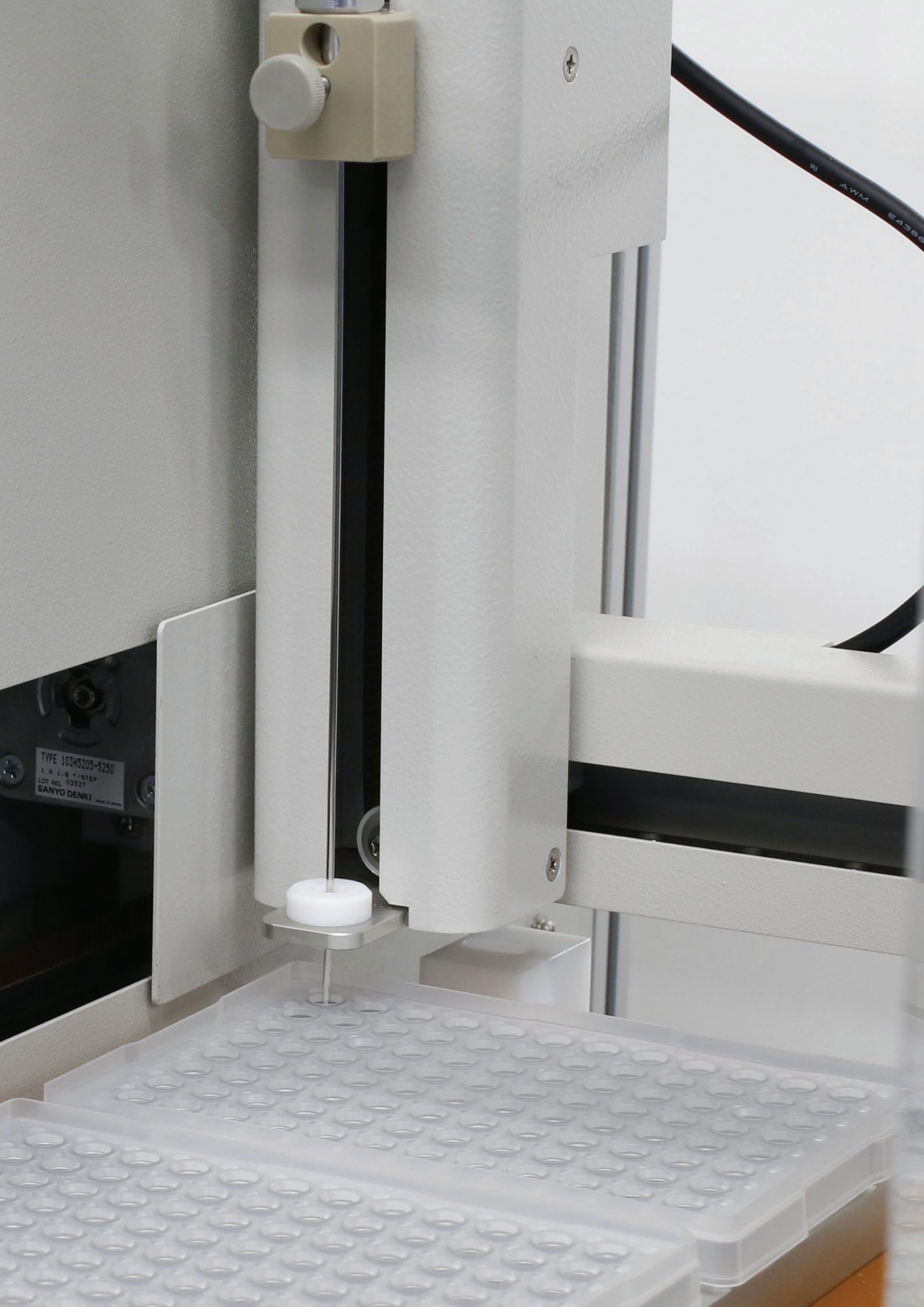
Circular Dichroism HTCD Plus

High Throughput Systems

JASCO

Performance
Innovation
Reliability


TYPE 103H5205-5250
1.8°/STEP
LOT NO. 03527
SANYO DENKI
AWM

For scientists in pharmaceutical, process- and bio-technology, and food chemistry labs who need reproducible automated measurements and reliable structural analysis software, the high-throughput circular dichroism (HTCD) system eliminates human error and bias in measurement acquisition and biomolecular characterization.

