HORIBA

Veloci

BIOPHARMA ANALYZER

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A-TEEM™ Molecular Fingerprinting

Absorbance Transmittance and a Fluorescence Excitation Emission Matrix (A-TEEM)

Overview

The Veloci A-TEEM BioPharma Analyzer contains innovative, column-free molecular fingerprinting technology designed for the biopharma and pharma industries. By integrating the selectivity of chromatography with the benefits of optical spectroscopy, Veloci offers a fast, simple, and cost-effective method for comprehensive component analysis in various industrial QC/QA life science applications. Unlike traditional methods such as chromatography and mass spectrometry, Veloci's A-TEEM™ Molecular Fingerprinting technology provides component analysis without time consuming and slow separations. This allows simplified workflows and drastically reduces ownership costs.

This versatile tool requires no sample preparation and is suitable for a wide range of applications, including monoclonal antibody discrimination, cell media monitoring, vaccine characterization, protein stability analysis, and AAV quantification. The Veloci A-TEEM BioPharma Analyzer enables label-free intrinsic fluorescence analysis, offering high accuracy and efficiency in research, production and QC/QA environments.

Key Benefits

- Selectivity of chromatography, but using spectroscopy.
- Superior sensitivity compared to HPLC and other spectroscopic techniques like absorbance, FTIR, and Raman.
- Hassle-free operation with no columns, mobile phase, or sample preparation needed. The lack of a mobile phase drastically reduces solvent usage and eliminates the cost of proper disposal.
- Cost-effective and user-friendly: Suitable for both research labs and production processes.

EzSpec Software

Veloci runs on EzSpec™ software, designed with user experience and data integrity. EzSpec™ Apps intuitively help you identify and select the analysis you want to perform. The navigation of EzSpec enables easy user interaction. EzSpec v2 Datastore database enables easy filtering and searching of all files.

Features for EEM and A-TEEM

- **SampleQ Application** for batch EEM/A-TEEM acquisition, processing and ASCII file export.
- **Batch EEM/A-TEEM Processing Tools** for subtracting a blank, data interpolation, applying inner-filter effect correction, Rayleigh masking, and RSU normalization.
- **3D-to-2D Profiling Tool:** Extracts 2D spectra from 3D data sets such as EEM/A-TEEM or Kinetic Emission Spectra.
- **Synchronous Scan** extraction tool from EEM/A-TEEM data.
- **Pass/Fail Application** for comparing new data to reference data in both 2D and 3D modes.
- **ASCII file export and PDF report generation.**
- Optional **EzSpec-P11 with PLATINALINK audit** for 21 CFR Part 11 and GMP.

EzPAT

EzPAT is a server written with OPC UA protocols to integrate control of Veloci with third-party orchestration software platforms. This server enables the Veloci and A-TEEM methods to be integrated into PAT process orchestrations that work in a GMP environment. For more information on EzPAT and integrating Veloci with your orchestration client, please contact the HORIBA Life Science team!

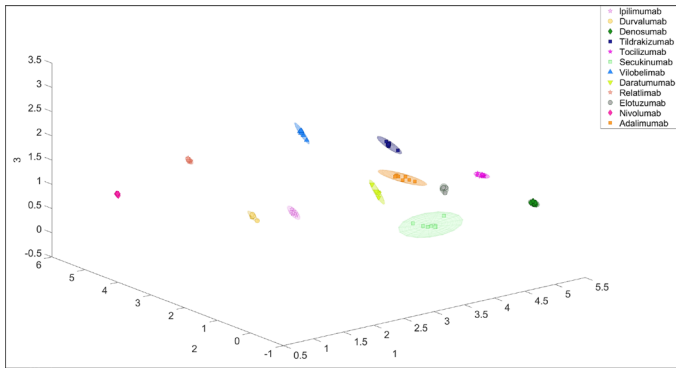
A-TEEM Direktor

A-TEEM Direktor multivariate analysis software is a software suite designed to empower scientists to extract meaningful insights from A-TEEM data. The guided workflow takes a user step-by-step through the modeling of A-TEEM calibration data sets. Prediction tools facilitate the application of calibrated models to predict class or concentration information from new sample data. PARAFAC, PCA, and PLS models, among others, are available for decomposition, classification, or regression analysis of A-TEEM data. For GMP labs, A-TEEM Direktor includes an audit trail, PDF report generation, and user login authentication.

