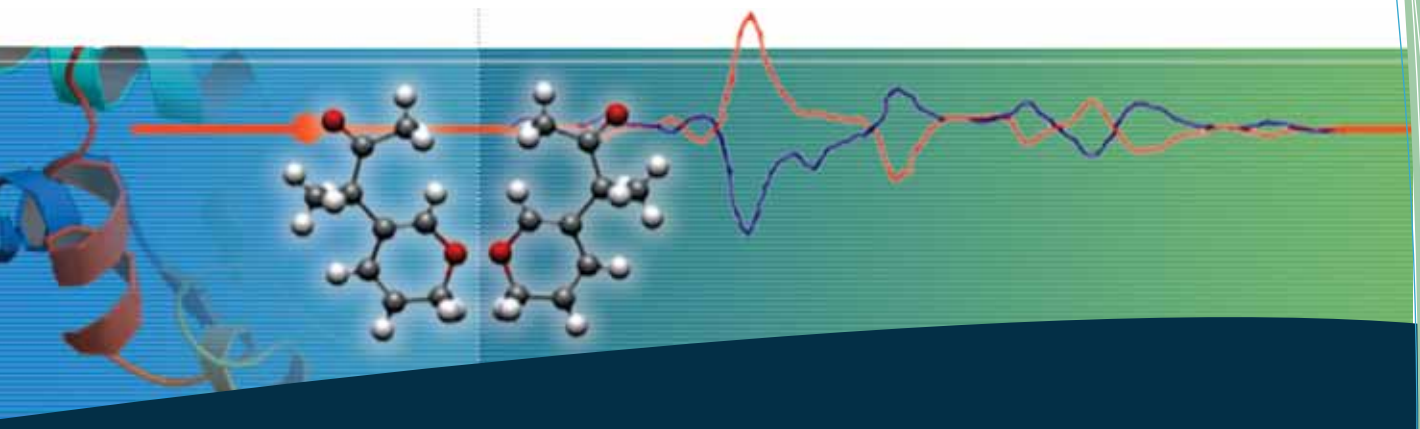
BioTools



Characterization Experts
Chirality & Biologics

Tools for
Discoveries
of Life

BioTools

To Our Customers

2010 marked the tenth anniversary of BioTools, Inc. We are a young rapidly growing company that has become a world leader in providing instrumentation and services to pharmaceutical and biotechnology companies in several niche markets. We are known for innovation - the company was created to bring to market dedicated instrumentation that no one else has dared to create, such as the Chira*IR*™ and Chiral*RAMAN*™. We are known for our unsurpassed customer support and education. We know each customer, their needs and their research, and we work to help them succeed with their applications. We are known for our knowledge, experience and dedication. We bring to you decades of collaborative efforts and research - we sell what we know.

Our core technology is vibrational spectroscopy. Our tools include instrumentation for:

- Vibrational Circular Dichroism (VCD)
- Raman Optical Activity (ROA)
- FT-IR Spectroscopy of Biomolecules
- Raman Spectroscopy of Biomolecules
- Unique Accessories
- Databases

We are very pleased to present our second full catalog, featuring an overview of our products and techniques. Please contact us to obtain more detailed information and to see how these new innovative tools can provide the solution to your research.

On behalf of all employees and consultants at BioTools, we want to thank you for your continued support. Our success could not be possible without you!

