the Analytical Scientist

SPECIAL SERIES:

Biopharma

EDITORIAL

Daddy, What's the Big Deal with Antibodies?

The (bio)pharma industry is booming, and so is our role in its success

"Daddy, what's the big deal with antibodies?"

It blew me off my chair when my 12-year-old daughter suddenly showed an interest in my work. Evidently, the question did not arise from the scientific articles and reports that she had spotted on my desk (I really need to find more time to process these), but rather from a discussion on COVID-19 immunity and testing between a virologist and a politician she had heard on television. And so I did what any responsible parent with a background in life science and biochemistry would do: I gave her a short course on antibodies and antigens, immunoglobulins M and G, T-cells, natural killer cells, innate and adaptive immunity…

As I rambled on with great enthusiasm, it eventually dawned on me that she is probably too young for my nerd babble. That is, until she asked THE question: "Why can't we use antibodies as medicines to treat COVID-19 infection?"

In the last two decades, antibodies have reshaped the pharmaceutical landscape and are today amongst the fastest growing and most lucrative therapeutics (six out of the top ten best-selling drugs worldwide are antibody-based). These biotechnology-derived products are being used successfully in the treatment of cancers and autoimmune diseases, amongst others, and are now also being evaluated as COVID-19 therapies.

Though antibodies are top-of-mind, the healthcare industry is also welcoming other protein-based products (antibody-drug conjugates, fusion constructs, replacement enzymes), as well as nucleic acid (plasmid DNA, mRNA) and cell-based products. All of these share a common denominator: intriguing therapeutic potential and extreme structural complexity. They are the new kids on the block, gaining rapid popularity amongst pharma visionaries, but remaining somewhat mysterious idols in the analytical community.

Oh, boy! How we love to get analytical autographs from those new rock stars, subject them to our newest tools, and spend weeks interpreting their data for discussion with our colleagues and collaborators. With all eyes on pharma and biotech as they are today, we live in challenging yet exciting times for analytical scientists. New and increasingly complex therapeutics and vaccines are being developed at an exponential rate. And, amidst this race, our community must move quickly while maintaining an eagle-eye view of our subjects.

In honor of our crucial role in this space, The Analytical Scientist is running a four-month special series celebrating biopharma in all its glory. Advances are lurking behind every corner, but which compelling stories will break the mold and make the difference. It's time to explore. You in?

Koen Sandra is CEO, RIC, Kortrijk, Belgium.

IN MY VIEW

Fast and Furious HOS Analysis?

Infrared spectroscopy is a useful technique for higher order structure analysis in the biopharmaceutical industry, but conventional systems lack pace and performance. It's time for microfluidic modulation spectroscopy.

The bar is rising for analytical techniques in the biopharmaceutical industry. Data quality used to be the only deciding factor, but other issues are now weighing in – notably, ease of use. Usability is becoming a defining characteristic of analytical tools for biotherapeutics labs looking to do more with less against aggressive timelines. As workflows are refined to maximize information flow, high-throughput systems with automated data acquisition and processing are becoming increasingly desirable. There is a great (and growing) appetite for innovative technologies that can serve this purpose across the biopharmaceutical lifecycle.

Higher order structure (HOS) analysis is crucial in biopharmaceutical development and commercial manufacture; such measurements characterize the secondary, tertiary, and quaternary folding and spatial arrangements that define the three-dimensional shape and interactions of biotherapeutic molecules. Those with a basic grounding in biology will know that changes in HOS impact functionality – and for biopharmaceuticals that can trigger loss of stability, increased aggregation, compromised efficacy, and increased immunogenicity. In short, quantifying and monitoring HOS across biopharmaceutical development and commercial manufacture is critical to understand, identify, and maintain conditions that will reliably deliver a safe and efficacious drug.

A raft of techniques are deployed for HOS characterization, but incumbent technology for secondary structure is currently ill-matched to industry needs (and is a primary target for improvement). Current techniques include far-UV circular dichroism (CD) and Fourier-transform infrared (FTIR) spectroscopy. And both have limitations.

Automated CD instrumentation allows the sequential application of far-UV CD and near-UV CD (for the assessment of tertiary structure) on a single sample set. Such an approach sits comfortably in modern labs, though sample preparation is essential as UV CD is most suitable for relatively dilute and simple solutions. The removal of many common formulation excipients that interfere with the measurement is a common requirement (1).

