. Pace, D. R. Preuss, *ibid.* **76**, 2247 (1982).
16. T. G. Dietz, M. A. Duncan, D. E. Powers, R. E. Smalley, *ibid.* **74**, 6511 (1981).
17. V. E. Bondybey and J. H. English, *ibid.* **73**, 42 (1980).
18. G. A. Ozin, *Catal. Rev., Sci. Eng.* **16**, 191 (1977).
19. D. M. Lindsay and G. A. Thompson, *J. Chem. Phys.* **77**, 1114 (1982).
20. D. P. DiLella, W. Limm, R. H. Lipson, M. Moskovits, K. V. Taylor, *ibid.*, p. 5263.
21. J. C. Miller and L. Andrews, *Appl. Spectrosc. Rev.* **16**, 1 (1980).
22. C. A. Baumann, R. J. VanZee, S. V. Bhatt, W. Weltner, *J. Chem. Phys.* **78**, 190 (1983).
23. V. E. Bondybey and J. H. English, *ibid.* **74**, 6978 (1981).
24. ———, *ibid.* **76**, 2165 (1982).
25. W. Demtröder et al., *ibid.* **51**, 5495 (1969).
26. R. Velasco et al., *ibid.*, p. 5522.
27. P. Ohez, P. Jaegle, S. Leach, M. Velghe, *J. Appl. Phys.* **40**, 2545 (1969); R. A. Bingham and P. L. Salter, *Anal. Chem.* **48**, 1735 (1976).
28. K. A. Lincoln, *J. Mass. Spectrosc. Ion Phys.* **2**, 75 (1969).
29. V. E. Bondybey, M. Heaven, T. A. Miller, *J. Chem. Phys.* **78**, 3593 (1983).
30. M. Heaven, T. A. Miller, V. E. Bondybey, *ibid.* **87**, 2072 (1983).
31. V. E. Bondybey and J. H. English, *ibid.* **79**, 4746 (1983).
32. V. E. Bondybey, G. P. Schwartz, J. H. English, *ibid.* **78**, 11 (1983).
33. P. E. Cade and A. C. Wahl, *At. Data Nucl. Data Tables* **13**, 339 (1974).
34. C. F. Bender and E. R. Davidson, *J. Chem. Phys.* **47**, 4972 (1967).
35. C. E. Dykstra, H. F. Schaeffer, W. Meyer, *ibid.* **65**, 5141 (1976).
36. M. R. A. Blomberg and P. E. M. Siegbahn, *Int. J. Quantum Chem.* **14**, 583 (1978).
37. R. O. Jones, *J. Chem. Phys.* **71**, 1300 (1979).
38. R. J. Harrison and N. C. Handy, *Chem. Phys. Lett.* **98**, 97 (1983).
39. B. H. Lengsfeld, A. D. McLean, M. Yoshimine, B. Liu, *J. Chem. Phys.* **79**, 181 (1983).
40. V. E. Bondybey and J. H. English, *ibid.* **80**, 568 (1984); V. E. Bondybey, *Chem. Phys. Lett.* **109**, 436 (1984).
41. J. M. Brom, W. D. Hewett, W. Weltner, *ibid.* **62**, 3122 (1975).
42. D. J. Frurip calculated the thermodynamic properties and equilibrium constants of Be₂ from our experimental data.
43. E. U. Condon, *Phys. Rev.* **32**, 858 (1928).
44. D. L. Rousseau and P. F. Williams, *Phys. Rev. Lett.* **33**, 1368 (1974).
45. K. K. Yee and R. F. Barrow, *J. Chem. Soc., Faraday Trans. 2* **68**, 1181 (1972).
46. J. G. Pruett and R. N. Zare, *J. Chem. Phys.* **62**, 2050 (1975).
47. M. Heaven, T. A. Miller, J. H. English, V. E. Bondybey, *Chem. Phys. Lett.* **91**, 251 (1982).
48. M. M. Goodgame and W. A. Goddard, *Phys. Rev. Lett.* **48**, 135 (1982).
49. A. B. Anderson, *J. Chem. Phys.* **69**, 4046 (1976); W. Klotzbüchen and G. A. Ozin, *Inorg. Chem.* **16**, 984 (1977).
50. J. Harris and R. O. Jones, *ibid.* **70**, 830 (1979).
51. P. Correa de Mello, W. D. Edwards, M. C. Zerner, *J. Am. Chem. Soc.* **104**, 440 (1982).
52. Y. M. Efremov, A. N. Samoilova, L. V. Gurvich, *Opt. Spectrosc. (U.S.S.R.)* **36**, 381 (1974).
53. D. L. Michalopoulos, M. E. Geusic, S. G. Hansen, D. E. Powers, R. E. Smalley, *J. Phys. Chem.* **86**, 3914 (1982).
54. S. J. Riley, E. K. Parks, L. G. Pobo, S. Wexler, *ibid.* **79**, 2577 (1983).
55. V. E. Bondybey and J. H. English, *Chem. Phys. Lett.* **94**, 443 (1983).
56. I thank K. Raghavachari for our useful discussions and T. Dunning for providing theoretical potentials of Be₂⁺ prior to publication.

