

Human Data Acquisition & Control

By John Benson

May 2020

1. Introduction

I have spent most of my career in the electric utility industry in three technologies that are all about data acquisition and control: supervisory control and data acquisition (SCADA), advanced metering infrastructure (AMI) and protective relaying. I have also written posts on all of these (below):

Supervisory Control and Data Acquisition: SCADA systems are still very important, and many potential readers that work for electric utilities and large facilities are likely to encounter them in the future, thus this six-part series was posted. The link below is to part-six of this series, which contains links to all of the other papers.

<https://www.energycentral.com/c/pip/scada-%E2%80%93-part-6-transmission-and-distribution-network-management>

Advanced Metering Infrastructure (AMI): In papers in this 4-part series we will explore the functions of the meter data management (MDM), the major advancements in commercial and industrial (C&I) meter technology, how advanced C&I metering led to AMI, how this market evolved and how it is evolving into the Internet of Things. The link below is to part 4 of this series, which contains links to the other three parts.

<https://www.energycentral.com/c/iu/ami-part-4-%E2%80%93-internet-things>

Initial Resilience, Part 2: In Part 2 of this series we look at protective automation, which involve protective relays and systems, as well as some suggestions to reduce the overall use of these, primarily effective vegetation management.

<https://www.energycentral.com/c/pip/initial-resilience-%E2%80%93-part-2>

This post will cover a different type of data acquisition and control which is used for humans, and more specifically their diseases. It came from a recent issue of Scientific American, and two articles therein (referenced below). However, there is huge difference in timing. Whereas the above utility technologies are a better part of a century old, the technologies we will review below are much younger.

2. Agents of Disease

We (the World's population) are very lucky that the COVID-19 Pandemic started in 2020, and not 20 years earlier. Although over a million humans lost their lives to COVID-19 and related diseases in the U.S., it could have been worse, much worse, except for recent major developments in biotechnology. World-wide, without these advances, it could have also been far worse than the current toll of this disease.

2.1. The Trip

In 1983 Kary Mullis was driving up to his cabin on the Northern Coast of California with his girlfriend, a chemist at the biotechnology company, where they had been hired to synthesize genetic fragments. Mullis had spent earlier years completing a Ph.D. at the University of California, Berkeley, where he would trip on LSD while making new

chemicals. His girlfriend had fallen asleep, and as he drove he had a vision of molecules dancing on the mountain road. It was then that the idea for polymerase chain reaction (PCR) came to him. He pulled over the car and scribbled down his thoughts. It won him a Nobel Prize a decade later.¹

2.2. PCR

At its heart, PCR is a method of making copies of genetic sequences. There are now many dozens of different kinds of PCR, but the most basic form that Mullis devised started with a tiny bit of DNA (Deoxyribonucleic acid) and then used various cycles of heating and cooling to replicate it. First, the process would heat the DNA to break its double helix structure into two strands. Next, it would cycle to a cooler temperature that would allow specially tailored primers to bind to specific target sequences within the strands. The samples would be warmed up again, and enzymes would get to work building off those primers to finish replicating the complementary DNA sequences. The cycle would then repeat. Ultimately it yielded a lot of copies of the target strands. Special fluorescent tags were later added to the process to flag the presence of those amplified short sequences of interest.

It became possible to use this method to detect the presence or absence of pathogens: if a virus was present in a person's blood sample, for example, the PCR machine would make a lot of copies of its sequence, and the fluorescent tags would shine brightly. If there was no virus, there would be only darkness.

The incorporation of fluorescent tags meant that the PCR machines could also indicate how much virus was in a person's system. If the fluorescent light shined more strongly and sooner in the replication cycling, it meant more virus was present. A PCR could not only detect DNA, it could also detect genetic material known as RNA (Ribonucleic acid). This opened up a whole new world of diagnostics because many viruses, such as HIV², are RNA based organisms. As the AIDS pandemic tore through the globe, doctors wanted to know how much HIV was circulating in their patients' bodies and whether the antiviral drugs they prescribed were working to keep the levels low. PCR could finally give them an answer.

2.3. Diagnostic Machines

The machines that did the analyses, though, required lab technicians with highly specialized expertise to prep samples and took half a day or more to return results. That changed after the U.S. Postal Service launched a competition for technology that could quickly screen mail for deadly anthrax spores, which a bioterrorist sent in letters to the offices of U.S. senators and journalists after 9/11. The winner, announced in 2002, was a GeneXpert prototype from Cepheid, a Silicon Valley diagnostics company founded in the late 1990s. The system automated many of the previously laborious sample preparation steps by using cartridges and valves that pull liquids through tiny channels and mix them together. And it returned results in minutes rather than hours. In the decades since, the GeneXpert platform has received approval to test for pathogens such as norovirus, chlamydia, tuberculosis and SARS-CoV-2.