Infrared spectroscopy has long been prized for its ability to measure secondary structures by probing the amide 1 band associated

"Clearly, there is a pressing need for more suitable technologies."

with stretching vibrations of the protein backbone. FTIR can measure more concentrated, clinically representative samples, and is particularly relevant for monoclonal antibodies because of its sensitivity to the β-sheet motif – a key feature of these clinically vital biologics. However, because of multiple limitations, it is reasonable to assert that FTIR is tolerated rather than loved by the industry… An inability to measure low-concentration samples without pretreatment, susceptibility to background drift, the need to separately collect buffer spectra (and the associated manual background subtraction), poor amenability to automation – all these issues hamper FTIR's use. Clearly, there is a pressing need for more suitable technologies.

Enter microfluidic modulation spectroscopy (MMS). The superior performance of MMS rests on two core technical advances: a high-power quantum cascade laser and a microfluidic transmission cell. The laser enables measurement across a broad concentration range with no sample preparation. The microfluidic cell then modulates the sample with a relevant buffer to deliver automatic background subtraction in real time. MMS systems are also highly automated, with self-monitored cleaning routines and 96 well-plate compatibility. The bottom line: acquisition of sensitive and reproducible data, with substantially less effort.

Such merits explain considerable enthusiasm for MMS from the biopharma industry and point to a bright future within the biophysical characterization toolkit. Industry leaders highlight its ability to demonstrate "high accuracy, linearity, sensitivity, and reproducibility" and "to detect very small protein structural differences, enabling a level of characterization not achievable using conventional FTIR methods" (2). Whether as a replacement for FTIR, for orthogonal measurements of secondary structure, or ultimately as a primary characterization tool for protein products, MMS shows how the right analytical tools can easily find a loving home in the biopharmaceutical industry.

Jeff Zonderman is Chief Commercial Officer, RedShift BioAnalytics Inc., Greater Boston, MA, USA

REFERENCES AVAILIABLE ONLINE

ONLINE

(Prote)omics in Next-Gen Drug Development

Collaboration between different omics fields will be key in supporting the next generation of medicines

Mark Rodgers is Senior Vice President, SGS Life Science, PA, USA

ONLINE

The Future of Nucleic Acid Therapies

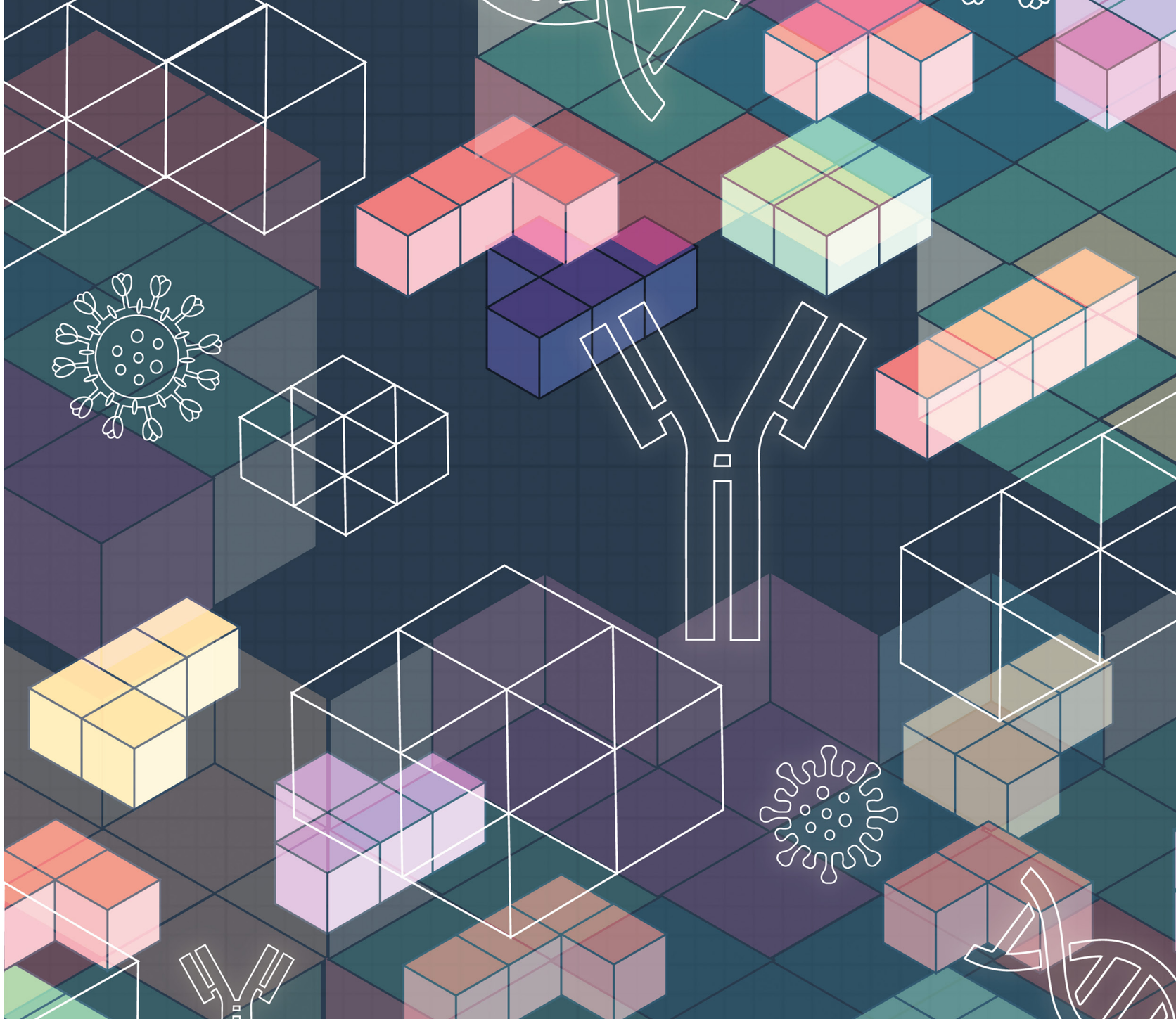
Medicines derived from genetic building blocks have the potential to transform patient care