The 1984 Nobel Prize in Physics

The 1984 Nobel Prize in Physics was shared between Carlo Rubbia and Simon Van der Meer. Rubbia and Van der Meer were recognized for "their decisive contributions to the large project, which led to the discovery of the field particles W and Z, communicators of the weak interaction."

The massive experiment, carried out at CERN, the European Center for Nuclear Research, which is located near Geneva, involved two major innovations. One had to do with accelerator science, the other with particle detectors. The results were announced early in 1983, making this one of the shortest "waiting" intervals in Nobel history.

Simon Van der Meer is a soft-spoken and gifted inventor with a high order of analytical ability. He was born in 1925 and is a graduate of the Technische Hogeschool in Delft. His invention of "stochastic cooling" is subtle and required insight and the ability to do rather complex, statistical calculations. It was a crucial element in the process of discovering the W and Z particles.

Carlo Rubbia, 50, is an exuberant extrovert, famous in his circle for unlimited energy and enthusiasm combined with a

broad-ranging and deep understanding of physics. He attended the Scuola Normale in Pisa, where his teachers frequently compared him with a famous predecessor, Enrico Fermi. In the course of his Nobel research, Rubbia worked hard on the accelerator problems, assembled the group of over 100 Ph.D.'s, and led them in the design and construction of the most complex particle detector ever built. He found time to fulfill his obligations as professor of physics at Harvard, helping, in the course of his commuting between Cambridge and CERN, to alleviate the financial plight of several airlines.

The identification of the W and Z culminates a 50-year history of the weak force. The first suggestion that the weak interaction is mediated through an intermediate boson field was made by Yukawa (1) in his 1935 paper which proposed that the strong forces holding nuclei together were communicated by a massive particle, later named the pion. Yukawa hoped that the exchange of pions would also do for the weak force. However, after the fall of parity in 1957, the structure of the weak force required a spin 1 (vector) mediator. The idea was taken up

by a very large number of theorists, gradually refining and embellishing the properties of the W and adding the neutral component, Z. It is the stuff of brave scholars to give proper credit here. The theoretical work culminated in the electro-weak theory, elegantly described by Sidney Coleman (2) for the 1979 Nobel Award to Sheldon Glashow, Abdus Salam, and Steven Weinberg.