Table of contents

Automated Protein Screening

The evaluation of secondary and tertiary structure is important in quality testing of protein and peptide based biologics. Circular dichroism (CD) is sensitive to a biomolecule's asymmetry and is ideal for pharmaceutical stability and processing studies, where even slight changes to the molecule or its environment can induce structural changes, altering its function. While CD measurements are known to be quick and easy to perform, the high-throughput system dramatically increases the amount of data obtained with automated measurements using two 96-well microplates and 120 vials.

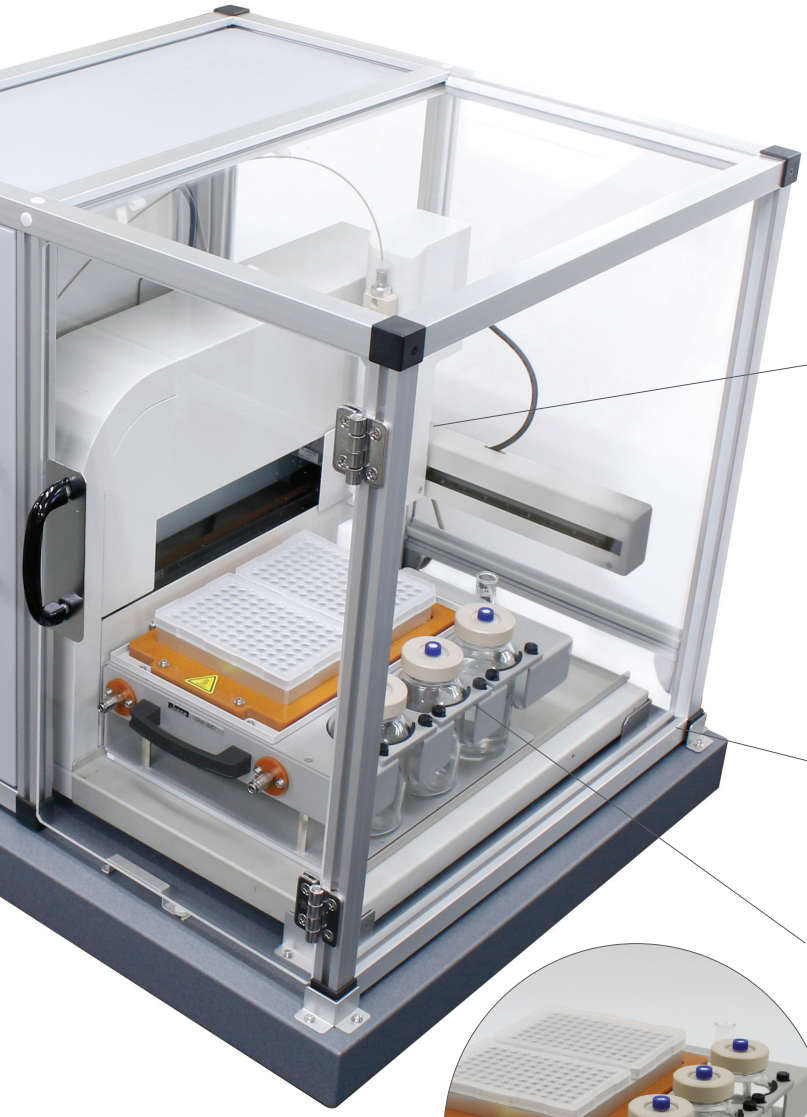
Flow Cell | Standard 1 mm pathlength cell: 25 µL
*0.2, 0.5 and 2 mm pathlength cells are options.

JFLC-515 | **Peltier Thermostatted Flow Cell Holder**
Accurate temperature controlled CD measurement accessory with a temperature range of 5 to 95 °C.

ADU-835 | **Drying Pump Unit**
Completely ejects sample from flow cell and tubing and dries flow path following the washing cycle.

ASP-849 | **Syringe Pump**
High-speed, high-accuracy pump for transferring a precise amount of sample to the flow cell.

The HTCD allows automated scanning measurements using pre-programmed parameters. The autosampler can be set to maintain the microplate rack or vial rack at a constant temperature to avoid sample denaturation or evaporation, and a system case further protects from sample contamination. The flushing method is pre-programmed for protein or DNA/RNA samples to eliminate sample carry-over, and the method is also customizable with up to three flushing solvents. The system allows samples to be recovered following measurement, and batch data processing includes secondary structure and comparability analysis.