Brian Carothers is Vice President & GM, Nucleic Acid Solutions, Agilent Technologies, Santa Clara, California, USA

FEATURE

Let's Get Biophysical

Nuclear magnetic resonance and hydrogen-deuterium exchange are uncovering key information to facilitate small molecule targeting of the SARS-CoV-2 envelope protein



The SARS-CoV-2 envelope protein is a small transmembrane protein found in the viral lipid envelope. In other coronaviruses, the envelope plays key roles in viral assembly, morphogenesis, and virus-like particle formation and release. And although the envelope protein is not solely responsible for replication, coronaviruses unable to express it are severely attenuated. In fact, envelope protein inhibition can severely mitigate replication in a number of other coronaviruses – these findings indicate that the envelope protein is a viable target for not only the development of antivirals, but also the generation of attenuated strains of the virus for vaccines.

With this in mind, we set out to analyze the envelope protein and use its structural information to identify small molecules that can impede its function. In doing so, we are focusing on small molecules that are approved for the treatment of other diseases; by repurposing them, we hope to identify novel therapeutic options that are already available – and approved. This will dramatically reduce the time needed to get these treatments to COVID-19 patients.

"This approach can measure the dynamics of the protein at atomic-level resolution over a range of timescales – and, because it is solution-based, it can measure dynamic events that are inaccessible to alternative methods like X-ray crystallography."

So how do we obtain the protein information we need? First, we obtain high levels of envelope protein using a bacteriophage T7 expression system. This is subsequently purified using a combination of fast-protein LC and high-performance LC, giving us samples of envelope protein at over 95 percent purity. For our biophysical experiments, we need milligram quantities of the protein. Nuclear magnetic resonance (NMR) and hydrogen/deuterium exchange MS (HDX-MS) are our methods of choice for probing the secondary and tertiary structures of the envelope protein to identify binding sites for potential small molecule inhibitors. This approach can measure the dynamics of the protein at atomic-level resolution over a range of timescales – and, because it is solution-based, it can measure dynamic events that are inaccessible to alternative methods like X-ray crystallography. If necessary, we believe we could use NMR to solve the high-resolution structure of the entire envelope protein.

Understanding the envelope protein will allow us to generate hypotheses regarding the specific roles it plays in SARS-CoV-2 replication. To aid with this, we are also developing a platform to generate mutant SARS-CoV-2 viruses, which will further our understanding of the envelope protein's role in the viral life cycle and support our biophysical findings.

We plan to complement our NMR studies with hydrogen–deuterium exchange MS, which extends the timescale over which we can extract dynamic information. The Waters COVID Innovation Response Team (of which we are a part) has been crucial in supporting and accelerating our progress both with material supplies, and expert input from Waters consulting scientists has been invaluable.

Overall, we are optimistic about the scientific community's efforts to provide us with effective treatments and vaccines against COVID-19. The sheer volume of work is encouraging – and, when such a monumental effort is made toward a single goal, we often see results sooner than expected. For example, the Altimmune vaccine developed at the University of Alabama at Birmingham is showing promising preclinical results – as does the vaccine from the UK'S University of Oxford, which appears to induce immunity with relative safety.

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Peter Prevelige is Professor, Department of Microbiology, the University of Alabama at Birmingham, Alabama, USA.