With best wishes for successful research and discoveries of life,

Rina K. Dukor, Ph.D. & Laurence A. Nafie, Ph.D. Co-Founders

Table of Contents

Vibrational Circular Dichroism

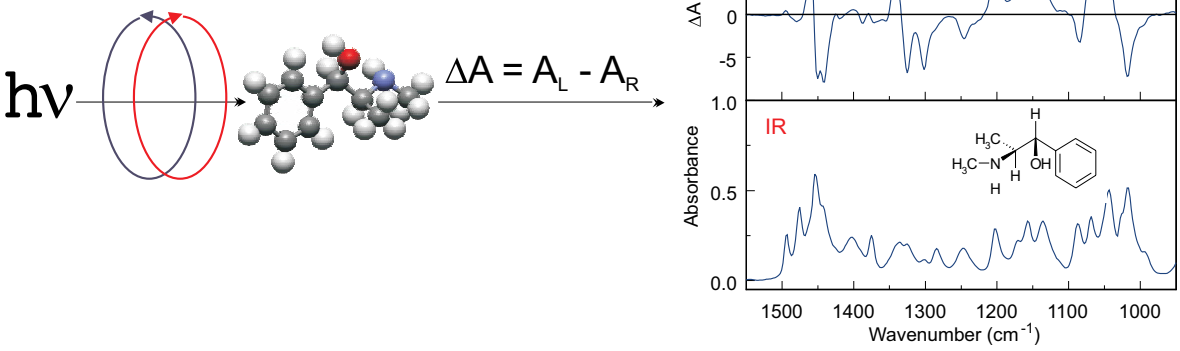
VIBRATIONAL CIRCULAR DICHROISM (VCD) WAS FIRST MEASURED IN 1973

In 1997, BioTools commercialized the technology by introducing the Chiral*IR*™. We are proud to be the first company to present a stand-alone dedicated VCD spectrometer and its powerful applications in the fields of chemistry and biology.

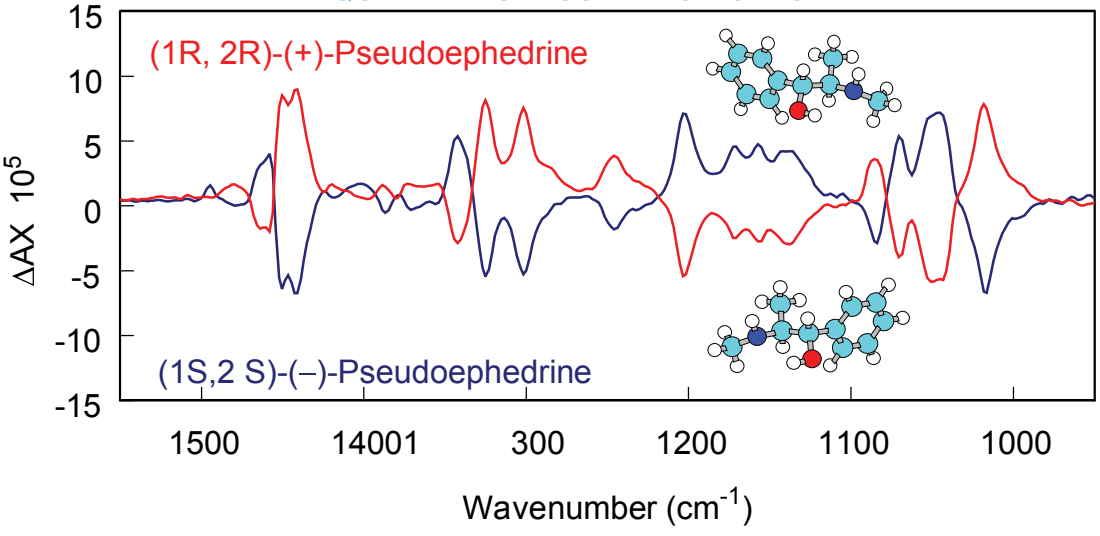
VCD is defined as the difference in the absorbance (A) of left minus right circularly polarized infrared radiation, $A=A_L-A_R$. VCD extends the functionality of electronic Circular Dichroism (CD) into the infrared spectral region where vibrational tranisitions in molecules are observed.

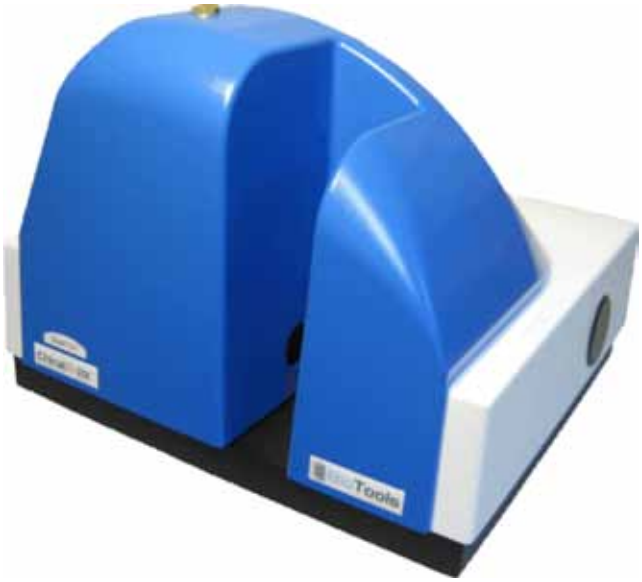
VCD combines the structural specificity of FT-IR spectroscopy with the stereo-sensitivity of circular dichroism. This gives access to multiple, well-defined bands that provide molecular quantitative information. Measurements can be done on solids and solutions.