Sampling Nozzle
with bias for piercing the plate sealer without risk of including debris.

ASU-800CD | Autosampler
Performs automated measurements using predetermined parameters.

SRA-841 | Rack for microplates
Holds up to two 96-well microplates and three flushing solvents (approx. 170 mL).

SRA-842 | Rack for sample vials
Holds up to 120 sample vials and three flushing solvents (approx. 170 mL).

Advanced Features

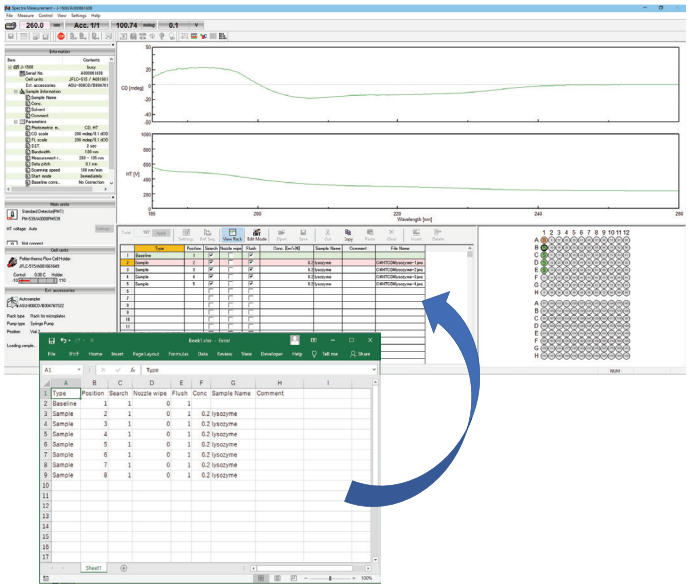
- Fully automated measurement of up to 192 samples (two 96-well microplates), or 120 sample vials
- Conventional and high-throughput measurement modes can be selected with ease
- Pre-registered flush method for protein or DNA/RNA samples can be selected to eliminate sample carry-over
- Retrofit capability to J-1500 CD spectrometer
- Drying system to eliminate sample dilution
- Flow monitor function to confirm sample can reach flow cell for proper measurement
- Measurement throughput of general protein sample is 7.5 min./sample

Spectrum Test Measurement

The [Sample Measurement] option allows a test measurement to be performed before running a sequence program, while the [Sequence Measurement] option begins the pre-programmed measurement sequence.

Sequence Program

A sequence program can be created on Spectra Manager, and can be imported using spreadsheet.



Open Access Function

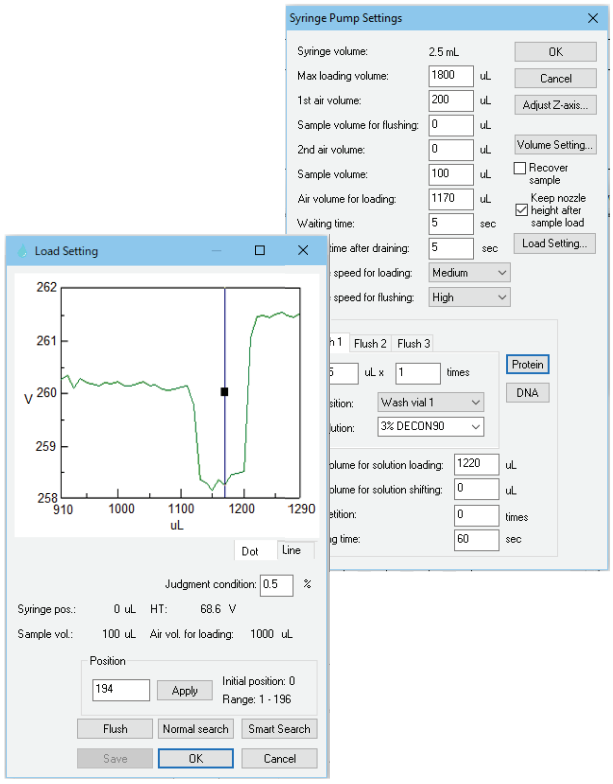
Allows the sequence to be edited during the measurement. Samples, baselines, and parameters can be added or removed, file names and locations can be changed, and sample information can be supplied.

