Lifting the veil

The growing commercial value of basic science research is impacting free cooperation in the community, says **S Ananthanarayanan**

ON the one hand, research in science is funded by the state and universities for the general benefit and the results are shared immediately, for maximum dissemination, application, follow-up and replication. On the other hand, such speedy sharing could eclipse the original researchers, denying them the credit and glory, the opportunity to capitalise and even the occasion to analyse the discovery and take the research to a creditable conclusion.

This conflict between the interests of the inventor and society has been a historical concern of states that wished to promote creativity, and the concern has given rise to now well developed patenting laws. The legal practice is said to have originated in Venice, Italy, in 1474, with a statute to protect the interest of inventors an innovators. The statute provided that once an invention had been put into practice and communicated to the state, imitators were prevented from making use of the invention for a period of 10 years. In this way, inventors were supported by the state to benefit exclusively from their creativity, and the state benefited with more inventions pouring in, to the common good.

But even without a statute, *letters patent* were being issued in England and elsewhere in Italy and there is evidence that in 500 BC, in the Greek city of Sybaris (now in southern Italy), "encouragement was held out to all who should discover any new refinement in luxury, the profits arising from which were secured to the inventor by patent for the space of a year".

But patents, even in modern law, are for industrial products. Scientific principles, theories, basic discoveries are outside the scope of patents. But this did not deter scientists driven by passion and love for their avocation — they only baulked at having to reveal their discovery early, even before they were able to polish their work and publish their findings in a prestigious journal. But universities and governments, which provide the funds for research, have imposed regulations of how fast the results of a scientist's work needs to be made available. It has even been provided that the data collected, which is not detailed in the announcement of the result, be made freely accessible.

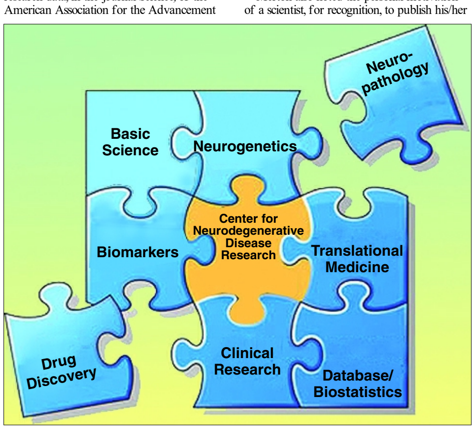
Changing conditions

But in modern times, when there is considerable privately funded research and the results of research are put to commercial use with negligible delay, the priorities of industrial products are crossing over to basic research findings. The growth of biotechnology and the use of genetic engineering in agriculture and pharmaceuticals has both increased the stake of private corporations in research as well as created resistance to time schedules for discoveries to be published.

While the conflict became significant in the area of biotechnology in the last decades, it is now affecting other important public domain areas like the discovery of green technologies, global climate change and molecular chemistry. Professor Jorge L Contreras, deputy director of the Intellectual Property Programme and senior lecturer in law at Washington University in St Louis, has published a review of the development of legal controls of research data, in the journal *Science*, of the American Association for the Advancement of Science.

Jorge L Contreras.

Robert K Merton.



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He builds up the idea of *science commons*, the mass of individual findings in science, free for all to access, like the free access that people in England enjoyed to land and pasture that was not private property. In the 1940s, sociologist Robert K Merton had observed a set of *norms* that were followed in the practice and culture of science. One of these is that scientists are willing to share their findings and experimental data with other scientists. Merton, who considered science an essentially collaborative activity, noted that this norm was essential for the practice and progress of science itself.

The sharing of findings, with bases, is also essential for validating discoveries and for the credibility of the finding. In fact, one of the hallmarks of a scientific finding is that it can be reproduced in suitable conditions by any researcher in any part of the world.

Merton also noted the personal motivation of a scientist, for recognition, to publish his/her discovery in the most reputed of journals. This has then created the tradition of the peer reviewed journal as the most important means of disseminating the results of research.

But there is a distinction between the results reported in a journal and the mass of raw data which forms the basis for the results published. Traditionally, scientists who desired to use the raw data of another scientist had to correspond and inspect or copy. In recent times, the means of access, through online data bases and computer networks, have expanded. The *science commons*, hence, covers much of the data of work in fields like high energy physics, astronomy or geoscience, which use facilities like particle accelerators and satellites in large laboratories, mainly funded by governments.

There were, accordingly, guidelines of the time within which data and the results of research were required to be published. This was in the range of 12 to 18 months, considering the time it normally took for the data to be converted into a formal paper, followed by review and acceptance. The *Human Genome Project*, which was an international drive to map the human genome, found this time limit to be too generous. The project was ambitious and had conscripted scientists from all countries and laboratories to collaborate. It was vital that resources were not wasted by efforts being duplicated. It was hence important that work done be reported immediately, for others engaged in the same area to stop or for others who depended on the result to make use of it.