The experimental threads begin with the searches for W's carried out in the high energy neutrino experiments of 1964–65 at Brookhaven National Laboratory in New York and at CERN. The W would be produced in association with a charged muon when muon-type neutrinos impinged on a material target. Subsequently the W would decay into another charged muon and a neutrino. The trick was to observe two muons, one having a transverse momentum of half the W mass. At this time, the W mass was completely unknown, but the non-observation of the above reaction established a lower limit to the W mass of about two proton masses. Soon thereafter, two U.S. groups developed a technique for seeking W's in strong interaction collisions where the entire energy and intensity of the primary beam of 26 billion electron volts (GeV) (at Brookhaven) was used in the production process. Now the limit was raised to approximately five proton masses. This line of research was abandoned in the 1970's when the advances in weak interaction experiments gradually established the credibility of the unified electro-weak theory and its predictions of the masses



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of the W and Z. These were close to 100 proton masses or 100 GeV. The predictions presented an irresistible challenge to experimentalists. The coup de grace of the new synthesis would be to produce W's and Z's in high energy collisions of ordinary particles and to observe the subsequent decays to lighter particles, as predicted by the theory.

The key experimental problems were fairly clear from the outset: (i) particles would have to be accelerated to energies high enough to permit the creation of the new, very heavy particles; (ii) the intensities of the accelerated particles would have to be large enough for reasonable numbers of W's and Z's to be produced during typical data collection periods lasting a few weeks or months; and (iii) the decay products of the conjectured particles would have to be detected efficiently and with enough resolution that potential background processes would not overwhelm the anticipated signals. The solutions to these problems on a short time scale were not so clear.

Rubbia and Van der Meer made strikingly original and important contributions in all of these areas and, together with their colleagues at CERN and elsewhere, put together in a remarkably short time an accelerator-detector complex that set new standards in particle physics. This complex continues to make frontier discoveries several years after the original W and Z discoveries were made.

The requisite energy was achieved by colliding beams of protons and antiprotons that circulated in opposite direc-

tions in the CERN Super Proton Synchrotron (SPS). The SPS was built in the early 1970's to provide beams of protons with energies up to 400 GeV that could be focused onto material targets for a wide variety of experiments. The SPS and its sister machine at the Fermi National Accelerator Laboratory (Fermilab) near Chicago were the highest energy accelerators in the world in the 1970's, but their protons were available only in batches every few seconds, and they could be used only with stationary targets. The maximum energy available for creating new particles when 400-GeV protons impinge on a stationary target is about 27 GeV, well below the 100 GeV thought to be needed for producing the W and Z particles. A conventional fixed-target accelerator would have to have a minimum of 5000 GeV in order to produce W's. However, if beams collide head on, the energy available for producing new particles is equal to the sum of the individual beam energies.

By the mid-1970's, colliding beams of electrons and their antiparticles, positrons, had become a powerful tool for studying the subnuclear world. It appeared that electron-positron colliders would be the method of choice for uncovering the W and Z bosons. Unfortunately, when accelerated to very high energies in storage rings, electrons and positrons radiate large fractions of their energies in the form of synchrotron radiation. Storage rings of ever increasing radius must be used to cope with the synchrotron radiation from higher energy beams. This problem does not arise

with protons and antiprotons because they are much heavier than electrons and positrons. The electron-positron colliders being built in the late 1970's would not reach even one-half of the energy expected to be needed for producing the Z^0 , and less than one fourth of the energy required for seeing the W's. In the 1970's, a colliding proton-proton machine, the intersecting storage ring (ISR), was constructed at CERN. This consisted of two intertwined rings of counterrotating protons intersecting in eight places. Each ring had a top energy of about 30 GeV. This was far from adequate. A colliding proton-antiproton machine based on an invention of G. I. Budker (3), was under construction in Novosibirsk in the Soviet Union and was designed to go to 25 GeV. Budker realized that antiproton-proton collision had the great virtue of requiring only a single storage ring in which protons and antiprotons counterrotate. The drawback was that antiprotons were rare particles and would have to be accumulated. Budker invented a method of dampening the oscillations of a beam of particles circulating in a storage ring. The dampening (or cooling) was accomplished in the Budker scheme by mixing the "hot" antiprotons with an accompanying intense, coherent (hence cool) stream of electrons. In 1968, Van der Meer invented an alternative scheme for cooling particles. This scheme, described below, was not widely known or understood at that time; for example, the 1974 proposal for the construction of ISABELLE contained a discussion of an antiproton collider option, but cooling was not included. By 1976, the principle of Van der Meer's stochastic cooling idea had been successfully tested on protons at the ISR (4).