Air Volume Auto Optimization

The air volume for sending sample to the flow cell is determined automatically (or manually) by photometric measurements, which allows sample volume optimization. This function helps to reduce the dead-volume.

Pre-programmed Flushing Function

The flushing method is pre-programmed for protein or DNA/RNA samples to eliminate sample carry-over, and the method is also customizable with up to three flushing solvents.



Automatic Calculation of Optical Constants

Optical constants are automatically calculated in the [CD Multivariate SSE] program when the path length and mean residue molar concentration are specified for the sample measurement.

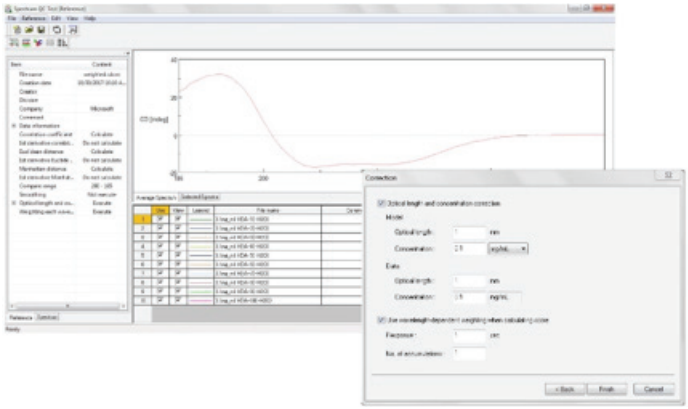
Batch Processing

Secondary Structure Estimation Analysis can be performed automatically on a large number of data files.

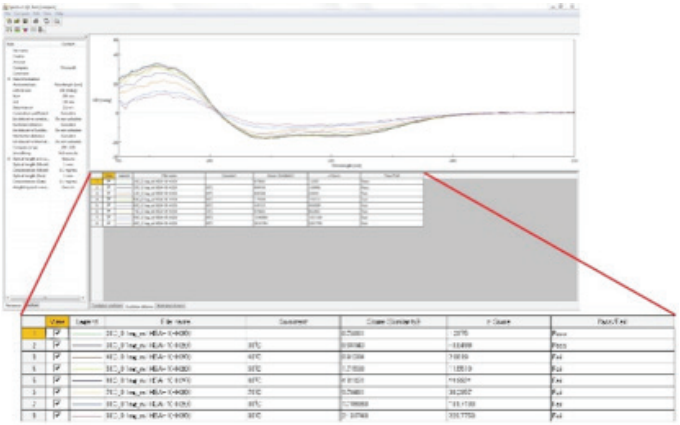
Powerful Analysis with Automated Post Measurement Processing

JWSQC-530 | Spectrum QC Test Program

The [Spectrum QC Test] program statistically evaluates the similarity and z-score between a measured sample spectrum and previously recorded reference data, effectively eliminating operator bias. To account for noise in the CD spectrum, calculated weighted scores are performed at each wavelength using the relation between the standard deviation of the noise and the high tension (HT) voltage of the CD spectrometer.

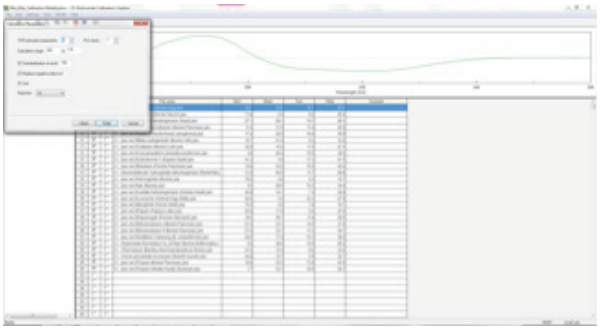


- Three algorithms are included: Correlation coefficient, Euclidean distance, Manhattan distance
- Sensitive to changes in spectral shape and intensity
- Optical pathlength and concentration correction for reference model and sample spectrum
- Pass/fail evaluation function using a z-score
- Compliant with 21 CFR Part 11

