PCR & The Biotech Revolution

Photo by Karl Mumm

A data innovation case study by copia

We live in a genomic age. The amount of important medical and biotech research happening today involving genes is staggering. And much of it goes back to the Polymerase Chain Reaction (PCR). The seeds of PCR development can be traced back to the 1970s, and the practical PCR machinery that fueled a biotechnology revolution started running in the 1980s. This innovation was quickly recognized with a Nobel prize in 1993, only about 10 years after its invention and approved patent application. PCR has accelerated the pace of innovation in biotech, and its contribution to society is immense.

WHAT IS PCR?

Simply put, PCR is a copying machine for DNA. DNA is naturally copied by living cells all the time, but getting a machine to do this job is a bit tricky. PCR solved a long list of problems enabling systems that rapidly produce exact copies of DNA sequences by repeating a series of automated steps.

A key part of the PCR process came about unexpectedly when scientist Thomas Brock discovered that microbes could survive in the hot springs of Yellowstone National Park — upending the long-established belief that such high temperatures would kill the microbes. Brock was able to grow these extremophile microbes in a lab, and he submitted samples to the American Type Culture Collection (ATCC) — a biological repository that, among other activities, preserves and distributes biological materials for the advancement of science. The availability of Thermus aquaticus (Taq) cells from ATCC allowed scientists to study how such organisms could survive in nearly boiling hot water, and Taq enzymes were used in the development of the PCR technique because this ability to function at high temperatures was well-suited for repeatedly replicating DNA.

In the early years, there were intellectual property fights over PCR, with questions about whether it should be locked up as a trade secret, or patented and licensed. While eventually PCR was patented and licensed liberally to research organizations, there were still a series of patent fights over the technology.

IMPACT

The immediate impact of PCR in the 1980s created a frenzy of work by producing a machine that could work much more efficiently than any human. The inventor of PCR, Kary Mullis, recounts that he was trying to increase demand for these tiny bits of DNA and succeeded in increasing demand a million-fold with PCR.

This automated system of copying DNA sequences spurred the genomic age. PCR makes it much simpler to detect and identify small amounts of DNA, so it is ideal for many disease diagnostics. In the mid-1980s, PCR was used to develop a screening test for sickle cell anemia. PCR continues to be used for diagnostic testing of a wide variety of diseases, including Lyme disease, Hepatitis C virus and Legionnaires' disease, and PCR is an essential tool for studying HIV, cancer and a long list of medical conditions.

In other biological research, PCR was used in the Human Genome project and is routinely used in all kinds of genetic studies. Without PCR, progress in stem cell research would be slower. Agricultural breeding techniques would not be as advanced without PCR. The study of genetically modified organisms (GMOs) would be more difficult without the ability to copy DNA rapidly, so determining the effects of GMOs on the environment or on human health would take longer.

In just the US, over 50,000 scientists use PCR techniques in their work. The global size of the PCR market — accounting for reagents, instruments, software and services — has estimates ranging from $5-$8 billion in 2014, possibly growing to $14 billion by 2020. The North American market is the largest segment with a roughly 40% share of the global activity. Together, Europe and Asia make up a little over 50%. These revenue estimates capture the business activity related to PCR, but there are wider impacts on society beyond the industry of biotech tools and services.

The criminal justice system would not be the same without PCR's role in forensics. PCR has exonerated wrongly-accused innocent people of serious crimes. Conversely, PCR has been used for convicting criminals as well. The idea that it only takes extremely small traces of blood or other sources of genetic material to determine the identity of a person is now widespread, and the PCR technique underlies a modern era of gathering scientific evidence at crime scenes.

Mainstream media has conveyed the capabilities of PCR to viewers of various crime shows, as DNA evidence commonly comes up near the end of many TV dramas. The premise of Jurassic Park relies on science fiction loosely related to PCR, describing dinosaur breeders copying the DNA found in an ancient mosquito. Science fiction has adopted many storylines based on genetic technologies, presumably based on PCR, from GATTACA to Blade Runner to re-boots of Spiderman and other superheroes. However, the topic of genetic research is also showing up in dramas based on reality such as Decoding Annie Parker.

This automated system of copying DNA sequences spurred the genomic age.

POLICY ISSUES AND IMPLICATIONS

The discovery of extremophile microbes in Yellowstone National Park was fortuitous in 1966. The National Park Service at the time didn't regulate how visitors to parks could take biological samples. The rules regarding bioprospecting simply didn't exist until 2006 when the National Park Service (NPS) published its Management Policies covering approved collection procedures and commercial use rules. The NPS further refined its policies in 2013 with its Benefits Sharing Handbook, allowing the NPS to receive monetary or non-monetary benefits from commercial ventures originating from authorized research at a national park.

Thomas Brock is not called a bioprospector by the NPS, but he collected samples from Yellowstone and deposited specimens he cultured at the American Type Culture Collection (ATCC). Brock was doing basic research and only wanted to advance science, saying, "Yellowstone didn't get any money from it. I didn't get any money, either, and I'm not complaining. The Taq culture was provided for public research use, and it has given great benefit to mankind."

Fortunately, the ATCC exists as a nonprofit biological resource center with a mission to generate new knowledge. Established in 1925, ATCC allows life science researchers all over the world to gain access to thousands of known cell lines and millions of cloned genes. Without its mission of sharing and distributing as a component of contributing to science, it might have taken longer for PCR to have developed. If the National Park Service didn't allow early forms of bioprospecting, innovations like PCR might not exist today.

The possibility of expanding trade secret laws may have changed the original decision on whether to keep PCR a trade secret or to patent and license it. Changes in patent laws might also have impacted both the way in which PCR was patented and licensed — as well as some of the early patent battles over the technology.

The original patents for PCR expired in 2005, and more advanced PCR techniques have been developed over the last 30 years. PCR equipment is a requirement for any advanced molecular biology lab, but the technology is getting cheaper and more available all the time.

A few crowdfunding projects have been funded to create open source hardware and software for PCR, aiming to bring PCR tools to classrooms, developing countries, cash-poor biotech startups, and biohackers everywhere.