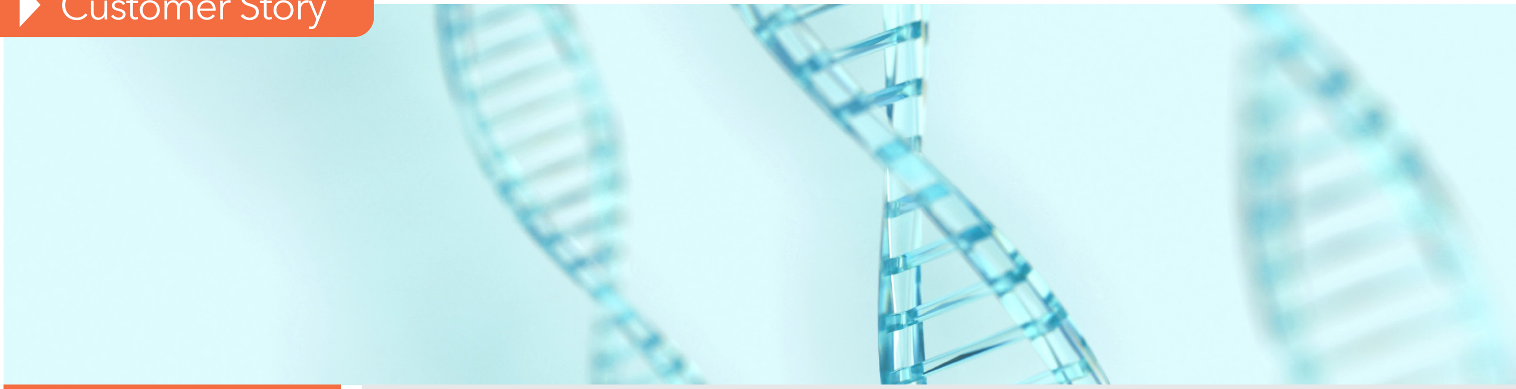
Customer Story



BIONANO GENOMICS

Challenge

Traditional sequencing technologies are entrenched as the standard of care and yet have narrow abilities to detect structural variants. Using optical mapping, Bionano Genomics' Saphyr technology can assess larger genomic events otherwise unobservable by alternate approaches. The company's development process, however, requires significant computational resources.

Breaking ground in genomic analysis

Statistical modeling enables the development of new, computationally intensive technology that more accurately identifies disease

As Director of Systems Engineering at Bionano Genomics, Pat Lynch, PhD, is on the forefront of a rapidly evolving industry, developing new genomic mapping technologies to address critical needs. Bionano, a San Diego-based genomic analysis company, seeks to advance genomics by complementing traditional sequencing-based analyses with an innovative, rapid optical mapping approach that uses whole genome imaging to identify large structural variants that are missed by the current standard practice.

Existing sequencing technologies break up DNA into small pieces for sequencing, then bioinformatically stitch the pieces together to form a whole genome. However such a process, known as short read sequencing, can result in gaps that interfere with scientists' ability to identify larger variations across the genome. "When you chop [the DNA] up into that small of a piece, you can miss some of the bigger events in the genome that may be occurring," Lynch explains.

Bionano's Saphyr® Genome Imaging System promises the ability to detect a much wider range of homozygous and heterozygous structural variation – and do so accurately and efficiently. Whereas traditional sequencing technologies can identify differences in a single DNA base pair, Saphyr looks at events that are roughly 500 base pairs and above.

With this capacity, investigators can evaluate different types of indicators that would be unobservable by other technologies, opening up diagnostic capabilities to a myriad of new conditions, including early detection for certain blood cancers.

Bringing statistical rigor to verification and validation

Moving from a previous role with scientific instrumentation giant Thermo Fisher to a startup like Bionano, Lynch relished the opportunity to try something different in the emerging technology space. After initially joining the company to start a verification and validation group, Lynch now leads the Saphyr instrument development core team.

Running this team requires a multitude of skill sets to continue to drive the technology forward. Working in areas from DNA isolation and labeling to the Saphyr instrument, the chip consumable and downstream software for both analysis and visualization, his team has a variety of needs when it comes to data analysis techniques, as each of these areas require significant data collection and testing.

One of the many roles of the Saphyr team is to test products like the sample prep kit and show that it meets all requirements, as well as validate that it works as intended outside the controlled atmosphere of the product development group.

