

Leaders in characterization

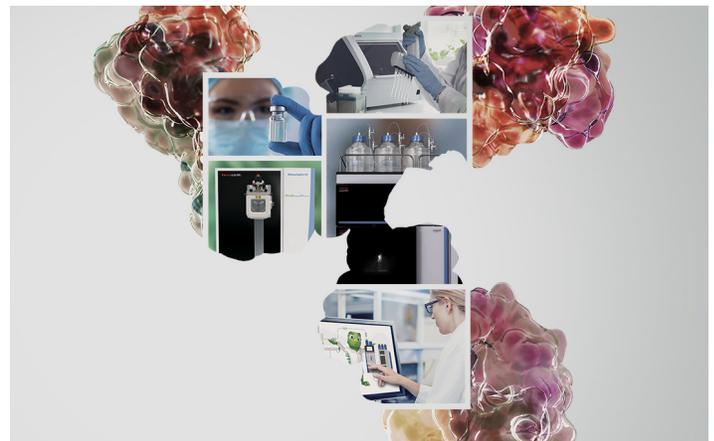
Bio-Techne Corporation

Delivering protein product quality through characterization expertise

With over 2,200 employees worldwide, [Bio-Techne Corporation](#) is a leading developer and manufacturer of high-quality purified proteins and reagent solutions— notably cytokines, growth factors, antibodies, immunoassays, biologically active small molecule compounds, tissue culture reagents, and cell and gene therapy workflow solutions, including T-cell activation technologies.

Bio-Techne products are integral components of scientific investigations into biological processes and molecular diagnostics, revealing the nature, diagnosis, etiology, and progression of specific diseases. They aid in drug discovery efforts and provide the means for accurate clinical tests and diagnoses.

R&D Systems, a Bio-Techne brand is located in company headquarters in Minneapolis, Minnesota, and has facilities that are specifically designed to produce high-quality reagents under current good manufacturing practice (cGMP) regulations, for the life-science industry. Protein reagent quality is only as good as scientists and the developed methods to characterize and control those products. R&D Systems proudly employs 750 highly skilled, and in-house industry-trained experts throughout their product development, quality control, and customer service departments.



Manufacturing of protein products through recombinant cell-culture processes deliver proteins with micro-heterogeneity stemming from genetic variations and delicate changes in the culture environment conditions. Understanding and controlling variables to deliver a well-characterized and appropriately quality controlled product requires great expertise. The Bio-Techne team has such expertise. They go above and beyond for their customers to understand the structural identity of the protein product and any associated contaminants using mass spectrometry.



“Since the 1980s we were among the first companies to mass-produce recombinant proteins; now we have almost 6,000 research-grade protein products, and over 50 produced under GMP control. Our products come with extensive quality testing with a focus on mass spectrometry-based analytics.”

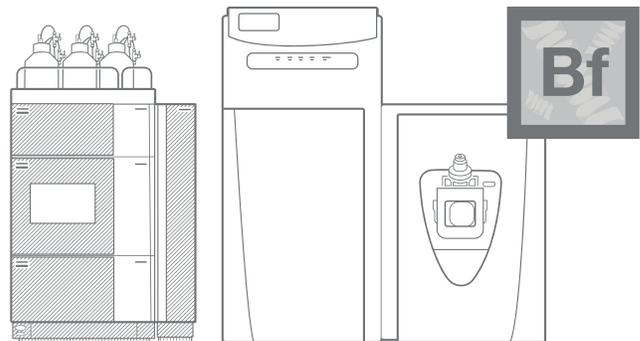
– Anthony Person, Ph.D.,
Sr. Director, Protein Business Unit, R&D Systems

A large part of R&D Systems’ business is bulk protein production for pharmaceutical companies. The protein product types are highly varied; anything from enzymes for small-molecule drug screening, or blocking-antibodies for immuno-oncology studies. A vast array of product types has one common feature—quality. The pharmaceutical customer demands quality and will always perform quality testing on receipt of inbound products. Consequently, R&D systems exhaustively test their proteins to ensure they deliver products they are confident in.