Thus, by the mid-1970's, the state of the art in colliding beam machines, both electron and proton, was well developed but was confined to energies far below those needed for W's and Z's. If normal evolutionary trends were to be followed, one could be confident that a new generation of accelerators would finally reach the desired goal within 10 to 15 years. But Carlo Rubbia was unwilling to wait so long. In 1976, together with three American colleagues, he proposed to Fermilab and CERN that their existing 400-GeV accelerators be outfitted with antiproton coolers and converted to proton-antiproton colliders (5). Fermilab was committed to building a new superconducting accelerator, but CERN formally accepted the proposal and gave the project unstinting support.

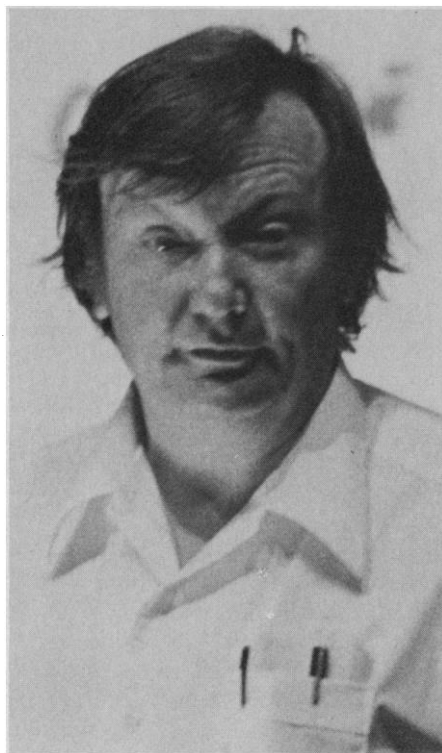
A superb group of accelerator physi-

cists and engineers under the leadership of Van der Meer and Roy Billinge soon began the preparations for transforming the SPS fixed-target accelerator into a storage ring for proton-antiproton colliding beams. One necessary change was to reduce the maximum beam energy to 270 GeV to avoid overheating the accelerator magnets during storage ring operations. The total collision energy of 540 GeV still seemed ample for producing W's and Z's, however.

By far the biggest problem facing the accelerator team was to produce and store enough antiprotons in the SPS to allow a chance of seeing the predicted new particles. Antiprotons do not exist in ordinary matter; they must themselves be produced in high energy particle collisions, albeit at energies considerably below those needed for the W and Z. At CERN, intense bunches of protons are extracted every 2.4 seconds from a lower-energy accelerator known as the proton synchrotron, and they strike a tungsten rod, making about one million antiprotons on average. These bunches of antiprotons must be accumulated for an entire day to obtain enough for storage in the SPS.

The accumulation of all these antiproton bunches presented a fundamental problem in accelerator physics. Gathering up many bunches of particles in an accelerator is like the problem of a man gathering a large load of firewood. Every time he tries to pick up a new log, one of the others falls out of his arms. In the case of accelerators, new particles are injected into stable orbits by the application of special pulsed electric and magnetic fields. If there are already particles on those orbits, the fields deflect them out of their stable orbits and they eventually strike the walls of the accelerator vacuum chamber and are lost from the beam. This is a consequence of a general law describing many physical systems known as Liouville's theorem. Thus after relatively few antiprotons are stored, the introduction of more will kick out as many as are added, and further accumulation of antiprotons is halted.