ONLINE

Charge Detection for Virus Protection

An emerging charge-detection technique allows MS analysis of super-sized molecules – including the SARS-CoV-2 spike protein

David Clemmer is Professor of Chemistry at Indiana University, Bloomington.

ONLINE

Small, But Mighty

Vaccines may hog the limelight, but small-molecule inhibitors could prove to be the secret weapon that addresses the pandemic

Brent R Stockwell is Professor of Biological Sciences and Chemistry, Columbia University, New York, USA.

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Achieving Harmony Amidst the Chaos?

Exploring the unique capabilities of Waters for accelerating biopharmaceutical research and development

Biopharmaceuticals exemplify the brilliance of modern science. With these molecules, we are able to help patients with various diseases – from the most common cancers to rarer orphan genetic ailments. When treating patients, the consistent quality of a biopharmaceutical or biosimilar is important to achieve the drug's desired efficacy and patient safety profiles.

Our "Subject Matter Experts" have closely followed the evolution of biopharmaceuticals and the concomitant changing analytical needs, developing innovative technologies specific for this exciting and growing market.

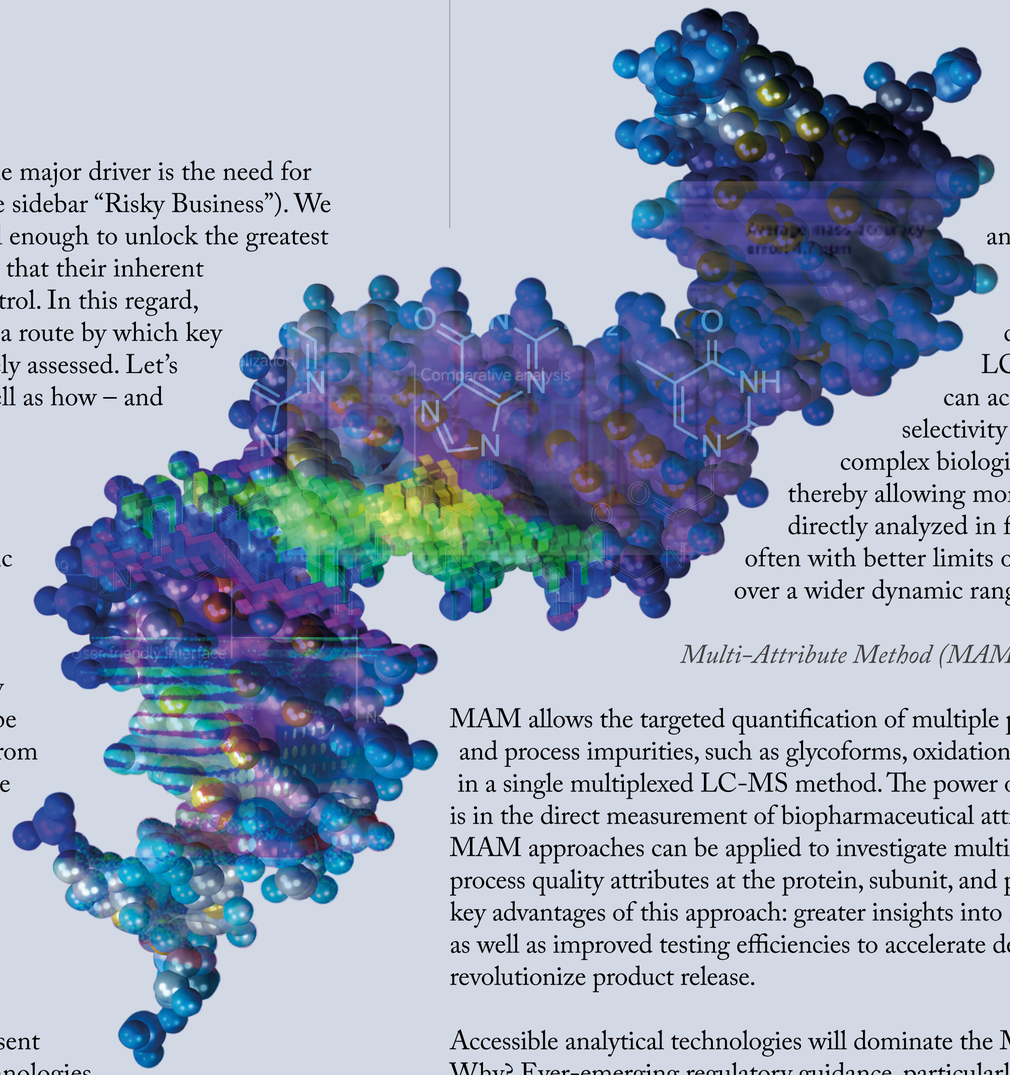
Analytical solutions

Analytical techniques play a crucial role across the lifecycle of biopharmaceuticals. How? By helping us to fully understand the product under development, including answers to crucial product lifecycle questions like "Have we continued to make the same drug that was produced for clinical studies?" But that's not all. Analytical techniques also allow us to explore the links between molecule structure and activity, physical and chemical drug stability, the impacts of dosage form and formulation on efficacy and shelf life, and the control of critical impurities.