Investing in tools that deliver confident characterization

R&D Systems employs an LC-MS system for protein characterization and quality control processes, comprising:

- Thermo Scientific™ Vanquish™ Flex UHPLC system
- Thermo Scientific™ Q Exactive™ HF Hybrid Quadrupole-Orbitrap™ mass spectrometer with BioPharma Option
- Thermo Scientific™ BioPharma Finder™ Software



The Thermo Scientific™ Q Exactive™ BioPharma platform offers 3 distinct high-resolution accurate mass (HRAM) operational modes that have been optimized for the top protein characterization workflows:

- High Mass Range (HMR) mode was designed specifically for intact therapeutic protein workflows to provide ease of use and flexibility.
- Protein mode ensures the isotopic resolution of subunits and facilitates top/middle-down sequencing.
- Standard mode enables performance for peptide mapping with unparalleled acquisition speed, mass accuracy, and spectral quality.



R&D Systems Laboratory, Minneapolis, Minnesota, U.S.A

“I believe Orbitrap™-based mass spectrometry was really a game-changing technology for us. We have been able to accelerate the structural characterization of complex protein products, bringing them to market faster; such as our recent introduction of the SARS-CoV-2 Spike protein products. We were able to fully characterize the glycan profile of the product with high confidence bringing a quality product to market in just a few months.”

– Anthony Person, Ph.D.

The Vanquish Flex UHPLC system is a fully biocompatible chromatography system that delivers new benchmarks in accuracy, precision, and sensitivity. With a design focus on uptime, robustness, and reliability, the system can be configured with multiple detection options. The system comes with innovative and reliable **Thermo Scientific™ Viper™ Fingertight Fitting connections** throughout that give you the performance you need with the ease of use you want.



Viper Fingertight Fittings provide tool-free connections designed for the entire fluidic pathway in all LC systems to improve chromatographic results.

BioPharma Finder software helps you take a simplified path for confident protein characterization across a range of workflows, including performing intact protein mass analysis, top- and middle-down analysis, peptide mapping, oligonucleotide mapping, host cell protein, or multi-attribute method workflows. It gives you access to workflows with novel deconvolution algorithms that facilitate comprehensive interpretation and data visualization, allowing you to characterize your biologics with speed and ease, generating complete results from easy-to-understand data visualization tools.

Investing in expert teams

The analytical core facility at R&D Systems focuses on protein development support and problem-solving. The team has over seventy-years of protein characterization expertise and is led by Mark Whittaker.

Alex Grill joined R&D Systems at Bio-Techne in 2015 and was tasked to set-up up a laboratory facility to deliver mass spectrometry excellence. Alex has a doctorate in pharmaceuticals from the University of Minnesota together with post-doctoral research in oncology drug delivery where he developed expertise in LC-MS using a range of technologies from Thermo Fisher Scientific. This experience enabled Alex to rapidly set-up the mass spectrometry facility at R&D Systems. However, the low-resolution LC-MS technology in the laboratory at the time limited the capabilities of the laboratory to small, low molecular weight protein studies; with manual data processing and interpretation. The company marketed some high molecular weight products for which the determination and control of low-level modifications were very challenging with the then available technology. So, in 2018 Bio-Techne decided to invest in the Q Exactive BioPharma platform.

The company manufactures proteins with size from circa 6,000 Da up to antibodies at 150,000 Da, and beyond. They needed a mass spectrometer that performed well across that entire range for both peptide and intact level characterization.

“The great thing about moving to the Orbitrap was there was no ambiguity in our characterization results anymore. The intact mass analysis performance and accuracy gave me the confidence to tell my colleagues in process engineering the exact nature of the protein variant or modification. It blew my mind the first time I saw the results”



“We knew if we could invest in a modern HRAM instrument, that could measure and resolve modifications at the intact level, we could turn our work into something even more useful for the company.”

