AppliedPhotophysics

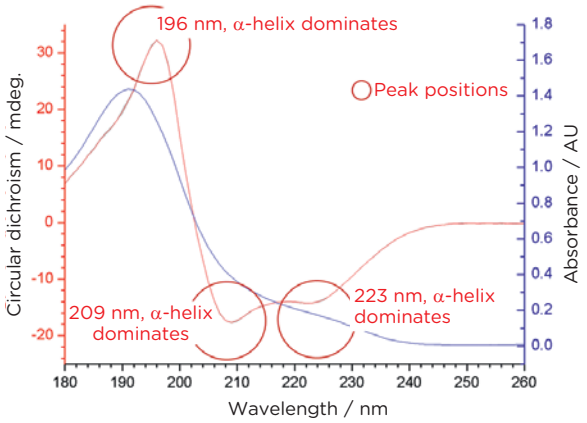
CHIRASCAN Q100
UNMATCHED PRODUCTIVITY AND PERFORMANCE

FULLY INTEGRATED, UNATTENDED OPERATION

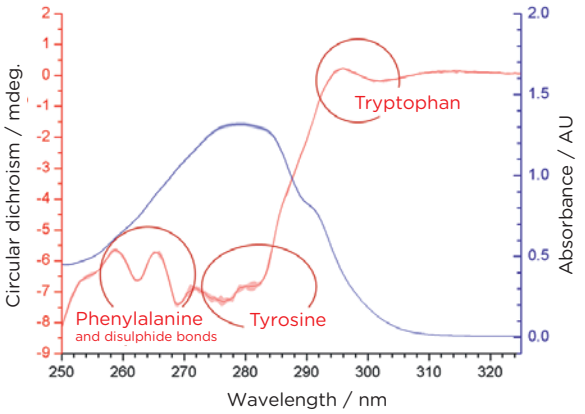
- Gain insight into Higher Order Structure (HOS) characteristics
- Make objective, statistically-validated HOS comparisons
- Achieve highest sensitivity and accuracy
- Ready to run – save days of operator time
- Obtain orthogonal data with simultaneous fluorescence measurements
- Optimize sample concentration and absorbance

GAIN INSIGHT INTO HOS CHARACTERISTICS

Characterize secondary and tertiary structure



Secondary structure, far-UV – signals from peptide backbone dominate, human insulin, Chirascan™ Q100

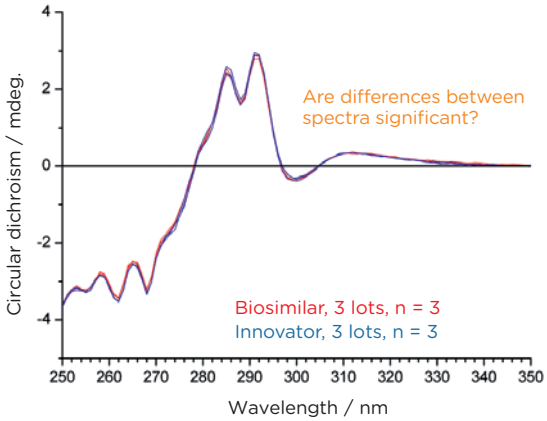


Tertiary structure, near-UV – signals from aromatic side chains and disulfide bonds of a mAb, Chirascan™ Q100

MAKE OBJECTIVE, STATISTICALLY-VALIDATED HOS COMPARISONS

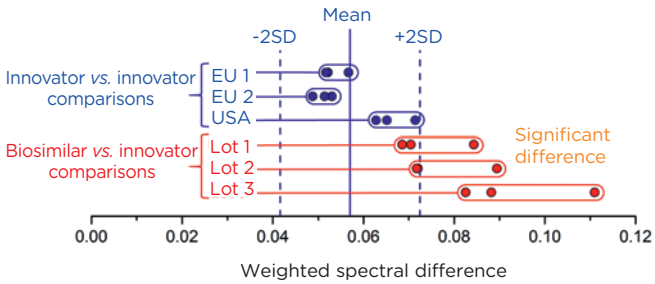
Detect minor differences and assess significance

Comparison of innovator and biosimilar tertiary structure



Tertiary structure, near-UV, tryptophan region. Spectra normalized for protein concentration by simultaneous absorbance measurements, 10 mm pathlength, Chirascan Q100

Rigorous statistical methods confirm significance of differences in tertiary structure



Tier 2 quality range test* applied with +/-2SD acceptance criteria to CD data expressed as weighted spectral differences**, HOS comparison data exported to Excel®.