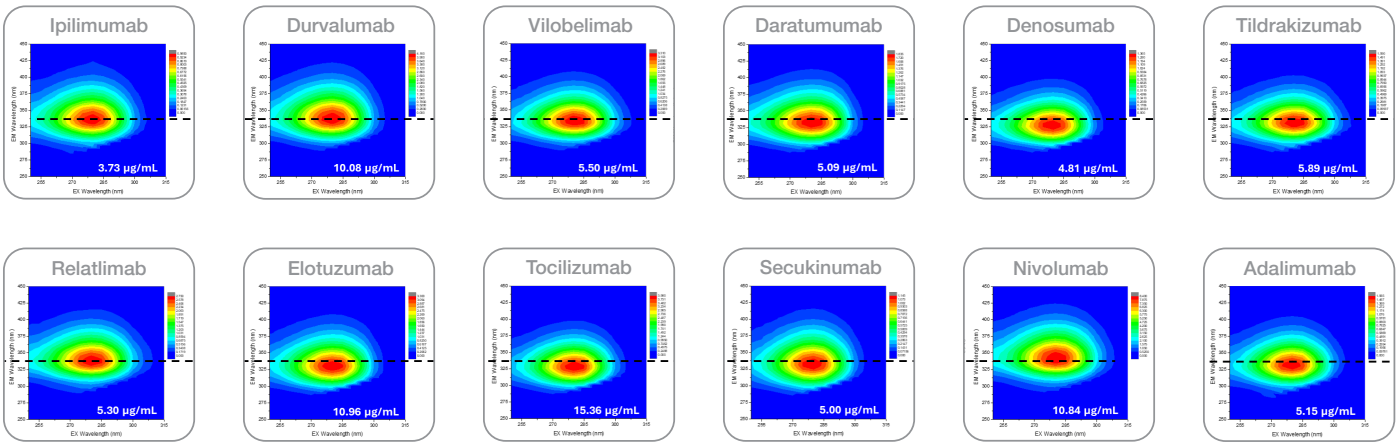
Monoclonal Antibodies (mAb)

Monoclonal antibodies (mAbs) are a significant part of the profiles of many biopharma companies' portfolio. Their composition of heavy and light chain units allows for extraordinary flexibility in design, and provides the ability to target extremely specific sites. The Veloci BioPharma Analyzer can be used to provide discrimination between extremely similar mAbs. By studying the intrinsic fluorescence of aromatic amino acids in the proteins, Veloci provides a label-free platform for investigating proteins in their natural state.

The Veloci BioPharma Analyzer can discriminate mAbs that have 90% or higher sequence homology as distinct from each other, as demonstrated in the PARAFAC plot to the right.

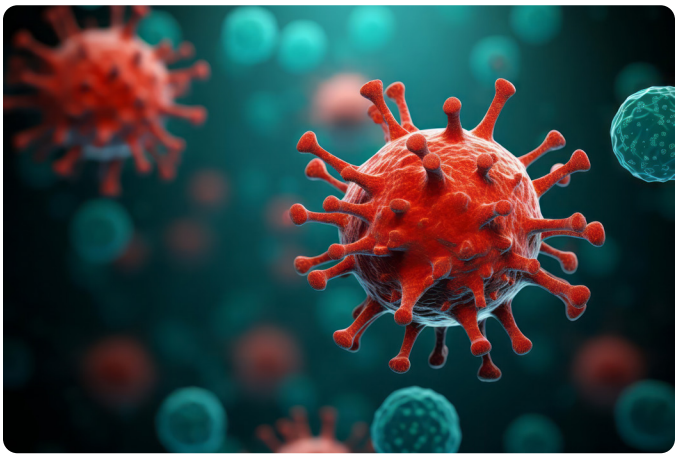


This study looked at two groups of commercially available mAbs, one with 90% or higher sequence homology and one with identical numbers and locations of aromatic residues. Measurements were taken in low PPM range (µg/mL) at 10 separate concentrations. We were able to discriminate all 12 mAbs in the study.