– Alex Grill, Ph.D., Scientist, R&D Systems

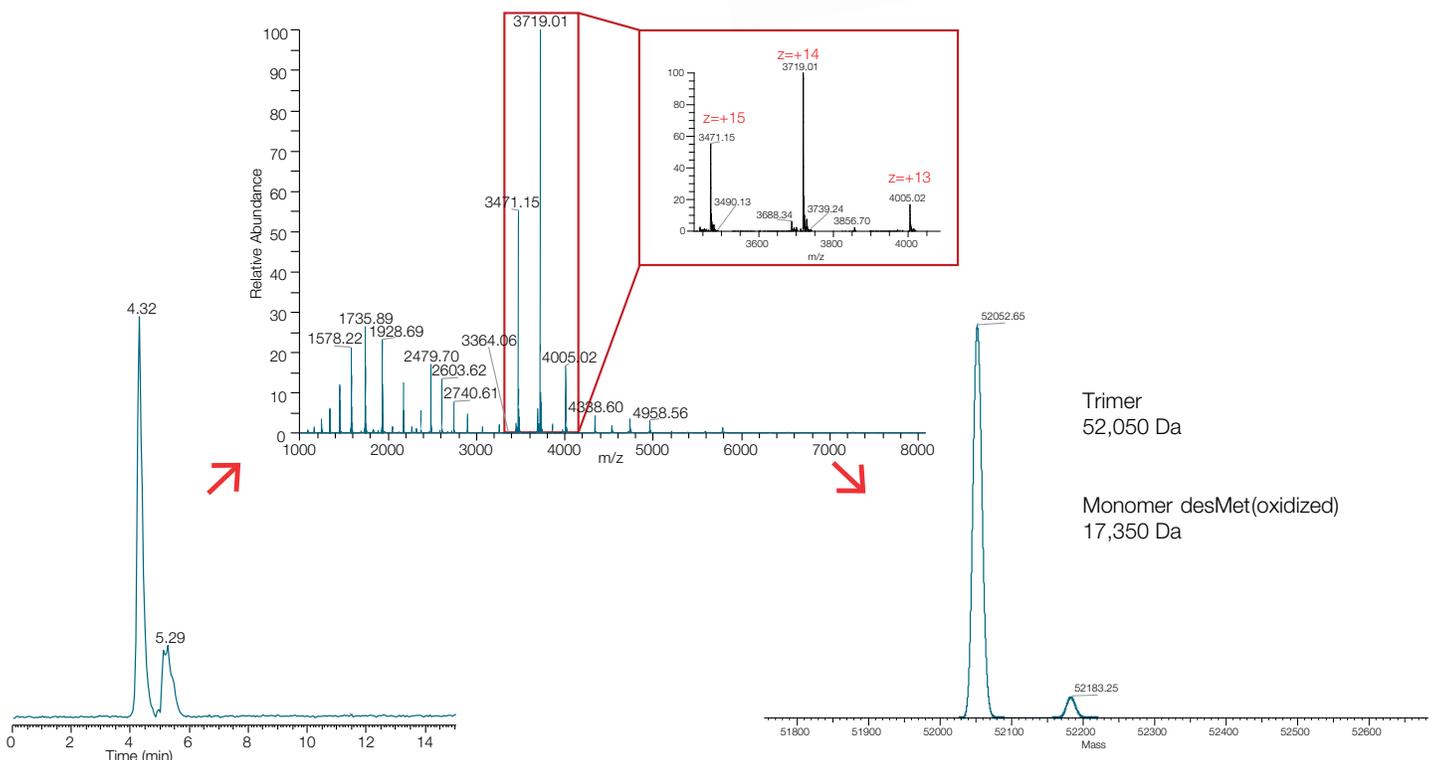
Solving problems fast

The team was able to provide structural insights to answer process engineering questions the same day. An example shown below is one of the R&D System’s TNF-alpha protein products. TNF-Alpha exists as a trimer, but occasionally size exclusion chromatography (SEC) molecular weight determinations using HPLC-UV would show that the mass didn’t align with the trimer expectations. The lot failed during manufacturing or there was an issue with storage, but the team needed to determine why. The product was then analyzed using a platform SEC-MS method. The LC-MS team was able to get accurate mass results that gave zero ambiguity in confirmation that the issue was due to the formation of an oxidized variant of the monomer. With root cause determined, the source could be traced to storage conditions and manufacturing controls implemented.