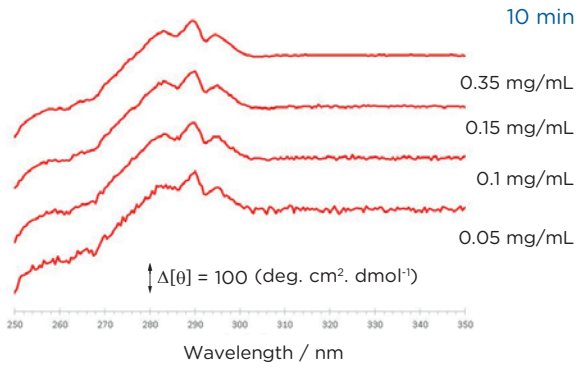
* Office of Biostatistics and Office of Biotechnology Products, CDER/FDA

** Dinh, Nikita et al., Anal. Biochem. 464 (2014): 60-62

ACHIEVE HIGHEST SENSITIVITY AND ACCURACY

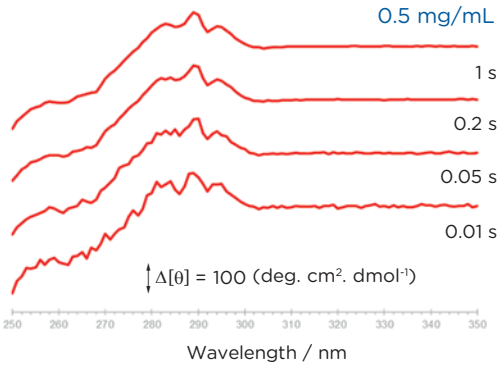
- Avalanche photodiode detector enhances sensitivity
- Increased signal:noise compared to conventional photomultiplier
- Accurate normalization from simultaneous measurement of absorbance and CD

Increased sensitivity when sample is limited



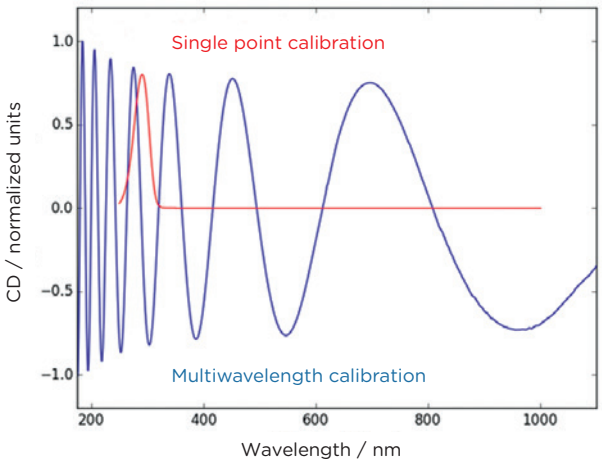
Tertiary structure of lysozyme – raw data, no smoothing, 10 min. baseline/10 min. sampling, n=3 scans, 0.5 nm step, 10 mm pathlength, spectra offset for clarity

Increased sensitivity for faster measurements



Tertiary structure of lysozyme – raw data, no smoothing, baseline corrected, n=3 scans, 1 nm step, 10 mm pathlength, spectra offset for clarity

- Accurate CD values across entire wavelength range
- Overcome challenges of chemical calibration
- Optics-based, multiwavelength calibration



Conventional chemical calibration methods require considerable skill in preparation. Standards, such as camphor-10-sulfonic acid (CSA), are unstable, photolabile and hygroscopic. In addition, single wavelength calibration (290.5 nm) assumes the same linear response at all wavelengths.

The optics-based, multiwavelength calibration method used in Chirascan Q100 overcomes these challenges. The correct calibration is applied to every wavelength to yield accurate CD values.

READY TO RUN – GENERATE HIGHEST QUALITY DATA

Chirascan™ Q100 is supplied with features and accessories required for acquisition and analysis of the highest quality CD data – from built-in temperature control during analysis to HOS comparison software.* A basic training program follows installation to familiarize users new to Chirascan.