When conducting such analyses, one major driver is the need for efficiency and cost-effectiveness (see sidebar "Risky Business"). We must understand our molecules well enough to unlock the greatest operational efficiencies without fear that their inherent variation exceeds our ability for control. In this regard, analytical characterization provides a route by which key molecular attributes can be effectively assessed. Let's take a look at those attributes, as well as how – and why – we study them…

Critical quality attributes (CQAs)

CQAs are the variants of therapeutic molecules that are measured and monitored to ensure that the final biopharmaceutical meets necessary quality, safety, and efficacy requirements. These qualities must be identified, assessed and controlled from development through to post-release process improvement campaigns per global regulatory requirements, but the structural complexity of biologics and their production represent an analytical challenge to ensure this control.



HPLC, UHPLC, and UPLC represent performance tiers of separation technologies for biopharmaceutical applications, with increasing performance based on decreasing chromatographic particle size. The quantitative power of optical detection is now being extended with the qualitative and quantitative capabilities of routine mass detection. Modern LC-MS platforms can achieve high analyte selectivity for characterizing complex biological samples, thereby allowing more attributes to be directly analyzed in fewer analyses – often with better limits of detection and over a wider dynamic range.

Multi-Attribute Method (MAM)

MAM allows the targeted quantification of multiple product variants and process impurities, such as glycoforms, oxidation, and deamidation, in a single multiplexed LC-MS method. The power of this approach is in the direct measurement of biopharmaceutical attributes, where MAM approaches can be applied to investigate multiple product and process quality attributes at the protein, subunit, and peptide level. The key advantages of this approach: greater insights into molecule variation, as well as improved testing efficiencies to accelerate development and revolutionize product release.

Accessible analytical technologies will dominate the MAM landscape. Why? Ever-emerging regulatory guidance, particularly for emerging novel therapies, for one reason – but user experience (or lack thereof) in organizations now looking to deploy LC-MS methodology for the first time is a critical factor. Although LC-MS has become the primary

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workflow for MAM, the use of LC-MS for product monitoring in manufacturing and QC product release presents a challenge to many companies; thus, a simple, robust, and user-friendly LC-MS platform will be essential to realizing the full value of MAM approaches, without requiring these organizations to reinvent themselves.

Physicochemical attributes

A similar concept of multiple attributes can be applied and another way to execute on this concept is an orthogonal approach of interrogating molecules on different platforms to ultimately obtain similar evidence. Physicochemical characterization digs into properties such as degradation and aggregation, which play a crucial role in understanding drug activity in biological systems. These studies take a compound from the process of biochemical characterization for CQA identification to biophysical characterization and functional assays. They generally comprise physical and structural studies, and provide information not easily detectable in other attribute-based analyses.

Harmonizing efforts

A broad range of complex analytical technologies are used together to draw a sufficiently clear picture of a given biomolecule. And, in the process, scientists may generate vast volumes of data.

More data (usually) means more communicated information, which is great – the information is used to keep patients as safe as possible, while ensuring efficacy. But the real demand is for robust and flexible solutions that can capture and then integrate the right data at the right time from all relevant sources. By harmonizing data streams, we can establish relationships within and between quality attributes, advancing our product knowledge, improving product quality, and boosting organizational efficiency. But true harmony will require that organizations come together in alignment and streamline workflows…

Waters: 21st century science

The right mix of technologies, data analytics, and professional support are needed to navigate biopharmaceutical discovery, development, and manufacturing. From sample preparation and separation chemistries to detection technologies that promise robust results, our integrated platforms have helped customers bring new and innovative molecules to the market for over 60 years. And we have no plans to stop!

We pride ourselves on intelligent informatics technologies that extract the most value from harmonized data, because we want to deliver clear benefits: deeper insights, reduced time to results, and lower costs. At the same time, our professional services organization is able to work closely with you to ensure you have the tools to meet today's challenges – and to help you rise to tomorrow's opportunities.

Harmonized Innovation

With a focus on tomorrow's opportunities in mind, we are continuing our quest for excellence by focused development in four important directions.