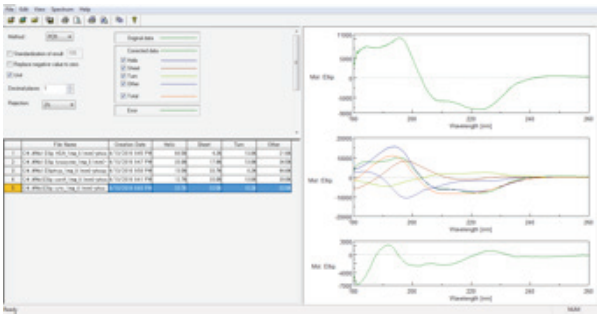


JWMVS-529 | CD Multivariate SSE Program

The quantitative multivariate analysis (PCR/PLS) program is used for the estimation of protein secondary structures from CD spectra. The reference data set includes 26 proteins with the option to add additional spectra. In addition, users can create their own unique reference data set.



- Verifies the calibration model using cross-validation
- Minimizes residual error in the concentration by calculating the abundance ratio
- Validates the analysis result using an F-test
- Verifies recalculation and calculated results (GLP/GMP compliant)
- Compliant with 21 CFR Part 11



Applications

Stability Evaluation of Antibodies

This shows the result of stability evaluation of antibodies (VHH model, Figure 1) by comparing the CD spectra of native and denatured antibodies using statistical analyses. Figure 2 shows the CD spectra of VHH for solutions with different pH values.

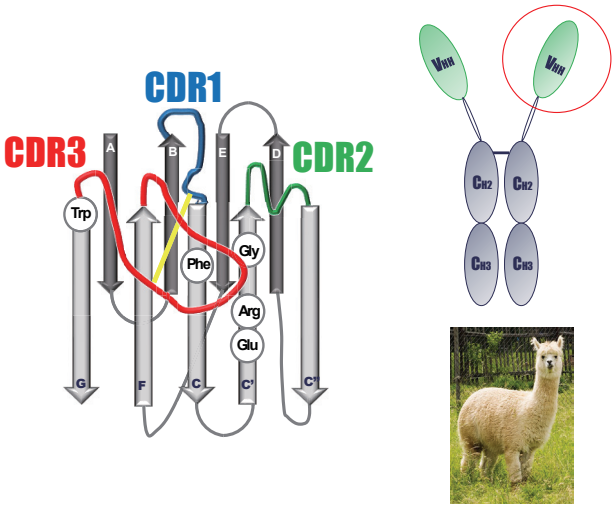


Figure 1. VHH model (Alpaca)

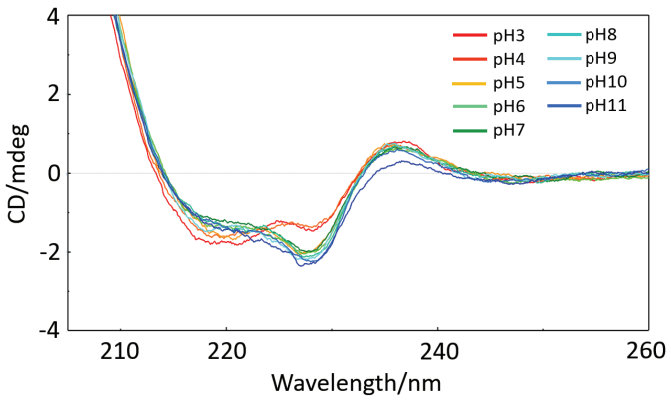


Figure 2. pH dependence of CD spectrum of VHH solution (NaCl conc. 200 mM)

Figure 3 shows the evaluation results for VHH structural changes with the pH and NaCl concentration. JASCO's unique program (Figure 4) can quantify the similarity of CD spectra using a statistical method, and can quantitatively evaluate CD spectral changes associated with structural changes in proteins.

