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Max Perutz, James Watson, John Kendrew and Francis Crick talk to a BBC presenter (centre) about their Nobel prizes in 1962.

What makes a great lab?

William Bynum reflects on the factors that have brought nine Nobel prizes to the UK Laboratory of Molecular Biology in Cambridge.

What makes an outstanding laboratory? There have been a number of these special places during the past couple of centuries, but none more so than the Laboratory of Molecular Biology (LMB) in Cambridge, UK, which is celebrating 50 years since it got its own building and, this week, 50 years since four of its scientists were awarded Nobel prizes — Max Perutz, John Kendrew, James Watson and Francis Crick.

Overall, the LMB can claim nine Nobel prizes for 13 staff scientists during its illustrious history, plus another eight for those who trained or worked there temporarily. As a unit within the Cavendish Laboratory at the University of Cambridge, the LMB had a distinguished pre-history. Few would have dared to predict that its independent existence would be so successful and productive. Seen historically, however, it shares characteristics with other outstanding laboratories. These include new methods of producing scientific knowledge, novel approaches to training researchers, the innovation and excitement that surround an emerging scientific field and, perhaps most centrally, the presence of a gifted individual with the personality and vision to make things happen.

The LMB can thus be seen as a modern exemplar of a species that goes back to the early nineteenth century. Previous centres of excellence had differing ambiences, which reflected the scientific cultures of their times. But all share a few important star qualities. In search of these, here I briefly examine three of the LMB's ancestors and its parent laboratory.

LABORATORY LIFE

Before the nineteenth century, most laboratories were places in which single individuals worked, sometimes aided by an assistant or two. Chemist Antoine Lavoisier (1743–94), with his wife at his side, was typical. Wives and servants often helped. Justus von Liebig (1803–73) changed this pattern definitively.

Liebig's chemistry laboratory at the University of Giessen in Germany opened in 1826 and acquired international renown. It attracted students from all over Europe and earned Liebig a reputation as a 'chemist breeder'. His lab was an early example of the research and teaching establishments that made the German universities the envy of many. It began as a single room, with a fire in the middle surrounded by work benches. Liebig's work on the compositions of chemical substances and their reactions was outstanding, and his focus on agricultural, industrial and biological issues gave his research a highly topical flavour.

He trained his protégés carefully, especially in qualitative analysis. Students flocked to him, with the result that European chemistry during the middle of the nineteenth century bore a distinctly Liebigian flavour as his students moved to influential positions elsewhere. The identification of state-of-the-art problems and the training of students to solve them characterize his achievements. Liebig's initiative was widely adapted in the natural and biomedical sciences throughout the German university system.

Training was also part of the brief of physiologist Ivan Pavlov (1849–1936), but he brought his own organizational genius to bear on the 'physiology factory' that he masterminded in St Petersburg, Russia, famously studying dogs. He adapted aspects of manufacturing to the production of scientific knowledge. Pavlov's staff were among the first to specialize in different tasks: surgical, chemical, dog handling. The dogs were also specialized. Many had permanent gastric fistulas; some had oesophageal or pancreatic ones or other surgical interventions that allowed Pavlov to examine physiology *in situ*.

Pavlov's 'laboratory' eventually occupied a whole building — already nearer to the modern usage of the word, and a far cry from the single rooms of most researchers of earlier times. As science has become more complex and cooperative, so the physical structures of laboratories have evolved faster than the language we use to describe them.

The next example reinforces this point: Thomas Hunt Morgan (1866–1945) and his Fly Room at Columbia University in New York. It was more than just a room. Modern experimental genetics was born there, with the fruitfly (*Drosophila melanogaster*) as the prize experimental subject. The fly's rapid breeding time and four large chromosomes made it ideal for examining how chromosomal events during meiosis and mitosis relate to the structural features of the adult. A chance finding of a fly with a white eye — instead of the usual red — led Morgan to the importance of the sex chromosome.

Morgan was a gifted scientist who surrounded himself with equally gifted students and postdoctoral researchers, including Alfred Sturtevant, Calvin Bridges and Hermann J. Muller. Although Morgan was a patrician from the US South, he ran his lab on egalitarian lines, with the consequence that historians still debate the relative contributions of the different parties. Morgan won a Nobel prize by himself in 1933, although he divided the money with Sturtevant and Bridges, to help to educate their children. Only Muller (who won his own Nobel in 1946 for his work on the effects of radiation on mutation rates) suggested seriously that Morgan sometimes exploited his students. Most believed that in the free interchange and mutual devotion to uncovering the genetics of the fruitfly was a formula that worked.

Liebig, Pavlov and Morgan each created something special. Their labs achieved international prominence, attracted talented scientists and bred further success. Each lab bore the stamp of the founder's ambitions and personality, and this relationship between the boss and the establishment stands out. Morgan's culture of egalitarianism provided a model for many successful modern laboratories, not least the LMB.

LAB SPECIATION

A kind of speciation can sometimes occur with laboratories. What is now the LMB began life ensconced in the Cavendish Laboratory, the centre of physics at the University of Cambridge and, by any reckoning, also among the most successful modern labs.