INFOGRAPHIC

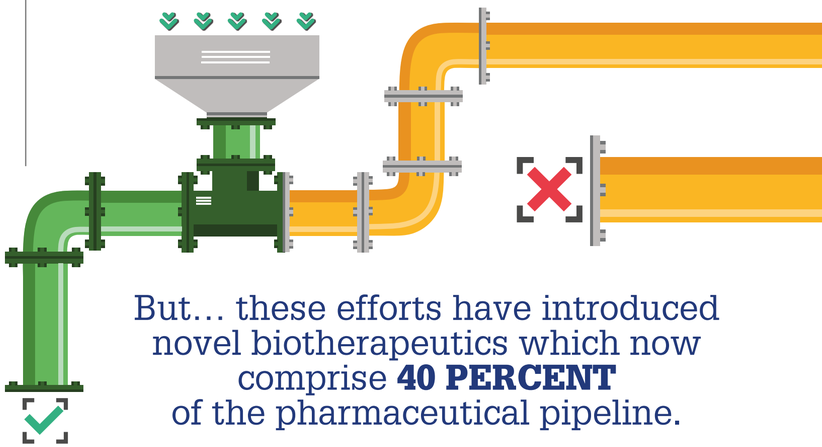
Risky Business

Of the tens of thousands of molecules screened in early R&D, few ultimately achieve approval and commercialization.

It can take a dozen years for a new drug to reach the market

… with a resulting cost of around

$2.6 BILLION



But… these efforts have introduced novel biotherapeutics which now comprise **40 PERCENT** of the pharmaceutical pipeline.

And **70 PERCENT** of the top-selling drugs are biologics

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Automating sample preparation to obtain consistent high-quality analytical samples

The Andrew+ liquid-handling robot from Andrew Alliance (a Waters company) simplifies complex workflows that are prone to pipetting and protocol errors, increasing confidence in results collected on downstream analytical platforms. It also improves productivity by relieving lab workers of repetitive and labor-intensive processes, while ensuring reliable and traceable sample preparation.

Enhancing LC analysis with routine mass detection

The ACQUITY™ QDa™ is a mass detector operating in both the small and large molecule space – and it has achieved its goal of deploying routine nominal mass detection as a robust and intuitive complement to optical detection. Using the ACQUITY™ QDa™, any scientist can – for the first time – consistently benefit from MS data without the need for specialized training or expertise.

The ability to track peaks in a peptide map by both mass and retention time accelerates method development, provides for quicker and more confident method transfer, and provides practical extension of sensitivity and dynamic range over optical based assays for targeted quantification. For scientists who would like to expand upon analysis of product attributes at the peptide and protein levels, the capabilities of the Waters BioAccord™ LC-MS System with SmartMS™ are the answer. This system takes usability for high-resolution LC-MS analysis to an entirely new level, with simple, automated setup, comprehensive system health monitoring, and simplified user-system interactions, one that is deployable across development, manufacturing, and into product release. The challenges posed by the adoption of traditional LC-MS platforms into organizations with limited MS experience are overcome by an integrated solution that combines streamlined workflows for biotherapeutic analysis that generate consistent and reproducible results.

Bridging attributes: from chemical to physical

Waters takes a common integrated approach in its instrument portfolio, including ownership of and strategic partnerships with myriad instrument companies. Our TA Instruments business, for example, offers higher-order structure instrumentation, such as differential scanning calorimetry – a technique typically used in formulation studies and is a great complement to Waters' hydrogen deuterium exchange LC-MS. Then there is the TA Instruments Affinity ITC (isothermal titration calorimeter), which is designed with the challenging demands of biopharma labs in mind, addressing association constants and its underlying enthalpic drivers from protein-antibody interactions to the formation of lipid nanoparticles. But our partnerships don't end there. Additional platforms in Waters' biophysical analysis toolkit include charge detection MS, infrared spectroscopy and grating coupled interferometry, available through partnerships with MegaDalton, RedShiftBio and Creoptix, respectively. Megadalton-sized molecules with human health relevance are natively characterized through simultaneous measurement of size and velocity using a charge detection MS from MegaDalton Solutions. Microfluidic modulation spectroscopy from RedShiftBio focuses on secondary structure and measurements of aggregation, quantification, stability, and structure. And Creoptix's grating coupled interferometry allows scientists to successfully determine affinity and kinetics from interactions in pure preparations, or even crude samples and biofluids, such as plasma.

Integrated data intelligence for streamlined acquisition, processing, and reporting of information

The Waters UNIFI™ Scientific Information System was the first informatics platform that combined chromatographic and high-performance MS data workflows into a single solution. Efficiency was amplified through the availability of modern data processing methods, while direct savings from reduced training needs and compliance expenditures on a common compliant-ready networkable platform made UNIFI difficult to ignore within both regulated and non-regulated lab organizations.