AVALANCHE PHOTODIODE DETECTOR

- Highest sensitivity (high signal: noise)

PHOTOELASTIC MODULATOR

- Converts horizontally polarized light to circularly polarized light. Alternates between left- and right-handed circular polarized light

MONOCHROMATOR

- Produces horizontally, linearly polarized monochromatic light
- Two polarizing prisms maximize light throughput

AIR-COOLED XENON LAMP

- Software-controlled
- Up-time recorded

ACTIVE NITROGEN MANAGEMENT SYSTEM

- Regulates purge gas consumption
- Software-controlled

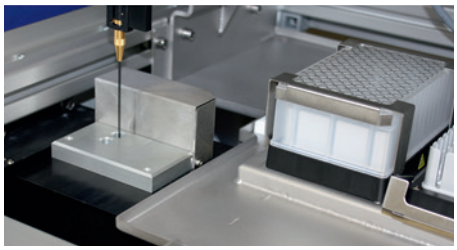
MOLECULAR SIEVE, ACTIVATED CHARCOAL FILTER

- Removes common gas impurities

FIXED FLOW CELLS

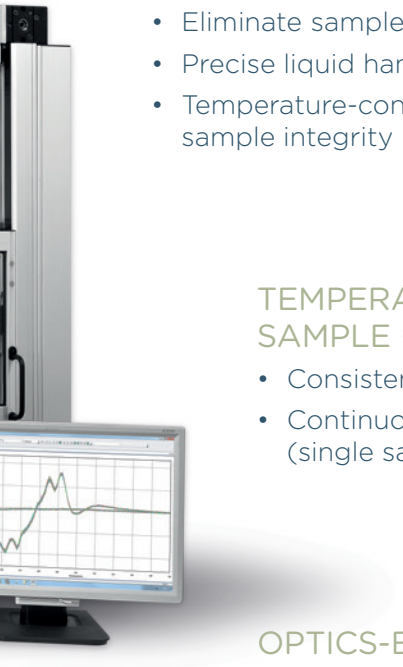
- Eliminates errors of cuvette handling
- Recognized by Chirascan Control to select run/wash/dry protocols
- Choice of pathlength to optimize concentration and absorbance

* Your local Applied Photophysics representative can supply specific details of components supplied for your region.



INTEGRATED AUTOSAMPLER

- Eliminate sample handling errors
- Precise liquid handling and reproducibility
- Temperature-controlled storage maintains sample integrity



TEMPERATURE-CONTROLLED SAMPLE CHAMBER

- Consistent analytical conditions
- Continuous temperature ramps (single sample mode)

OPTICS-BASED, MULTIWAVE-LENGTH CALIBRATION

- For CD accuracy at every wavelength

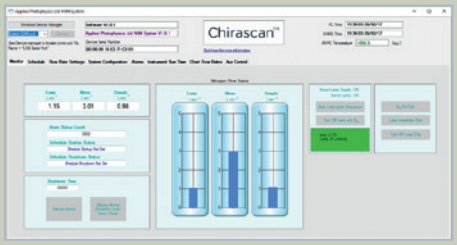
CUVETTES AND HOLDERS

- Selected for far- and near-UV CD analysis of biomolecules (single sample mode)

WATER CIRCULATOR

- Dissipates heat from sample chamber and sample storage Peltiers

CONTROL AND ANALYSIS SOFTWARE



CHIRASCAN CONTROL

- Easily defined run parameters and store routine protocols
- Saves time with scheduled start-up/shutdown of lamp and N_2 supply
- Fail-safe lamp switch-off if N_2 flow drops
- Ensures O_2-free conditions with N_2 purge
- Recognizes flow cell to select optimal run/wash/dry protocol

HOS COMPARISON SOFTWARE

- Generate statistically-validated comparisons

GLOBAL THERMODYNAMIC ANALYSIS

- Derive melting points and enthalpies from multiwavelength, thermal denaturation experiments (single sample mode)

UNMATCHED PRODUCTIVITY – SAVE DAYS OF OPERATOR TIME

- Prepare 96-well plate
- Select experimental conditions

- Unattended operation

- Inspect raw data
- Automatically average/baseline correct
- Statistical analysis for HOS comparison

A 50-fold increase in operator productivity is readily achievable. Assuming a seven hour working day and a set-up time of 30 minutes, the Chirascan Q100 system analyzes 48 buffer-sample pairs over 24 hours. In comparison, an experienced operator can process up to 14 samples per day using a manual system.