The National Institute of Health and the Department of Energy first adopted a limit of six months. But even this was considered excessive and in the convention of HGP workers in Bermuda in 1996, it was agreed that results needed to be published immediately, preferably within 24 hours.

While such rapid reporting was understandable in the conditions of the HGP, there were other motivations, like the concern for academic recognition and "credit" and the right of a researcher to have priority over his/her "own" data that pressed for giving the researcher more time. This, in turn, has led to policies that favour different "data latency" approaches.

An example is the NIH policy of 2007 for NIH-funded Genome-Wide Association Studies. Gwas data is to be released rapidly, but the "owners" are protected in that the users of the data are not allowed to publish or present any related results for 12 months. This time allows the data generators to finalise their own publications but still leaves the data available for general use.

Private agencies provide greater protection, at the cost of overall advancement. A typical case is the International Serious Adverse Events Consortium, which allows 12 months before the data is made public. Different agencies then provide different periods of blocking the use of the data released, or a "rights latency".

A problem with the early release of results is that this comes in the way of securing a patent because the laws of most countries would consider a discovery that has been published to be "already in the public domain". This difficulty is then approached through "defensive patenting" where the consortium files the patent on priority with a commitment to subsequently contribute the rights to the public.

Professor Contreras says similar approaches need to be followed to develop policies that balance the priorities native to different fields of research. A policy of *science commons* weighted in favour of data users would not find many contributors, but if the policy were too much in favour of the data generators, advancement of science would suffer. However, a technology of fixing optimum latencies is developing.

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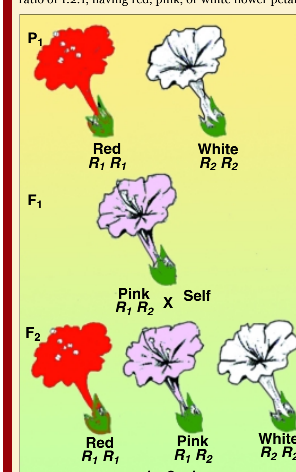
Decoding dominance

What happens when the phenotype of the heterozygote falls between those of the two homozygotes? **Tapan Kumar Maitra** explains

IF dominance were universal, the heterozygote would always have the same phenotype as the dominant homozygote and we would always see the 3:1 ratio when heterozygotes are crossed. If, however, the heterozygote were distinctly different from both homozygotes, we would see a 1:2:1 ratio of phenotypes when heterozygotes are crossed. In partial — or incomplete — dominance, the phenotype of the heterozygote falls between those of the two homozygotes. An example occurs in flower petal colour in some plants.

Using the four-o'clock plant (*Mirabilis jalapa*), we can cross a plant that has red flower petals with another that has white flower petals; the offspring will have pink flower petals. If these pink flowered F_1 plants are crossed, the F_2 plants would appear in a ratio of 1:2:1, having red, pink, or white flower petals



Flower color inheritance in the four-o'clock plant ~ an example of partial, or incomplete, dominance.

respectively. The pink flowered plants are heterozygotes that have a petal colour intermediate between the red and white colours of the homozygotes. In which case, one allele (R_1) specifies red pigment colour and another allele specifies no colour (R_2; the flower petals have a white background colour). Flowers in heterozygotes (R_1 R_2) have about half the red pigment of the flowers in red homozygotes (R_1 R_2) because the heterozygotes have only one copy of the allele that produces colour, whereas the homozygotes have two copies.

As technology has improved, we have found more and more cases in which we can differentiate the heterozygote. It is now clear that dominance and recessiveness are phenomena dependent on which alleles are interacting and on what phenotypic level we are studying. For example, in Tay-Sachs disease, homozygous recessive children usually die before the age of three after suffering severe nervous degeneration; heterozygotes seem to be normal. As biologists have discovered how the disease works, they have made the detection of the heterozygotes possible.

As with many genetic diseases, the culprit is a defective enzyme — protein catalyst. Afflicted homozygotes have no enzyme activity, heterozygotes have about half the normal level and, of course, homozygous normal individuals have the full level. In the case of Tay-Sachs disease, the defective enzyme is hexoseaminidase-A, needed for proper lipid metabolism. Modem techniques allow technicians to assay the blood for this enzyme and to identify heterozygotes by their intermediate level of enzyme activity. Two heterozygotes can now know that there is a 25 per cent chance that any child they bear will have the disease. They can make an educated decision as to whether or not to have children.

The other category in which the heterozygote is discernible occurs when the heterozygous phenotype is not on a scale somewhere between the two homozygotes, but actually expresses both phenotypes simultaneously. We refer to this situation as codominance. For example, people with blood type AB are heterozygotes who express both the A and B alleles for blood type. Electrophoresis allows us to observe proteins directly and also gives us many examples of codominance when we can see the protein products of both alleles.