It was Van der Meer, beginning in 1968, who broke through this seemingly hopeless situation in a series of profound and beautiful studies of the statistical properties of the motion of large numbers of particles in accelerators. The essence of his idea is that with suitable arrangements of pickup electrodes and amplifiers, the actual orbits of individual particles can be measured. From the orbit information, correction signals can be generated to modify each particle's trajectory to some common one. This



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technique, invented by Van der Meer and refined by him and others, notably Hugh Hereward, Dieter Möhl, Frank Sacherer, and Lars Thorndahl, all of CERN, is known as stochastic cooling. Cooling refers to the fact that the density of particles in the beam is increased when such a pickup and correction system is applied, much as the density of a gas is increased when it is cooled. Cooling allows all particles in the machine to be "parked" out of the way of the newly incoming particles without violating Liouville's theorem. The pickup and correction system then moves the fresh particles to the parking orbit, allowing another batch to be injected into the machine, and the entire process is repeated until the desired number of antiprotons is accumulated.

The key to measuring and correcting individual particle orbits is to make the measurement in a very short time. Because the particles are distributed at random around the circumference of the accelerator or storage ring, if the time is sufficiently short, only one particle will be detected by the pickup electrodes and correction amplifiers. The correction signal can then be sent directly across the storage ring in time to meet the particle at a correction electrode, the particle having taken a longer circular path. Making such measurements and corrections in very short intervals of time implies a very large bandwidth for these electronics systems. In practice, it is not possible

to achieve bandwidths large enough for the ideal correction scheme described here, and signals from other particles tend to mask the desired signal, thus limiting the number of particles that can be cooled. Nevertheless, significant cooling and accumulation can still be obtained in real systems.

Stochastic cooling for the SPS proton-antiproton collider was provided by a special storage ring, called the AA (antiproton accumulator) ring, built by the CERN accelerator group. It uses several sets of pickup and correction electrodes and special large-bandwidth amplifier systems. After antiprotons are collected in the AA ring for about 24 hours, the dense beam is transferred to the SPS along with a beam of protons, and colliding beam experiments can begin. The beams continue to circulate in the SPS for several hours. The development of the AA ring is a monumental achievement in accelerator science.

As the accelerator activity progressed, Rubbia devoted his energies to constructing the detection apparatus needed to observe the W and Z particles. He assembled a collaboration of 135 physicists from 12 universities and laboratories in Europe and the United States to build the large general-purpose detector known as UA-1. This large device, weighing over 2000 tons and using tens of thousands of sensitive electronics channels to record the products of proton-antiproton collisions, set a new standard for detectors in colliding beam experiments. As the instruments of modern science grow more complex, the requirements for large collaborative groups is an ever increasing phenomenon. Among the many sociological problems raised, one is the fair assignment of recognition. In the case of the 1984 Nobel award there is very little, if any, controversy about the selection of Rubbia and Van der Meer.

It was widely recognized that detectors for proton-antiproton colliding beam experiments must be capable of handling very large numbers of particles produced in these violent collisions. It is not uncommon for 100 particles to be created in a single proton-antiproton interaction. Thus, detectors for these experiments are inherently very complex. The important new ingredient that Rubbia emphasized in his design of UA-1 was the need to measure accurately the energies and directions of as many of these particles as possible over the full space surrounding the collision point. His reason was that a characteristic signature for new phenomena would likely be the emission of neutrinos. Neutrinos themselves pass through any practical detector without

leaving a trace, but by measuring all of the other particles in the event, the presence of neutrinos could be deduced by imbalances of energy and momentum. Next, Rubbia used multiple detection techniques along the paths of all particles so that electrons, photons, and muons could be identified with high reliability. These particles are also harbingers of new physics. Such considerations were essential because only about one W or Z particle was expected for every hundred million proton-antiproton interactions.

As in the case of the SPS-AA complex, UA-1 was constructed in an amazingly short time, and it began to take data in 1981. A second major detector known as UA-2 was also constructed during this period. It was built by a collaboration of approximately 60 physicists from six European institutions, under the leadership of Pierre Darriulat and Luigi DiLella, both of CERN. The UA-2 is somewhat simpler than the UA-1 apparatus, but it is used to deal with many of the same physics questions.