AAVs (Adeno-Associated Viruses)

Adeno-associated Viruses (AAV) are small viruses (~20 nm) that infect humans. Several of their properties make them extremely attractive as viral vectors for the delivery of selective gene therapies. Most relevant of these is the fact that they can infect dividing and quiescent cells without integrating into the host genome. Quantification of both the capsid and the genome titers is considered a Critical Quality Attribute (CQA) for AAV production. Dosage and potency are directly affected by the Empty/Full ratio of the capsid and its payload.



By measuring the intrinsic A-TEEM fluorescence fingerprints of the capsid of AAVs, it is possible to not only differentiate AAV subtypes, but to also quantify the empty/full ratio. Even when non-fluorescent payloads like cDNA are integrated, they have a quenching effect on the intrinsic fluorescence. The stronger the quenching effect, the fuller capsids are present. By making use of this phenomenon, it is possible to quantify the empty/full ratio of AAVs in a label-free manner without the need of an analytical centrifuge which is the current gold standard for industry.

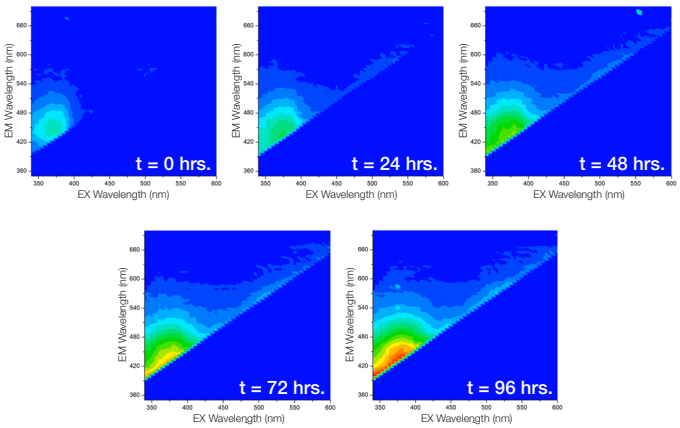
Vaccines

Standard separations-based approaches for vaccine characterization are too slow to keep up with the industry demand for rapid analysis. However, typical vaccine formulations (extremely low protein concentration, aqueous solutions, with confounding excipients) make these particularly challenging samples for the “standard” spectroscopic toolbox (Raman, FTIR, NIR). The capabilities of A-TEEM make it highly suited for the analysis of vaccines. A-TEEM has been used to differentiate vaccine formulations, detect aggregation, identify amino acid substitutions and post-translational modifications, screen for batch-to-batch variation, and perform QC measurements for batch release.

Protein Stability and Aggregation

Stability in proteins is a Critical Quality Attribute (CQA) across the biopharma industry. Proteins can be affected in many ways during post-production due to a variety of factors, however one of the main concerns is protein aggregation. This can be caused by factors such as heat exposure, shaking, too much pressure at filling, or just random entropy. Regardless of the cause, protein aggregation results in misfolding and causes the API to lose potency and specificity, increasing the risks of side effects.

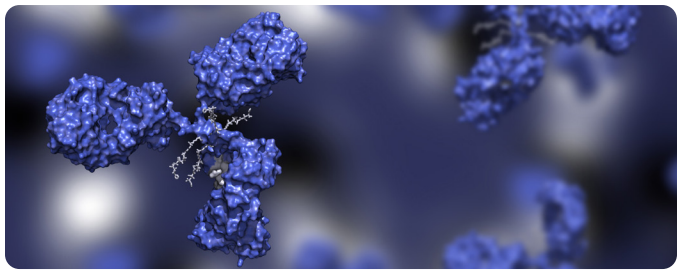
To prevent aggregation, it is crucial to detect the process as early as possible. The Veloci BioPharma Analyzer can be used to detect and monitor these aggregates as they form.



You can see the A-TEEM molecular fingerprint signal grow over time as the aggregates form. This work mirrors established literature indicating that certain structures, mainly β-sheets, have an intrinsic fluorescence profile that can be monitored in real time as more of them accumulate.

Antibody-Drug Conjugates

Antibody-Drug Conjugates (ADCs), are a hybrid therapy, usually used for cancer treatment, designed to target cancerous tissue while sparing healthy areas. They consist of a target antibody, often a mAb, that specifically targets a receptor solely expressed in cancerous tissue. That antibody is then linked to an extremely cytotoxic compound via a linker. Upon binding to the unhealthy tissue, the linked compound is then absorbed into the tumor cells, which are destroyed.