OBTAIN ORTHOGONAL DATA WITH SIMULTANEOUS FLUORESCENCE MEASUREMENTS

Controlled through Chirascan software, the CCD fluorometer generates emission spectra in seconds providing secondary structure CD, absorbance and tertiary structure fluorescence data in a single experiment.

Chirascan CCD fluorometer: Use with flow cell pathlengths 5 or 10 mm or one-piece stoppered cuvettes: 2.0 mm/800 µL or 4.0 mm/1400 µL

OPTIMIZE SAMPLE CONCENTRATION AND ABSORBANCE

Fixed flow cells

Selecting a suitable flow cell with optimal pathlength is critical to acquisition of high quality data. Each flow cell consists of a digitally-recognized cartridge containing a thermocouple and a quartz cell. Replacement cells are available.

For secondary structure (far-UV) analysis			
	Performance with highly absorbing buffers	Performance when limited sample available	
Flow cell pathlength 0.1 mm	••••	•	Supplied with Chirascan Q100
Flow cell pathlength 0.2 mm	•••	••	Used together with 10 mm pathlength flow cell. Enables use of a common sample concentration for secondary and tertiary structure analysis
Flow cell pathlength 0.5 mm	••	•••	
Flow cell pathlength 1.0 mm	•	••••	

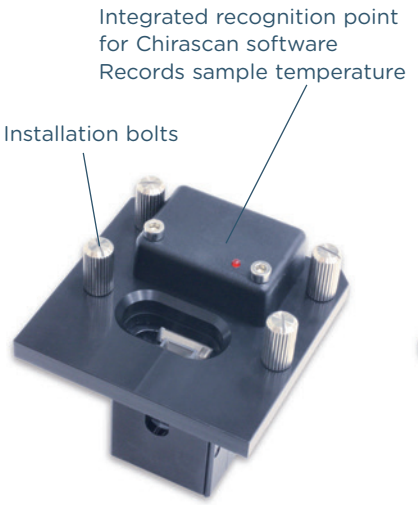
For tertiary structure (near-UV) analysis	
Flow cell pathlength 10 mm	Supplied with Chirascan Q100
Flow cell pathlength 5 mm	Used together with 0.1 mm pathlength flow cell. Enables use of a common sample concentration for secondary and tertiary structure analysis

CUVETTES AND HOLDERS FOR SINGLE SAMPLE ANALYSIS

Cuvettes for Chirascan systems are manufactured from far-UV quartz to enable analysis of secondary structure. The range of cuvettes and compatible holders provides full flexibility when optimizing sample concentration and absorbance.

For secondary structure (far-UV) analysis	
0.5 mm 175 µL one-piece stoppered cuvette Adaptor for 0.5 mm and 1 mm one-piece cuvettes	Supplied with Chirascan Q100 Not suitable for fluorescence, certified free from strain birefringence.
1.0 mm 350 µL one-piece stoppered cuvette	Not suitable for fluorescence; requires adaptor
2.0 mm 800 µL one-piece stoppered cuvette for autosampling systems	Simultaneous measurement of secondary structure by CD and tertiary structure by fluorescence; no adaptor needed
4.0 mm 1400 µL one-piece stoppered cuvette	Simultaneous measurement of secondary structure by CD and tertiary structure by fluorescence;. No adaptor needed
For tertiary structure (near-UV) analysis	
10 mm 3500 µL one-piece stoppered cuvette	Supplied with Chirascan Q100 Suitable for fluorescence
5.0 mm 1750 µL one-piece stoppered cuvette; Spacer for 5 mm pathlength cuvettes	Not suitable for fluorescence; requires spacer

For secondary structure analysis with rapid cell cleaning. Scan further into the far-UV Not suitable for fluorescence or for use with chiral buffers
Adaptor for demountable/slide cells
0.01 mm 3 µL demountable/slide cell
0.1 mm 30 µL demountable/slide cell
0.2 mm 60 µL demountable/slide cell
0.5 mm 150 µL demountable/slide cell