Both the UA-1 and UA-2 experiments resulted in a number of important observations during the early running. Most notable was the detection of very clean

jets of hadrons that follow from the quark-gluon substructure of protons and antiprotons. By the end of 1982, enough data had accumulated for signs of the long sought W's to be seen. The signature was quite clear; each group of investigators had a few events containing a very energetic electron produced at large angles with respect to the colliding beam direction, but with no other visible particles to balance the electron's transverse momentum. In early 1983, both groups published their findings, which were fully consistent with predicted properties of the W boson. UA-1 had six events (6), whereas UA-2 presented four events (7). Soon thereafter, both groups obtained equally convincing evidence for the Z^0 . In this case, the production rates are expected to be lower than those for the W, but the experimental signatures are easier to interpret. By the end of 1983, Rubbia's group had collected some 50 W events and five Z^0 events, and the experimenters were using the data to learn more about the nature of the production process. Given the previous successes of the unified electro-weak theory, these results were immediately accepted as conclusive evidence for the existence of

the W and Z bosons. This exploit closed the 50-year-old quest for a clarification of the weak force, but the technique that evolved opens a new phase of research in elementary particle physics. Henceforth, all new colliding beam accelerators and detectors will look back on the model pioneered by the 1984 Nobel laureates in physics.

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References and Notes

1. H. Yukawa, *Proc.-Math. Soc. Jpn.* **17**, 48 (1935).
2. S. Coleman, *Science* **206**, 1290 (1979).
3. G. I. Budker, *At. Energ.* **22**, 246 (1966).
4. S. Van der Meer, "Stochastic damping of betatron oscillations in the ISR CERN" ISR PO-72-31 [see also *Phys. Rep.* **58**, 73 (1980)].
5. D. B. Cline, P. McIntyre, F. Mills, C. Rubbia, Fermilab Report TM 687 (1976).
6. UA-1 Collaboration, *Phys. Lett. B* **122**, 103 (1983); *ibid.* **126**, 398 (1983).
7. UA-2 Collaboration, *ibid.* **122**, 476 (1983); *ibid.* **129**, 130 (1983).

RESEARCH ARTICLE

B Lineage-Specific Interactions of an Immunoglobulin Enhancer with Cellular Factors in Vivo

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Enhancers are DNA sequences that increase the level of transcription from some promoters when placed within several kilobases of them (1, 2). Mouse immunoglobulin heavy chain genes contain a tissue-specific enhancer, which is located in the intron separating the V region J segment and the constant region (Fig. 1) (3-5). The immunoglobulin heavy chain genes are extensively transcribed in myeloma cells. Cloned copies of these genes are also efficiently transcribed when transfected into cells of the B lineage but not in non-B cells such as L cells, HeLa cells, or lung cells (3, 4).

Analysis of deletions showed that removal of a portion of the intron of the immunoglobulin γ_{2b} gene greatly reduces the level of transcription of the gene upon its transfection into myeloma cells (3). Further experiments revealed that restitution of a 990 base-pair fragment of DNA from the intron to these deletions restores high level transcription in myeloma cells and that this restoration is

independent of both the position and the orientation of the fragment (3). A smaller fragment, 307 base pairs in length (Fig. 1, base pairs 376 to 683) is capable of enhancing transcription in myeloma cells from heterologous promoters and genes such as β -globin and SV40 T antigen (4).

How enhancers work is not known. Although viral transcription enhancers function in most cells regardless of species or tissue of origin, they are most active in cells that are the virus's natural hosts (6-8). The immunoglobulin heavy chain enhancer has a somewhat more restricted tissue specificity and functions most efficiently in cells of the B lineage (3, 4). It seems likely that enhancer activity is related to and dependent on specific cellular factors. In the case of an enhancer showing tissue specificity one might expect to find proteins binding to the enhancer only in cells in which the enhancer is active.

Proteins that interact with specific sequences can prevent or increase the methylation by dimethyl sulfate (DMS)

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