The newest versions of these existing UNIFI applications – augmented by totally new applications for attribute-based monitoring studies – are being released on our interoperable platform: waters_connect ™. The combined power of a common network environment supporting LC-optical and LC-MS for product characterization and attribute monitoring can be recognized on this modern informatics platform. Here, the hope is that organizations of all sizes will be able to realize the potential of these platforms in terms of scientific knowledge, productivity, and financial savings.

FOR MORE INFORMATION ON ALL THESE TOPICS, PLEASE READ THE FULL-LENGTH ARTICLE AND VISIT THE WATERS BIOPHARMACEUTICAL MARKET WEB PAGES

SOLUTIONS

Copycat Chemistry: Uncovering Counterfeit Drugs

As fraudsters get more sophisticated, it's vital that counterfeit analysis keeps pace

The US Food and Drug Administration (FDA) defines counterfeit medicine as a fake medicine that is contaminated, contains the wrong or no active ingredient, or contains the right active ingredient at the wrong dose (1). These "knock-offs" have caused significant harm to public health, and though many steps have been taken to deter fraudsters, fake pharmaceuticals remain a serious issue in both developing countries and the Western world. In fact, the Pharmaceutical Security Institute reported 5,081 crime incidents in 2019 – an all-time high – and the COVID-19 pandemic has only exacerbated the problem (2). Earlier this year, Interpol's annual Operation Pangea reported an increase of around 18 percent in seizures of unauthorized antiviral medication, and more than 100 percent increase in seizures of unauthorized chloroquine (3) – a direct response to the coronavirus outbreak.

It is clear that counterfeiters will stop at nothing to make a profit, so what can be done to combat fraudulent pharmaceuticals? There are a number of measures in place around the world to detect counterfeits, including track and trace packaging, blockchain technology, and monitoring of online pharmacies. But with the global market for counterfeit medicines continuing to expand, it will become increasingly difficult to keep our supply chains safe. Here, we discuss the growing need for sophisticated chemical analysis of the drugs themselves, and our approach to telling the real products from the fakes.

Identifying a fake

The analytical methods used to detect counterfeits vary widely in the equipment, training, and preparation involved. For more detailed characterization needs, NMR, GC, HPLC, and MS are the more popular techniques, but they demand more extensive training and preparation of samples. On the other hand, spectroscopic techniques offer a faster and less labor-intensive route to counterfeit identification. Some of the more popular techniques include Raman, near-infrared spectroscopy (NIR), and mid-infrared spectroscopy (MIR). In addition, having access to energy dispersive X-ray (EDX) and UV-Vis spectroscopy is useful when additional information is needed on a specific product; for example, to uncover provenance or link multiple cases together.

Typically, there is a progression of techniques that any counterfeit screening lab will run through to confirm or deny the authenticity of a product. Each and every case is different but, as a general rule, our team will start with a morphological examination of the sample, which involves examining the size, shape, and color of the suspect product, and looking for any inscriptions or engravings. We often use microscopy in this work, so we can take high-resolution images of the samples if we need to – especially if we start to see any evidence of foreign matter, or visual clues indicating inauthentic manufacturing processes or materials.

We'll then move on to a more detailed analysis of the sample. We usually rely on spectroscopic techniques – primarily because spectroscopy provides very specific data for what we consider to be a minimal investment of time and resources. In contrast to chromatography, where you spend maybe 90 percent of the time preparing and running your samples, and 10 percent interpreting the data, with spectroscopy it's almost the reverse. Moreover, it is non-destructive in nature – a key benefit when you're working with a limited amount of sample, which can be used as evidence in court proceedings.

Raman spectroscopy is our go-to technique, but the same principle applies across all our vibrational spectroscopic approaches. Suspect drugs are scanned using a laser, which results in a change in the energy state of the scattered light by the different chemical functional groups present in the suspect product. The resulting spectral fingerprint can then be compared against the fingerprints of known drugs. Notably, our lab ensures that spectral fingerprints are consistent across different batches of the same Bristol Myers Squibb product – we measure the degree of fingerprint variation across batches, validating with products from other manufacturers. In this way, we can ensure that fingerprints are unique for each and every type of medicine we produce.

Knowing your limits

Our approach to counterfeit detection depends on the product we are testing and the limitations of certain techniques. For example, highly colored samples are problematic for Raman spectroscopy – with the more powerful lasers of a benchtop instrument, you can end up burning your sample. With limitations in mind, it's also important to have a complete toolbox of complementary techniques at your disposal. This way, you can piece different data together to get a complete picture of a drug.