The Cavendish opened in 1874. Its first director, James Clerk Maxwell (1831–79), was arguably the most important physicist between Newton and Einstein. A genial man blessed with a fertile mind and remarkable ingenuity, Maxwell contributed to many problems in physics, and he completed the work on electromagnetism begun by Hans Christian Ørsted, Michael Faraday and others. He showed that the Sun's light comes to us through electromagnetic waves, and at the same time predicted the range of radiations that has been central to modern science and modern life.

Many of these advancements came from the Cavendish, beginning with J. J. Thomson (1856–1940) and his discovery of the electron in 1897. His was one of many Nobel prizes from the Cavendish, and like all leaders of successful laboratories, he was a good talent spotter. And successful labs attract ambitious and talented individuals. Ernest Rutherford (1871–1937) came from New Zealand to the Cavendish because of Thomson and his group. He thrived there, and after stints in Montreal, Canada, and Manchester, UK, he succeeded Thomson as director in 1919. He brought with him from Manchester James Chadwick, rooting nuclear and atomic physics firmly in the Cavendish during the early decades of the twentieth century.

Until it got its own building in 1962, the LMB was simply a research unit within the Cavendish. Of its early workers, the most important was Max Perutz (1914–2002), whose style and personality shaped the LMB. Perutz came to England in 1936, hoping to work with Frederick Gowland Hopkins, the pioneer Cambridge biochemist. A meeting with the X-ray crystallographer J. D. Bernal, then still at the Cavendish, convinced the young Perutz that X-rays could provide the tools to solve the molecular structures of proteins. It took Perutz a further year to get horse haemoglobin crystals that were suitable for analysis using X-ray diffraction techniques. Because of the Second World War, it was seven more years before he could return to this molecule, his life's work. Even though he had lived in England for several years before the outbreak of war, he was treated as an enemy alien and incarcerated for nine months during 1940, in Britain and Canada. He spent the rest of the war back in Britain designing aircraft carriers.

Encouraged by Lawrence Bragg, then director of the Cavendish, Perutz returned to studying haemoglobin, joined by John Kendrew (1917–97). The beginnings of the LMB date from 1947, when the UK Medical Research Council (MRC) began supporting the work of Perutz and Kendrew. The original name of their group was the MRC Unit for Research on the Molecular Structure of Biological Systems. Perutz described himself then as a chemist working in a physics laboratory on a biological problem: a fairly accurate summary of the inputs into the field dubbed 'molecular biology' in 1938 by the Rockefeller Foundation administrator Warren Weaver.

Perutz and Kendrew pursued a promising avenue of molecular biological research, but haemoglobin is such a complex model that they soon added the simpler myoglobin to their agenda. Hugh Huxley joined the group in 1948, but turned to studying the biophysical dynamics of muscle contraction: an early example of the widening range of biological problems in the unit's remit. The increasing international reputation of the group's work brought talented young scientists to Cambridge, including physicist Francis Crick as a research student and biologist James Watson as a postdoc.

> ***"A single administrator, Audrey Martin (and her dog Slippers), looked after things."***

A successful laboratory generally breeds more success, with implications for size and ethos. Bragg was appreciative of the group's prominence, but the Cavendish was chronically short of space in post-war austerity Britain. So in 1957 Perutz, aware that Frederick Sanger from the biochemistry department also needed more space, wrote to the MRC about housing the molecular biologists in a new laboratory. Unsurprisingly, negotiations were slow given so many vested interests, but money was found. The present building, in Hills Road, Cambridge, expanded on more than one occasion and, still growing, was opened by Queen Elizabeth II in May 1962. There were then about 25 staff members and the same number of visiting workers. In October, there was a party to celebrate the Nobel prizes of Perutz and Kendrew in chemistry, and Watson and Crick (with Maurice Wilkins) in physiology or medicine.

BRIGHT BEGINNINGS

The party in 1962 was just the beginning. Over the past half-century the LMB has been at the centre of molecular biology, the discipline at the heart of the life sciences. New groups in developmental biology, immunology, cell biology and neurobiology attest to the expansion of the field. The growth has often been opportunistic, clustered around individuals such as Sydney Brenner, César Milstein, Aaron Klug and Michel Goedert. The simpler rules of only a generation ago (the original procedures for producing monoclonal antibodies were not patented, for instance) have given way to the contemporary competitive world of biotechnology.

As the laboratory has grown, its administrative structure has inevitably become more complex. Until Perutz retired in 1979, it had no director. Perutz didn't want to be one, and it meant he could retain his lab space after retirement. Instead, the lab had a loose management committee, which met occasionally and saw its main job as attracting outstanding talent to the lab. Perutz kept the bureaucratic structures of the laboratory minimalist, and until 1973 a single administrator, Audrey Martin (and her dog Slippers), looked after things. The egalitarianism that Morgan had fostered at Columbia was effectively duplicated in Cambridge, an ethos encouraged by the lab's successive directors — Sydney Brenner, Aaron Klug, Richard Henderson and Hugh Pelham — as each has presided over an ever-larger operation. The LMB now has some 400 workers, about half permanent staff and the rest students and visiting scientists.

It is easier to describe success than to explain it, but several of the characteristics that typified earlier exemplars are also part of the core ideology of the LMB. New techniques, new disciplines, new ways of tackling old problems and the ethos of collegiality have continued to characterize the lab. So has the key personality of Perutz, whose influence shines even after his death. The achievements of the lab's first half-century have been rewarded by even more new buildings, due to open in 2013. Long may the LMB flourish. ■

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