¹ Roxanne Khamisi, "COVID Set Off a Boom in Diagnostics, Scientific American, March 2022 Edition (hardcopy), page 41, To order a copy of a Scientific American issue: call (800) 333-1199.

² Human immunodeficiency viruses, over time, these cause acquired immunodeficiency syndrome (AIDS).



Cepheid says there are now more than 40,000 GeneXpert machines around the world, up from 23,000 in 2020. (The diagnostics branch of the major biomedical company Roche also has a PCR machine for clinics that is about the size of a coffee machine.) Increasingly, they are found at doctors' offices and at locations such as border crossings rather than just at centralized labs. In September 2020 Cepheid received FDA authorization for a GeneXpert test that looks simultaneously for influenza A and B, SARS-Co V-2 and a pathogen that is particularly dangerous in young kids called respiratory syncytial virus. The test results, which can come back in about half an hour, help clinicians

know what specific antiviral to give if a patient is sick-Tamiflu for influenza for example, and Paxlovid for COVID. That is all the more' crucial during a pandemic when your infection determines your isolation behavior.

Author's comment: A few days after a family gathering on Christmas Eve 2021, I started feeling sick and running a fever. My medical provider, Stanford Health Care, has an Urgent Care Facility, and I went there. No one was sure whether I had Flu or COVID-19, since both were circulating and had similar symptoms. Fortunately the Urgent Care Facility had the above-described "...GeneXpert test that looks simultaneously for influenza A and B, SARS-Co V-2..." A few hours later, I knew that I had COVID-19. This was in spite of being vaccinated and boosted. Fortunately it was Omicron and mostly cleared in a few days since I was fully vaccinated.

IT WAS NOT UNTIL the past decade or so that scientists established global surveillance systems that rapidly tracked outbreaks of viruses. Testing for pathogens fell to individual labs, and molecular diagnostics approaches such as PCR were expensive or unavailable. Furthermore, to do PCR testing for viruses of interest, scientists needed specific probes that would recognize a genetic sequence in the pathogens. But they lacked easy tools to create these probes. The barriers to conducting PCR and the dearth of repositories to upload such data made tracking the ebb and flow of viruses in populations spotty.

In 2012, the California Department of Public Health received several reports of a mysterious polio-like disease striking children. It manifested as the sudden onset of muscle-weakness in limbs, sometimes also leading to slurred speech and difficulty moving the eyes. The sick children did not have poliovirus, and health authorities ruled out other possible culprits, including West Nile virus, stroke and botulism. What the children did have was an obscure virus called enterovirus D68, or EV-D68, which had first been identified decades ago. It had recently been linked with acute flaccid myelitis. Although some children make a full recovery from this condition, it can cause permanent paralysis and even death.

Around the same time that acute flaccid myelitis became associated with EV-D68, BioFire Diagnostics, a Utah-based molecular biology company that is now a subsidiary of the global diagnostics giant bioMérieux, began offering a comprehensive PCR-based respiratory test. It looked for 17 viruses and three bacteria in a single deep nasal swab taken from a patient.

Although the respiratory panel does not test specifically for EV-D68, it tests for the presence of the general family of viruses to which it belongs. BioFire wanted to find a way to catch EV-D68 outbreaks so that doctors and public health officials could know to keep patients from infecting others. Along with its academic partners, the company developed and tested an algorithm that was trained on past data to predict hotspots of EV-D68. The real proof of the approach came in 2018, when the algorithm alerted researchers to the emergence of EV-D68 that summer. Nationwide Children's Hospital in Columbus, Ohio, was one of the first places the algorithm identified with a possible uptick in cases of the virus; the team there confirmed the algorithm was right. As a result, the hospital implemented EV-D68 testing to catch cases early and prevent it from spreading.

2.4. Data Acquisition Systems

A related surveillance platform that uses BioFire's PCR test collates data from different sites across the U.S. and other countries around the world on respiratory viruses such as influenza, rhinovirus and now coronavirus, as well as more than a dozen gastrointestinal pathogens. Unlike the cumbersome data-collection protocols of the past, surveillance systems that continuously collect data directly from connected PCR machines have the potential to be used to detect outbreaks, including those of foodborne disease.

