JMP CUSTOMER STORY

# Riffyn

Researchers at Imperial College London used the intelligent process development software Riffyn Nexus® in concert with its JMP® add-in to develop and validate a reagent- and instrument-agnostic SARS-CoV-2 diagnostic assay – all within nine weeks.

## CHALLENGE

A series of national lockdowns in response to the COVID-19 pandemic posed unprecedented disruptions to the global supply chain as early as December 2019. Scientists at Imperial College London quickly recognized the urgent need for a novel diagnostic workflow that would enable labs to utilize whatever reagents and instruments they had available while being resilient to further supply chain disruptions.

## SOLUTION

Open-access high-throughput synthetic biology workflows managed from end to end within Riffyn Nexus enabled researchers to randomize and dynamically iterate experiments, taking advantage of all the statistical power JMP has to offer.

## RESULTS

In just nine weeks, researchers had developed and validated a novel qPCR diagnostic assay for SARS-CoV-2 that could process up to 1,000 samples within 24 hours. With its adaptability to a range of reagents and liquid-handling instrumentation systems, the assay was scaled to National Health Service Diagnostic (NHS) labs across London. Ultimately, the NHS has run more than 700,000 tests based on researcher Michael Crone's innovation in 2020, in addition to over 100,000 at Imperial College London.

## Rapid innovation in COVID-19 diagnostics accelerated testing at a make-or-break moment in the pandemic

The high rates of community spread even in the earliest stages of the COVID-19 pandemic had epidemiologists and clinicians around the world urging widespread diagnostic testing to contain the damage wrought by SARS-CoV-2, the virus that causes COVID-19. Scientists racing to develop patient and community-level diagnostics for the novel coronavirus, however, soon encountered a major setback: Government lockdowns had caused a severe disruption to the global supply chain, and access to critical liquid-handling instruments and chemical reagents was limited.

In the UK, the National Health Service (NHS) had access to only a few reagent suppliers, and only enough supply to support 34,000 COVID-19 tests per week. As the disease spread, the national testing capability was soon overwhelmed. Labs desperately needed new diagnostic assays that could be adapted to their existing reagent inventory and instrumentation, enabling the NHS to overcome procurement challenges and contain the virus.

### Unprecedented supply chain challenges – and urgency – demand flexibility

"We tried to predict where the bottlenecks would be initially," explains Michael Crone, a doctoral student in the Department of Infectious Disease at Imperial College London. In early January 2020, Crone and his colleague Paul Freemont, Professor of Synthetic Biology and Co-Director of the London Biofoundry at Imperial, reached out to colleagues in China for insight into the challenges that were arising.

After receiving reports that supply chain shortages were limiting RNA extraction efforts, Crone explains, the team at Imperial decided to explore how existing platforms might be repurposed for the RNA extraction process at accredited facilities in the UK. "We had to be very flexible with what we were willing to use – we couldn't just say 'this is the ideal scenario,'" he says. "Instead we had to say, 'This is what's in stock, so can we test X and make sure that it works?'"

Long before even the first news of COVID-19 emerged, Crone, originally a medical doctor, was working to develop more efficacious patient- and community-level HIV diagnostics.

The approach revolved around what he calls "the highest throughput kind of optimization" – exploring a parameter space and then applying it to an individual reaction. "I was interested in the applications of mixing clinical medicine with synthetic biology," he explains.

Recognizing the potential SARS-CoV-2 diagnostic applications for the assays they had in development, Crone and Freemont began looking into ways to repurpose HIV diagnostics technology in the COVID-19 context, and within both procurement and financial constraints. Doing so required a more streamlined, process-centric approach to experimentation that could enable them to explore, iterate experiments, and ultimately develop and validate a new diagnostic on an unprecedentedly short timeline. They turned to Riffyn Nexus, an enterprise cloud-based scientific process data system that unites data storage and analysis all into one workflow. Riffyn, Crone says, was instrumental in achieving the research team's endpoint.

## Riffyn Nexus contextualizes data processes

In contrast to a traditional approach in which scientists might record data in a structured database or electronic version of a paper lab notebook with attached Excel files, Riffyn Nexus enables scientists to use a different paradigm for data capture and organization, thereby accessing the best of both worlds. "To a certain extent," Crone adds, "it's like designing your experiment with the data processing in mind.

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>
> **Michael Crone**
> Department of Infectious Disease

"Traditionally, labs have quality management systems where you can record the lot number, but if you actually have to go back and work out what went wrong, it can be very, very difficult… With Riffyn Nexus, if you've designed your process in such a way that you're recording the information you need, it's quite easy to go back and work out any difference between two experiments and identify what most likely caused the variation."

In addition to the iterative processing of historical data, Riffyn Nexus offers another hugely valuable feature: seamless integration with JMP, a software widely recognized as the industry leader in design of experiments (DOE). "Riffyn strategically chose to partner with JMP for visualization and complex data analysis, as opposed to spending resources reinventing the wheel," Herm explains.

## All the benefits of JMP® and Riffyn Nexus in one package means statistically robust, iterative, randomized experimentation

Riffyn Nexus' JMP add-in is central to the new innovation. "With design of experiments, you can store the data in a particular way," Crone explains. "It makes randomization a lot easier and exports to a specific format, which I can then use directly on our lab automation equipment. It's become quite a nice workflow."

The use of Riffyn Nexus and its JMP add-in enables researchers to evolve and iterate experimental designs flexibly – as well as to automatically pull historical data into new designs. The tool set offers randomization and a menu of options for DOE including full factorial and custom designs with data ranges populated automatically.

This end-to-end data capture, storage, analysis and visualization workflow is part of the main value proposition of the system: With its JMP add-in, users have access to state-of-the-art DOE features side by side with the capabilities Nexus has to offer. "The Riffyn-specific JMP DOE add-in is really streamlined," Herm says. "It can do in an afternoon what would have otherwise required a week or more of work for potentially less compelling results. JMP is a statistical software package that does DOE properly."

Ultimately, Riffyn Nexus and JMP, Crone says, change the way scientists think about processes and data. And by streamlining the myriad steps involved in a data capture workflow, the system reduces the potential for human error – and saves time. "You can actually think about the concept behind the DOE instead of copy-pasting or looking at your SOP or ELN entry and wondering whether it's going to be categorical or continuous and what the ranges should be," Herm explains. "Riffyn Nexus takes all of that work that is prone to error – and is exhausting – and does it for you. You can then focus on what's actually important, which is making a good design." And with clocks ticking for the NHS to roll out more widespread test-and-trace efforts, that accelerated development schedule could not have been more crucial.

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**Zoey Herm**
Senior Scientist

## An automated clinical diagnostic test for SARS-CoV-2 is validated for clinical use in just nine weeks

Within just nine weeks between January and March 2020, Crone and his colleagues had successfully validated RNA extraction and RT-qPCR workflows – a worldwide standard – in addition to two novel detection assays based on CRISPR-Cas and loop-mediated isothermal amplification methodologies. All three are the subject of a paper published in Nature Communications in September 2020. To date, the qPCR diagnostic workflow has been installed across London, adding capacity of 1,000 tests per machine per day. Furthermore, to date the NHS has run more than 700,000 tests based on Crone's innovation, in addition to over 100,000 at Imperial College London.