Cartridge/cuvette holder for single sample mode (supplied)

Cartridge/10 mm pathlength flow cell (supplied)

Cartridge/0.1 mm pathlength flow cell (supplied)

PRODUCT SPECIFICATIONS

Performance characteristics	
Spectral information	Circular dichroism (CD), absolute absorbance (UV), fluorescence (optional)
Isothermal analysis, typical measuring time	Minimum 48 buffer-sample pairs in 24 hours
Isothermal analysis, maximum throughput	Up to 4 x 96 individual runs (with additional 2 x 96 well microplates, optional)
Isothermal analysis, typical sample consumption (automated mode)	Tertiary structure, 10 mm pathlength, cell width 4 mm: mAb 0.7 mg Secondary structure, 0.1 mm pathlength, cell width 5 mm: mAb 0.16 mg
Thermal denaturation (thermal ramping), single sample mode	Full spectrum per 1°C, continuous ramp rate 1°C/min.
Automation	Unattended operation, 30 minute set-up

Technical specifications	
Light source	150W air-cooled Xenon arc lamp
Monochromator	Two polarizing prisms to maximize light throughput
Detection	Avalanche photodiode
Wavelength range Note: quartz prisms within monochromator limit measurements to wavelengths > 163 nm	163 nm to 1150 nm Typical wavelength range for biomolecule analysis 180 nm to 350 nm
Wavelength resolution	±0.1 nm
CD calibration	Optics-based, multiwavelength Accuracy ±1% determined across wavelength range (selected wavelengths)
Measurement error on absolute absorbance	< 0.01 AU (simultaneous measurement of CD and absorbance signals)
Bandwidth	160 nm: up to 2 nm 180 nm: up to 4 nm 200 nm: up to 7.5 nm 240 nm: up to 16 nm
Bandwidth precision	±0.1 nm at 267 nm
Stray light	< 3 ppm at 200 nm
Typical Root Mean Square (RMS) noise values, no sample in place, 1 nm bandwidth, 2 s digital integration time – no smoothing, no rolling average	0.03 mdeg at 185 nm 0.03 mdeg at 250 nm 0.03 mdeg at 500 nm
Baseline stability (16 h drift test)	< 0.4 mdeg
Sample temperature during analysis, coolant at 15 °C or above	Hardware tolerance: -20°C to +105°C Typical range for biomolecule analysis: 4°C to 95°C
Sample temperature during on-instrument storage	0-70°C, accuracy +0.2°C

Data handling and storage	
PC operating system	Microsoft® Windows® 7 Professional, 64 bit
Data storage and export	Secure SQL database. Exportable as .csv

Compliance	
Electrical safety and other regulatory requirements	EU legislation, Low Voltage Directive: 2014/35/EU Standard: IEC/EN 61010-1:2010.Standard: IEC/EN 61010-1:2010. USA National Registered Testing Laboratory (NRTL) under OHSA Federal code 29 CFR 1910.7. Canada. Approval agency TUV-SUD. Standard: UL 61010 1:2012, CAN/CSA C22.2 No. 61010-1:2012 EU Restriction of Hazardous Substances Directive (ROHS) 2011/65/EU Standard: EN 50581:2012 (Cat 9 Monitoring and control instruments) EU electromagnetic compatibility directive (EMC) 2004/108/EC Standard: IEC/EN 61326-1:2013 (EMC Class A Group 1)

Physical and environmental specifications	
Instrument weight and dimensions (WxDxH)	160 kg, 195 x 65 x 120 cm
Operating conditions: temperature	20 to 25°C controlled to within 1.5°C
Operating conditions: humidity	20 to 80 % non-condensing
Nitrogen requirement (flow rate, pressure, purity)	> 5 L per min, > 4 bar, > 99.998%
Electrical requirements (Voltage, Frequency, Power)	100 to 240 VAC; 50/60 Hz; UPS rated to ≥1500 VA

Ordering information

To order Chirascan systems or accessories, please contact your local Applied Photophysics representative to discuss your specific requirements or submit your enquiry online at www.photophysics.com.

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