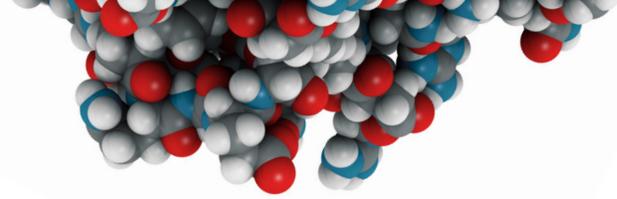
The protein development team delivers a range of analytical tests for various internal and external customers. Consequently, they nurture expertise in both chromatography and mass spectrometry together with a variety of physical-chemical and spectroscopic methods. The team delivers troubleshooting projects for key process engineering functions within R&D Systems. Mark Whittaker leads the team and has been with Bio-Techne for almost 20 years. The protein development department was specifically built to increase front-end analytical capability to answer customer-specific analytical questions, both pre- and post-purchase.



Thermo Scientific™ MABPac™ SEC-1 Size Exclusion Chromatography HPLC Columns for high-resolution separation of monoclonal antibody (mAb) analysis.



Native SEC-MS chromatogram of TNF-alpha separated on a MABPac SEC-1 column, showing mass spectrum and deconvoluted mass spectrum confirming trimeric form and oxidized impurities in under 10 minutes



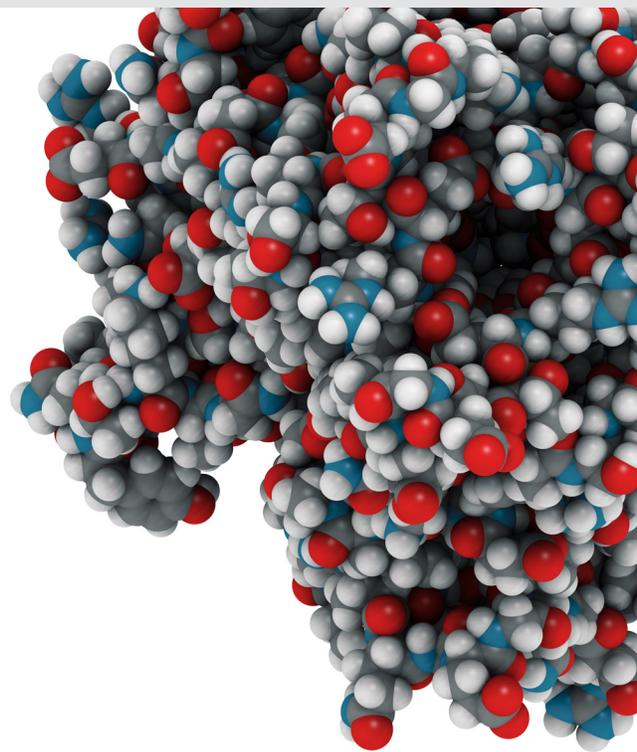
“It was a big change for us. It gave us the freedom to look at a range of experiments. Alex did a fantastic job of developing the SEC-MS method. The technology was productive fast. It was a good opportunity for us to leverage the right equipment at the right time. And, with the right support network at Thermo Fisher Scientific—from sales, service, and through to application support. We’ve had a great experience.”

– Mark Whittaker, Ph.D., Manager, Protein Development, R&D Systems

Successful deployment

“We’re very ambitious and committed to quality. We try to give our customers, both internal and external, 24-hour turnaround time in their analytical results. Our clients look to solve problems fast. They look at both cost-efficiency and speed of turnaround of results. We look to develop methods that can answer questions, with high confidence, fast.”

In the past Bio-Techne outsourced its HRAM LC-MS testing of intact large molecular weight proteins. Investing in bringing that capability in-house enabled quicker decisions and greater efficiencies and an altogether better customer/product delivery service.



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For more information on products from R&D Systems at Bio-Techne please visit www.bio-techne.com

Find out more at thermofisher.com/NativeMS

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