One of our major limitations, until about 4 years ago, was the inability to routinely analyze biologics spectroscopically because of their size and complexity – and their low concentration in the aqueous solutions in which they are often formulated. That meant running more traditional, labor-intensive tests using MS or NMR that also consume the precious sample. To overcome the problem, our team at Bristol Myers Squibb developed a benchtop method for Raman analysis of biologics, using a special sample preparation technique called drop coat deposition (DCD) [See sidebar]. So far, the method has enabled us to stay ahead of biologics counterfeiters.

Smarter, faster, more productive

The bad news is that counterfeiters are getting smarter and they are learning from their mistakes; over the years, we've seen counterfeit products get better in quality. As this continues, it's going to become harder for us to tell the difference between authentic and fake drugs. All manufacturers must continue to keep pace with emerging trends by employing the most cutting-edge technology in their counterfeit screening labs.

We're not only on the hunt for the latest technology, but we are also increasingly looking into portable technology. In fact, we're currently working on a handheld version for our biologics analysis using a portable Raman spectrometer. Miniaturization boosts flexibility and coverage by enabling any time, any place testing – but it does tend to come with a trade-off in terms of performance. That said, we've typically found that the benefits outweigh any drawbacks; for example, portable instrumentation allows us to roll out analytical technology in manufacturing sites across the world, and even in the hands of non-scientists, which improves efficiency and empowers the user.

As well as miniaturization, we also see an increasing need for user-friendliness. As counterfeiters get more sophisticated and widespread, it's inevitable that we're going to have to increase testing, which means more people outside of the lab environment conducting analyses. Whether it's the patient, the pharmacist, or someone else along the supply chain – these tools must be accessible to those without professional training. The software and sensor might increase in sophistication, but the usability must be streamlined and simple.

It's true that counterfeiters are getting increasingly intelligent in their approach. At some point, they will likely find a way to fool our packaging and tracking authentication systems. But being able to get the exact same chemical composition as a regulated product? Unlikely – and that's why counterfeit analysis labs need to stay ahead of the game.

REFERENCES AVAILIABLE ONLINE

Ravi Kalyanaraman is Director, Global Quality Analytical Science and Technology group with Global Product Development and Supply, Bristol Myers Squibb Company, US

Scott Huffman is Associate Director, Global Quality Analytical Science and Technology group with Global Product Development and Supply, Bristol Myers Squibb Company, US

ONLINE

Drop Coat Deposition Raman

With a growing number of counterfeit biologics cropping up worldwide, drop coat deposition Raman offers quick and accurate fingerprint analysis for proteins

SITTING DOWN WITH

Safety Guaranteed

Sitting Down With… Nadine Ritter, President, Global Biotech Experts, Maryland, USA

Who inspired you to pursue a career in science?

Back in the 1960s and 1970s, children's after-school cartoons in the USA were accompanied by a mascot-type character. New Orleans had a mascot known as "Morgus the Magnificent." Morgus wore a lab coat and had a gothic laboratory filled with bubbling beakers and funny-looking lab assistants. I was totally engrossed by it all. Ever since then, I longed for a life in the laboratory.

How was the landscape for women in science back then?

Women faced many difficulties in the early 1970s – particularly in funded academic research. Funding was difficult to acquire and women's research was rarely reviewed. In the 1980s a group of women from the NIH formed a professional society to combat the issue: The Association for Women in Science. I became actively involved during my college years in Houston. I soon found myself leading the Houston chapter, and later the chapter in Chicago. We focused on mentoring young women in science by helping them to obtain the information and skills needed to conduct their research. We also advised on how to deliver talks, organize meetings, and manage teams; many pioneering women scientists were involved in this effort, and I was fortunate to work alongside them and learn from them.

When did you move into pharma analysis?

I trained as a protein chemist and molecular biologist at Rice University in Houston, and worked for over a decade at one of the biggest medical complexes in the world: UTHSC-Houston. There was no modern recombinant biotechnology industry at that time, but the1980s ushered in a boom regarding our ability to scale up and express target proteins like monoclonal antibodies. It was then that I made the switch from academia to industry to work in biopharma analysis, after being recruited to work as a protein chemist at Abbott Laboratories.

Did you ever anticipate the move from academia to industry?

No – I thought I'd spend my entire career in academia, eventually becoming a beloved faculty member at a prestigious university, giving profound lectures to adoring students – just like my own favorite professors! But NIH funding was tight. It was a challenging time and a future in academic research was uncertain. It made sense to move to a new position in industry with people whom I trusted, but it was a scary transition. At that time, leaving academia meant you no longer existed. Many colleagues warned me that I was "giving up." I'd say that I wasn't giving up. I was going to do the same protein chemistry, just in a more applied manner.

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SPOTLIGHT ON...

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