While in a typical biology setting 90-95% performance may be considered successful, slight inconsistencies in the manufacturing process can significantly alter outcomes, and ultimately affect a customer's ability to achieve the results they need. To ensure reproducibility, Lynch says, the team "needs to put statistical rigor behind [all verification and validation efforts]. We do a variety of different analyses depending on which part of that workflow we're dealing with.

"A lot of times we'll do a capability analysis, for example, to make sure that given the data … we have this certain capability and can show the frequency that we expect it to be successful in a broader range of customers."

Understanding their customers' needs pushes Bionano to continually pursue greater data quality. "When you're making tens or hundreds of thousands of parts, you want pass rates of 99.9%," Lynch explains. "What percentage of time are customers going to be successful? We gauge from that what's acceptable."

jmp
Statistical Discovery.™ From SAS.

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>
> Pat Lynch, Director of Systems Engineering

Statistical methods for non-programmers

The importance of these analyses dictates the need for a powerful and comprehensive tool that can address the various requirements of the Saphyr core team; and Lynch needed a straightforward tool to help his team ease into the statistical realm. "I'm not a programmer," he explains, adding that a user-friendly and intuitive platform can enable engineers to bypass time-consuming coding without sacrificing the ability to perform complex analyses.

After being introduced to JMP® at a previous company, he slowly began exploring its simpler functions, but it wasn't until he came to Bionano that he began to unlock the software's greater potential.

"When I moved to Bionano, one of the first things I wanted to do is make sure I got a JMP license," says Lynch. Despite having only a three-week JMP course under his belt, he had a hunch that it would be the right tool as he stepped into his new role. As he explored new features within JMP, others at Bionano took notice and followed suit. "I became proficient and tried to encourage others to try JMP," Lynch adds, noting that by providing some informal training, uptake of JMP expanded across the team and has since become a core tool.

'Time is equal to money on computational platforms'

Current sequencing technologies have the benefit of years of use in the medical field, making them the standard of care for certain diagnoses and thus firmly entrenched. Despite new options like Saphyr, replacing widely used techniques takes significant effort and momentum.

"It's a slow process that requires convincing labs and users of the value, while also providing the technology at a cost that's affordable," Lynch adds. To do this, the Saphyr team has to differentiate its technology in the marketplace, give customers the information they need and provide reliable costing to encourage change.

Having recently released compute-on-demand functionalities, Bionano gives customers the ability to complete their computationally intensive bioinformatics analysis with a cloud provider and using the same visualization software, instead of having to purchase an expensive, dedicated server. However, understanding the actual costs of this service is complicated – how do you set a fair price for customers when every data set is different?

JMP software has allowed Lynch's team to evaluate multiple factors within data sets to determine a prediction expression for more accurate cost forecasting. Using this approach, Bionano can provide customers with a clearer range of expected costs, ensuring customers are not over- or undercharged and allowing them to proactively budget for these services.

"Time is equal to money on computational platforms," Lynch explains. The more predictive the team can be, the better they can set expectations. Without JMP, it would be more difficult for Bionano to charge accurately, and customer confidence and experience would suffer.

"I can't think of how [without JMP] we would be able to pull as many variables in to come up with some sort of expression that would take that data and turn it into predictive computational hours. We likely would have had to take the quantity of DNA and [desired] coverage and do a linear regression," Lynch says.

Not afraid of uncharted territory

With this powerful new approach to genomics, Lynch and his team seek expanded human clinical applications. Saphyr is particularly suited for applications where the traditional technology is unattractive or unreliable – recently, Saphyr technology has been adopted for lab testing for FSHD, a type of muscular dystrophy that is seen as a repeated segment in the genome and traditionally is diagnosed through an old technology using radioactivity, "stuff that people don't really want to use," Lynch explains. Providing not only an alternative but in many cases, a safer and more effective approach, Saphyr has the potential to transform diagnostics – and with JMP, Lynch's team can continue to pursue the analytical sophistication necessary to achieve these goals.

Solution

Engineers use JMP® to build predictive models, beginning by reducing all data quality metrics to those input variables identified as statistically impactful. Baseline models are then applied to subsequent data sets to streamline resource allocation.

Results

In one example, engineers consolidated a resource-intensive pipeline by modeling computational time for optical map assembly in JMP. Statistical approaches like this help Bionano Genomics speed innovation cycles and open the door to new diagnostic applications.

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