In many ways, this approach-combination PCR tests that cast a wider net to look for more possible pathogens in a given sample signals the future of PCR. "Their instruments are phoning home, which is totally cool," Greninger³ says of the BioFire disease-tracking platform, explaining that the broad net it casts could help show where unexpected outbreaks are occurring. The COVID pandemic has made it clear that testing people for viruses even if they are asymptomatic can help identify those who would not otherwise know they are infected, prompting them to isolate before they pass the pathogen unknowingly to others in their community.

3. Control

In just 17 years, messenger RNA therapies have gone from proof of concept to global salvation. The Pfizer-BioNTech and Moderna vaccines for COVID-19 have been given to hundreds of millions of people, saving countless lives.⁴

In 2005 Katalin Karikó and I (Drew Weissman) created a way to make mRNA molecules that would not cause dangerous inflammation when injected into an animal's tissue. In 2017 Norbert Pardi and I demonstrated that modified mRNA, carried into human cells by a fatlike nanoparticle, protected the mRNA from being broken down by the body and prompted the immune system to generate antibodies that neutralize an invading virus more effectively than the immune system could do on its own. The Pfizer-BioNTech and Moderna vaccines both use this mRNA-liquid-nanoparticle "platform"-known as mRNA-LNP. In large clinical trials, it prevented more than 90 percent of the people who received the vaccines from becoming ill.

³ Alex Greninger, assistant director of the clinical virology labs at the University of Washington Medical Center,

⁴ Drew Weissman, "Messenger RNA Therapies Finally Arrived," Scientific American, March, 2022 Issue (hardcopy), page 54. To order a copy of a Scientific American issue: call (800) 333-1199.

These extremely promising trials, and massive studies of people who have since received the vaccines, have finally given us sufficient information about the safety and efficacy of mRNA vaccines in humans. The platform outperformed more conventional approaches, in which vaccines are grown in laboratory cell cultures or chicken eggs. The rapid development also accelerated investment in further research that is now underway. And because the U.S. Food and Drug Administration and similar regulatory agencies are now familiar with the technology, assessment of new therapeutics should come readily.

Messenger RNA vaccines instruct cells to create proteins that induce an immune response to an invader such as the SARS-CoV-2 virus, training the immune system to attack future infections of the actual pathogen. They are easier to produce in large quantities than conventional protein therapies (genetically engineered versions of natural human or pathogen proteins) and monoclonal antibody therapies (lab-produced molecules that attack viruses in the same way that human antibodies do). And once a reliable manufacturing facility is built, it can quickly switch to a new mRNA vaccine or drug, unlike protein or monoclonal facilities, which must reengineer production from the ground up for each new therapy.

Success has inspired researchers, companies and government labs to pursue mRNA therapies for many infectious diseases, including influenza, cytomegalovirus, herpes simplex virus 2, norovirus, rabies, malaria, tuberculosis, dengue, Zika, Hrv; hepatitis C and the entire family of coronaviruses. In each case, researchers are determining exactly how mRNA-LNP vaccines induce potent antibody responses.

The Defense Advanced Research Projects Agency is even experimenting with mRNA delivery of monoclonal antibodies that could be tailored for previously unidentified infectious diseases, with the goal of supplying reliable manufacturing of such remedies within 60 days.

The concentrated COVID-19 work has also helped make mRNA a leader in nucleic acid therapeutics approaches that can produce nearly any protein made by a specific cell. The technique is starting to be applied, and it could fight diseases in more convenient, less invasive and less expensive ways. For example, the FDA has approved gene therapy for sickle cell anemia, and it is working in the U.S., although it requires marrow to be extracted from a person's bone, treated and reinserted; mRNA therapy could be delivered to marrow with a straightforward injection into a person's arm. If that works, sickle cell treatment could be greatly expanded in countries where the condition is widespread...

Drew Weissman is an American physician-scientist best known for his contributions to RNA biology. Weissman is a professor of medicine at the Perelman School of Medicine at the University of Pennsylvania (Penn). He and his research colleague Katalin Karikó have received numerous awards including the prestigious Lasker-DeBakey Clinical Medical Research Award...⁵

For additional information go to the site linked below:

<https://www.med.upenn.edu/apps/faculty/index.php/g275/p20322?msclid=46b2779ec0c011ec9b53e1e6787ed404>

⁵ Wikipedia article on Drew Weissman,

https://en.wikipedia.org/wiki/Drew_Weissman?msclid=46b53313c0c011ecb633dbbe3133371f