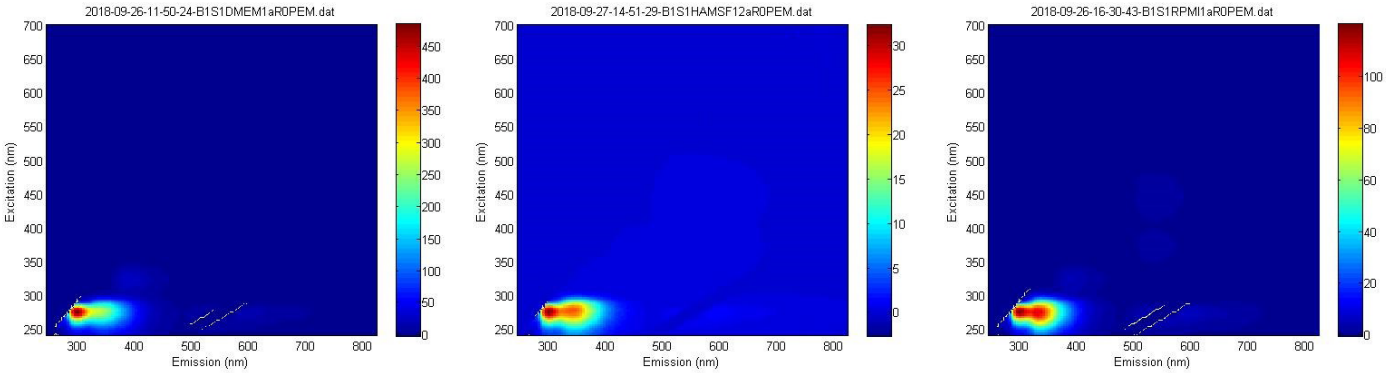


Veloci A-TEEM molecular fingerprints can discriminate between the mAb portion of the drug, the payload, and the linker. Monitoring the process of the linker attaching to the mAb and to the lab is crucial to the production process as the starting materials are quite expensive to produce. Monitoring the reaction in real-time allows the user to see how much free material remains, versus reacted final product, allowing users to control the endpoint of the reaction.

Cell Media Monitoring and Bioreactor Monitoring

Cell culture media for bioreactors are usually prepared as an aqueous solution and provide everything a cell line needs for optimal growth, as well as product yield and quality. Even subtle variations in composition can have a noticeable impact on the growth rate of the cell culture and its yield. Thus, identifying and analyzing cell culture media is important. As a result, the pharmaceutical industry has begun to turn to spectroscopic methods, such as fluorescence, for cell culture media analysis, due to the speed of testing, minimal sample handling requirements, and lower cost when compared to mass spectrometry and chromatography.

Of particular interest are Fluorescence Excitation-Emission Matrix molecular fingerprints complemented by simultaneous Absorbance and Transmittance measurements (A-TEEM). Cell culture media in bioreactors, typically prepared as aqueous solutions, provide essential nutrients for cell growth and product yield. Even small compositional changes can significantly affect cell culture outcomes, making accurate analysis crucial. The pharmaceutical industry increasingly uses fluorescence spectroscopy, particularly A-TEEM, for its speed, minimal handling, and cost-effectiveness, compared to mass spectrometry and chromatography.

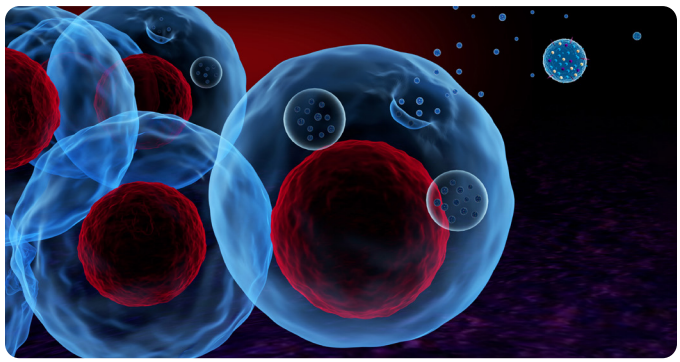


Examples of cell culture media A-TEEM™ molecular fingerprints. The media shown are from the samples DMEM1 (left), HAMSF12 (middle), and RPMI1 (right).