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Secrets of the deep

Oceanography emerged as a modern science in the post-war years – and the British role was key. **Rob Sharp** hears about those heady days of improvisation and experimentation

IN the first half of the 20th century scientists misunderstood the ocean's currents and had only a murky understanding of plate tectonics and the fauna of the briny deep. Experts squinted through homemade cameras at ocean bottoms thinking they were as barren as the moon. But empirical techniques have evolved and modern oceanography — that is, the chemistry, zoology and geology of 71 per cent of the world's surface — is now a cutting-edge science. Today, scientists embarking on a research project can gird themselves with an arsenal of probes, microchips and electronic microscopes to model complex currents, for example (handy when investigating oil spills, as in the Gulf of Mexico recently), or to sniff out spawning whales.

It was Britain that kick-started this revolution. In 1949, the government funded the country's first National Institute of Oceanography based in Surrey. It proceeded to push back the frontiers of the discipline until its eventual dissolution in 1973. Its work underpins many of today's oceanographic methods, such as employing "floats" — buoy-like devices equipped with sensors that measure the ocean's properties — or using tags embedded in whale blubber which can be tracked by satellite. This month, some of the organisation's former members have published a book, *Of Seas and Ships and Scientists*, brimming with tales of halcyon days on — and under — the ocean waves. The institute certainly holds water with contemporary scientific players.

"It was a very influential era," says Nick Owen, director of the British Antarctic Survey, and also a marine biogeochemist. "In many ways it was the end of the beginning, propelling us into the integrated science we see today. Before, there were many different specialists — geologists, chemists — pulled in to work in oceans. Now, one can be an 'oceanographer', and talk the same language as everyone else working within your field."

The Nio's methods were unconventional. Its first director, George Deacon, would appoint staff without seeing their CVs or resorting to recruitment boards or interviews. "When I arrived, he asked me what I wanted to do, and I replied that the UK should investigate the ocean floor with photography," Anthony Laughton, a retired geophysicist, remembers. "He replied, 'Go ahead.' This was Deacon's style of recruitment in those days." Laughton had been all set to become a nuclear physicist but was told his low white blood cell count made him susceptible to radiation poisoning. So his career was launched as much by luck as by aptitude.

This gung-ho attitude was useful, given its context. After World War II, Britain's pursuit of sea science was sinking, which was surprising since, historically, many of its most famous researchers have been sea lovers. Isaac Newton is best known for his laws on thermodynamics; he also researched how the world's tides work. Edmond Halley, one of Britain's astronomical *éminences grises*, equally took an interest in South Atlantic geomagnetism. But despite their best efforts, from the mid-19th century, it was the New World that led scientific forays into the deep.

Britain hit back. Motivated by nationalist notions, the post-war British Admirality asked Deacon to study sea waves, hoping to better understand how to coordinate amphibious landings. By the end of the organisation's 24-year reign it had cleared up mysteries in weather, water, health, energy, disasters, ecosystems and biodiversity; the UK was back on top.

So what was it like conducting experiments at sea for endless, sleepless nights? "We had the feeling we were a community," says John Gould, an expert in measuring ocean currents. "We went off to sea on small ships for months on end, and there was very little communication back to the lab in Britain. We communicated by radio or not at all. It produced a unique bond among those who went to sea, and cemented friendships with those technical people who stayed behind, on whom we were dependent."

Gould was on call "24 hours a day", when he wasn't "sleeping, eating or washing". Thankfully he never suffered from seasickness and could focus on predicting oceanic weather instead. Some research was done on land. Sometimes, the researchers' working lives collided with those of other countries. Gould recalls going to sea in the 1960s with a group of Russians, many of whom were obliged by their superiors to bunk down in conditions that were vastly inferior to those of their English counterparts. The Russians were prevented from publishing their findings for peer review until decades after Gould's conclusions appeared in print. In those Cold War days, "due to secrecy, we were not allowed to see the echo-sounder (a device that uses sonar technology to map the ocean floor) or to send messages about the work", he writes.

Periods of isolation and budgetary and political constraints stretched the researchers' powers of innovation. Working with the Nio's engineering department, Laughton designed and built the first camera capable of capturing pictures at colossally high pressure. It allowed his team to see burrows harbouring the *benthos*, the organisms that live on the deep seabed. These images provided the first evidence that sufficient nutrition was available to allow for life at such depths. Afloat on a different sea, Gould improvised by filling baby feeding bottles with jelly and oil and lowering them into the water to detect subtle changes in current direction and velocity. Many of these experiments with "floats" — used to measure temperature and salinity — are still in widespread use today.

Such experiments propelled oceanography into the 21st century. At the beginning of Laughton's career, scientists believed tectonic plates moved up and down — not sideways. By the time he retired, the study of the spreading and interlocking tectonics of the ocean-floor, like tessellations in a Roman bath, was appearing on university syllabuses around the world. Laughton personally proved that Arabia had rotated away from Africa to create the Gulf and the Red Sea.

Making waves: oceanography has developed as a discipline, advancing our knowledge of areas from seismology to health

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