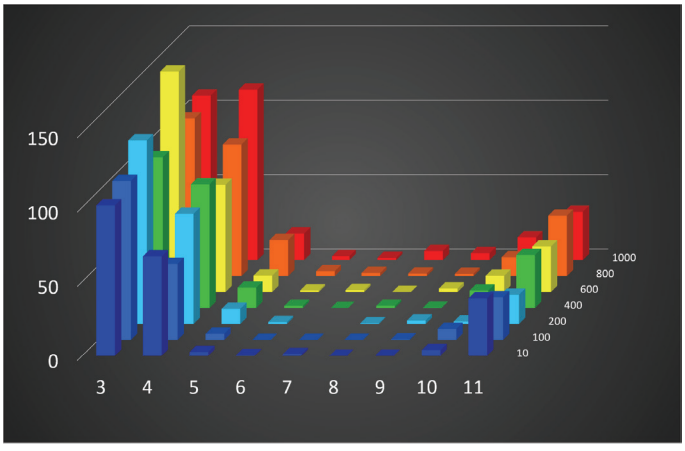


Figure 3. 3-D Histogram of Z-score vs. pH vs. NaCl concentration

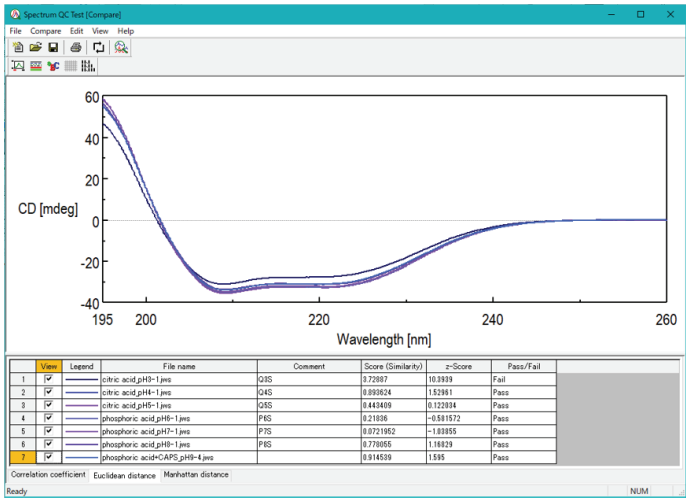


Figure 4. Spectrum QC Test program

The Z-score shows that the structure of VHH changes greatly as the pH becomes higher than 10 or lower than 5 and as the NaCl concentration becomes larger.

*Special thanks for collaboration; Prof. Kouhei Tsumoto, School of Engineering and Institute of Medical Science, The University of Tokyo

Figure 5 shows a plot of the Z-score obtained by HTCD and Tm obtained by denaturation temperature measurement. The high correlation between the Z-score and the denaturation temperature suggests that a Z-test is a very useful primary screening method before conducting a thermal denaturation analysis, which generally requires a great deal of time.

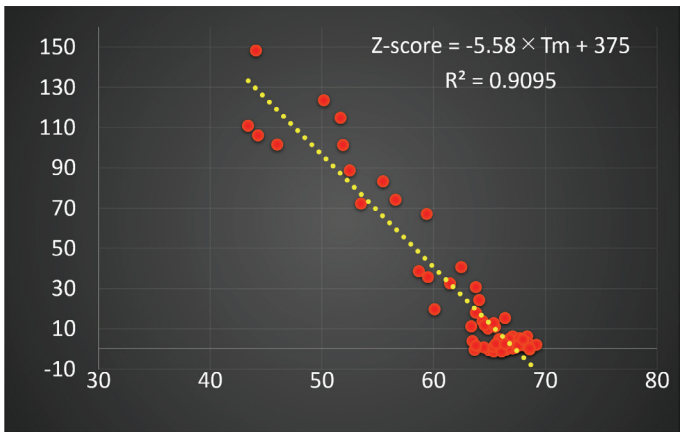
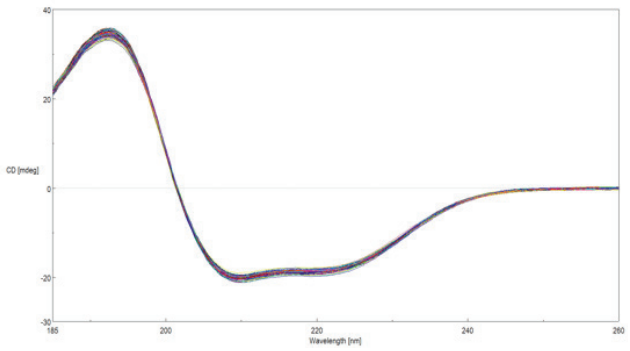