Exosomes

Exosomes are small extracellular vesicles, 30-150 nm in diameter, which have been determined to play a crucial role in extracellular signaling. They have been observed in both prokaryotic and eukaryotic organisms, meaning they are incredibly widespread in nature. Exosomes bud off from their parent cells in a sealed package, taking the properties of their parent cell walls with them and encasing many intracellular components with them. Many bioactive markers have been found encased in exosomes, including proteins, lipids, DNA, and RNA.

This cargo's diversity has led to exosomes having many roles within the body, including immune regulation, tissue regeneration, cancer progression, and neurodegenerative diseases. They can be released by healthy or diseased tissue, and their composition correlates with the health of their parent cell, giving them significant potential for diagnosing diseases. In addition, since exosomes are already carrying cargo from cell to cell, it has been shown that replacing that cargo with therapeutics could lead to more reliably targeted delivery of therapeutics.



The Veloci BioPharma Analyzer discriminates between different subtypes of exosomes using label-free intrinsic A-TEEM fluorescence. This is crucial when isolating exosomes from tissues to ensure you only have the species of interest. As discussed with AAVs, A-TEEM fluorescence signals are sensitive to whatever is contained within molecules and their natural state. The result can be a boost in fluorescence signal, or a quenching effect like what was observed with AAVs. Regardless, the Veloci platform can discriminate between subtypes of exosomes, and can be used to study whatever is internalized

For more information, visit HORIBA.com/Veloci.

Discover the Future of Molecular Fingerprinting with the Veloci A-TEEM™ BioPharma Analyzer

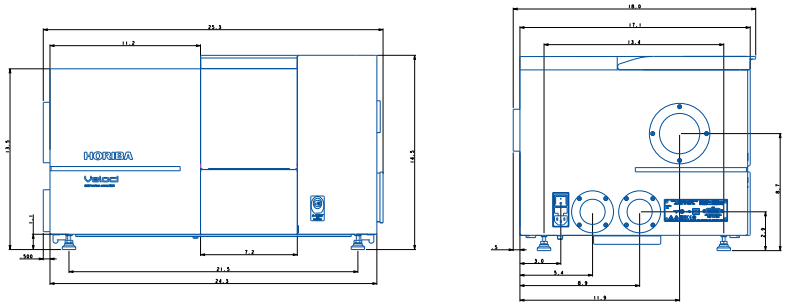
Technical Specifications

Veloci BioPharma Analyzer	
Detection Limit	Parts per billion (sample and wavelength dependent)
Excitation/Absorbance Wavelength Range	200 to 800 nm
Fluorescence Emission Wavelength Range	250 to 800 nm
Wavelength Accuracy	+/- 1 nm
EEM/A-TEEM Acquisition Rate	As fast as 60 seconds (sample and wavelength dependent)
Optional Accessories	Remote fiber optic probe, Autosampler with flow cell
Minimum Sample Volume	70 microliters
Sample Handling, Internal	Cuvette and solid sample holders
Sample Handling, External	Autosampler (96 sample maximum)
Light Source	Xenon arc lamp
Validation	Complies with US Pharmacopia
Dimensions (W x D x H)	25.3 in x 18 in x 14.5 in; 642.6 mm x 457.2 mm x 368.3 mm
Weight	32.72 kg (72 lbs.)

PC Requirements

EzSpec™ Software	
Operating System	Microsoft Windows® 10 Pro or 11 Pro, English version operating system
Memory	16+ GB RAM minimum
CPU	Intel i7 processor or better
GPU	Non-integrated Graphics Processor Unit (GPU)
Internet	Internet access, convenient but not required
Touch Screen	Touchscreen compatible, but not required

Dimensions (Unit: inches)



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IMS

The HORIBA Group adopts IMS (Integrated Management System) which integrates Quality Management System ISO9001, Environmental Management System ISO14001, and Occupational Health and Safety Management System ISO45001.
We have now integrated Business Continuity Management System ISO22301 in order to provide our products and services in a stable manner, even in emergencies.

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