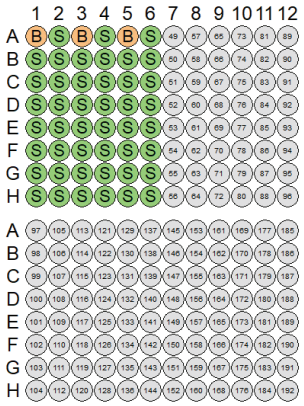
Figure 5. Plot of Z-score vs. Tm

In the screening analysis, 10.5 hours are required to measure CD spectra for about 84 samples with different pH values and salt concentrations. The Z score is then calculated using [Spectrum QC Test] program. It then takes 140 minutes to measure Tm values for about 12 selected samples (2 sets of six simultaneous measurements) using a turret-type cell changer and the temperature interval measurement program to vary the temperature from 20 to 82 °C. The HTCD Plus allows the entire set of samples to be evaluated in only about 12 hours.

Small Pathlength Cell Reproducibility

Since CD is an absorption technique based on Beer's Law, the sample concentration and pathlength are critical to obtaining good CD data. Strongly absorbing samples and/or buffers can be measured by either decreasing the concentration or cell pathlength. However, for some samples the working concentration cannot be modified. The 0.2 mm pathlength cell allows for strongly absorbing samples to be accurately and reproducibly measured in the far-UV with the HTCD Plus system.

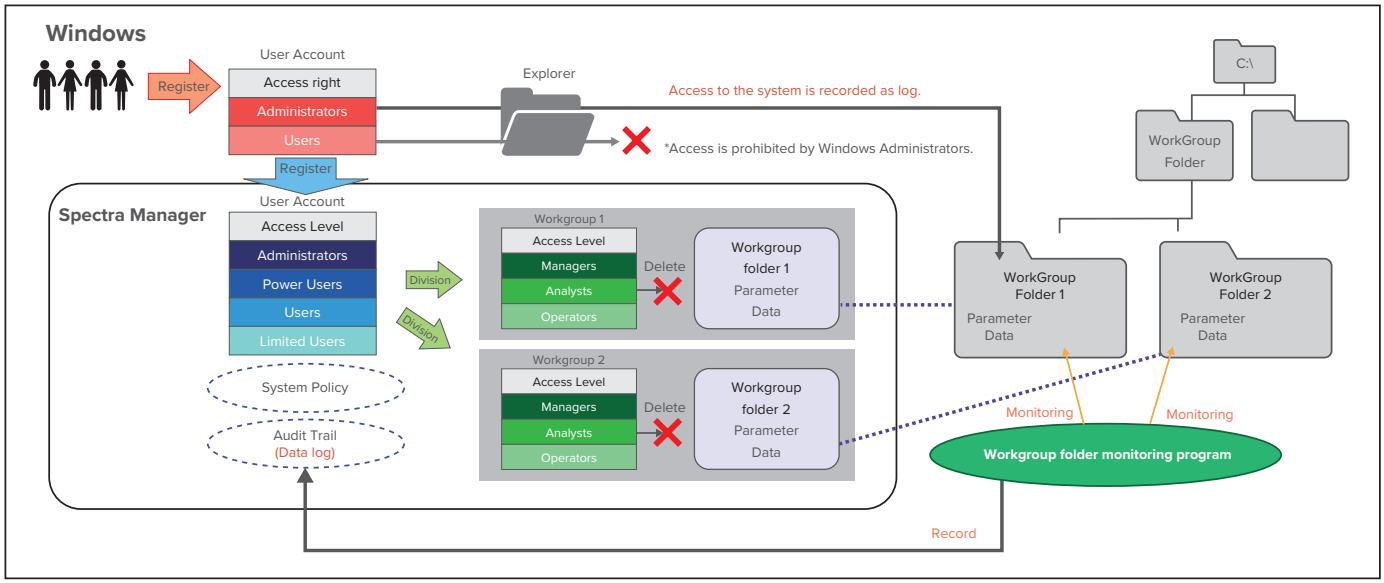




Far-UV spectra of 184 bovine serum albumin samples (BSA, 0.5 mg/mL) and the corresponding well microplate set up for baseline and sample measurements.

Regulatory Compliance with Spectra Manager CFR™

JASCO Spectra Manager is designed and developed under ALCOA+ and is a total solution platform to create accurate and complete data.



Data Integrity

User Management

Based on the dual security category ([Access Level] and [Work Group]), it is possible to manage different authorization process in flexible and independent as total analysis systems, instrumentations and analytical applications.

Enduring Electronic Record

Based on prohibiting function to delete electronic record and to overwrite save, and also functions for backup and restore data, electronic records can be saved properly and can be searched accurately during the data lifecycle.

Audit Trail

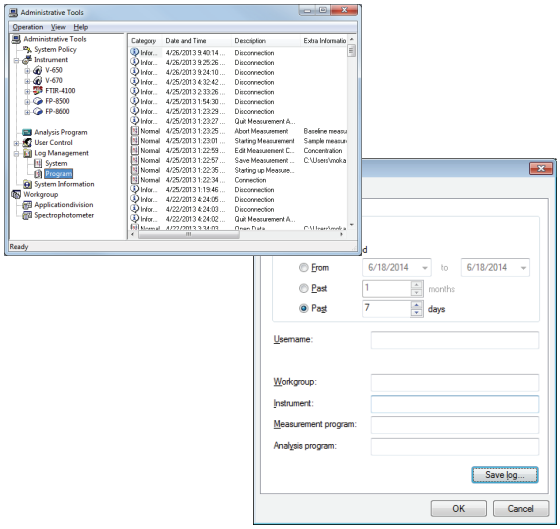
It is categorized as 3 different records (system log, application log and data log), and it is recorded. Each log can be filtered and displayed under recorded date, user name etc, and it can be exported for audit trail review.

Computerized System Validation

Spectra Manager CFR is developed and manufactured properly under quality control system adapted ISO 9001, and adapted CSV standard.

User Account Security

Based on functions to prevent duplicate account or to protect password, and to prevent unauthorized access, administrative authorizations as system access and electric signature etc., can be managed strictly.



HIGH-SPEED AUTOMATED BIOMOLECULAR ANALYSIS SYSTEM

The J-Series HTCD Plus system brings walk up automation with open-access unattended measurement, analysis and reporting for laboratories that can't afford to wait.

JASCO CORPORATION
2967-5, Ishikawa-machi, Hachioji-shi, Tokyo 192-8537 Japan
Tel: +81-42-649-5177 Fax:+81-42-646-4515 Web: www.jasco.co.jp
Japan

JASCO INTERNATIONAL CO., LTD.
11-10, Myojin-cho 1-chome, Hachioji-shi, Tokyo 192-0046, Japan
Tel: +81-42-649-3247 Fax: +81-42-649-3518 Web: www.jascoint.co.jp/english/
Australia, Hong Kong, India, Indonesia, Korea, Malaysia, New Zealand, Pakistan,
Philippines, Russia and CIS countries, Singapore, Taiwan, Thailand, Vietnam

JASCO INCORPORATED
28600 Mary' s Court, Easton, Maryland 21601, U.S.A.
Tel: +1-410-822-1220 Fax: +1-410-822-7526 Web: www.jascoinc.com
Argentina, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Guatemala, Mexico,
Paraguay, Peru, Puerto Rico, United States of America, Uruguay, Venezuela

JASCO EUROPE S.R.L.
Via Luigi Cadorna 1, 23894 Cremella (LC), Italy
Tel: +39-039-9215811 Fax: +39-039-9215835 Web: www.jasco-europe.com
JASCO Deutschland www.jasco.de | **JASCO UK** www.jasco.co.uk | **JASCO France** www.jascofrance.fr
JASCO Benelux www.jasco.nl | **JASCO Spain** www.jasco-spain.com
Algeria, Austria, Belgium, Cyprus, Denmark, Egypt, Finland, France, Germany, Greece, Hungary,
Israel, Italy, Jordan, Kuwait, Luxembourg, Morocco, Netherlands, Norway, Poland, Portugal, Romania,
Saudi Arabia, South Africa, Spain, Sweden Switzerland, Tunisia, Turkey,
United Arab Emirates, United Kingdom, Yemen

JASCO CHINA (SHANGHAI) CO., LTD.
Room No.D, 10F, World Plaza, 855 Pudong South Road, Pudong New Area, Shanghai, China
Tel: +86-21-6888-7871 Fax: +86-21-6888-7879 Web: www.jasco-global.com
China

ISO-9001
ISO-14001
CERTIFIED

Products described herein are designed and manufactured by ISO-9001 and ISO-14001 certified JASCO Corporation

DE6401-2103-01