ONE MEASUREMENT GIVES TWO SPECTRA: FT-IR AND VCD



ENANTIOMERIC PAIRS OF CHIRAL MOLECULES GIVE EQUAL AND OPPOSITE VCD SPECTRA

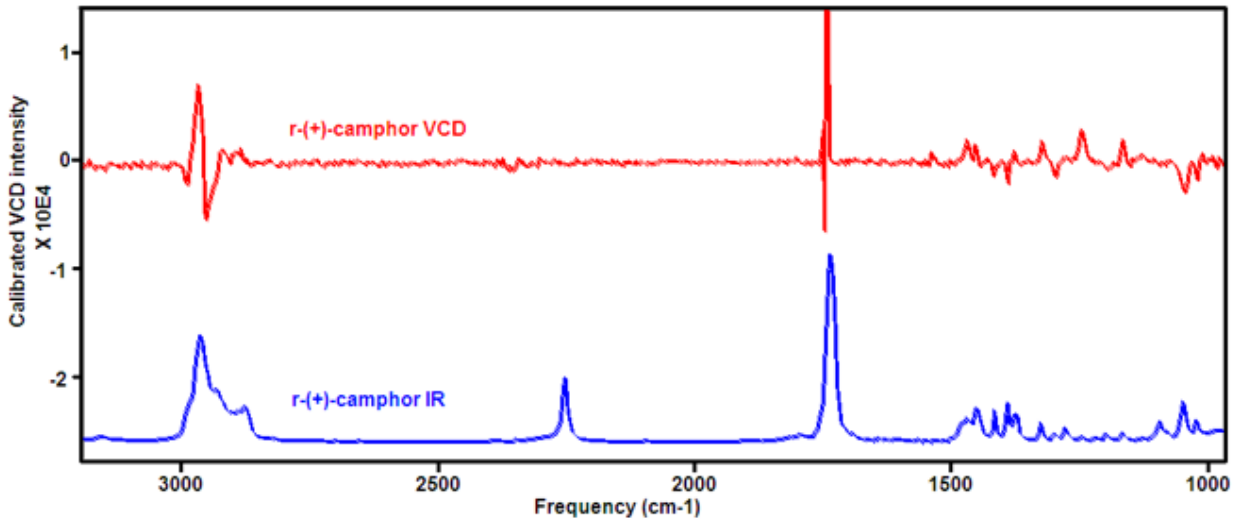




Chiral*IR-2X*™ Instrument

UNIQUE ADVANTAGES OF THE CHIRAL*IR-2X*™ SPECTROMETER

- Dual Source increases signal-to-noise (S/N) ~3.6 times over any singular-source system
- Exclusive stage for elimination of cell artifacts with *Sync*RoCell™
- Complete spectral range of measurement 4000-850 cm^{-1} (no change of filters required)
- Baseline offset from zero less than ± 2 x 10^{-5} absorbance units
- 30-48 hour hold detector time
- Simultaneous collection of IR & VCD Interferograms (AC & DC)



- Upgrade availability to patented Dual*PEM*™ technology which allows artifact-free measurement of solids
- Factory aligned baseline resulting in immediate and routine operation
- Digital signal processing - no lock-in or electronic filter needed
- Permanently aligned
- Lifetime warranty on scan mechanism
- Training and support by the experts with unprecedented experience in design and applications of VCD
- Micro measurements with new *VCDμ*Sampl*IR*™
- Chiral*IR*™ comes with standard IR cells but many other options are available such as *Bio*Cell™ and temperature control (p. 17)

Chiral*IR-2X*™ Options

Chiral*IR-2X*™ IS ALSO AVAILABLE IN THE NEAR-IR REGION

The instrument can also be configured for coverage from 2000 to 4000 cm^{-1} or from 4000 to 10000 cm^{-1}

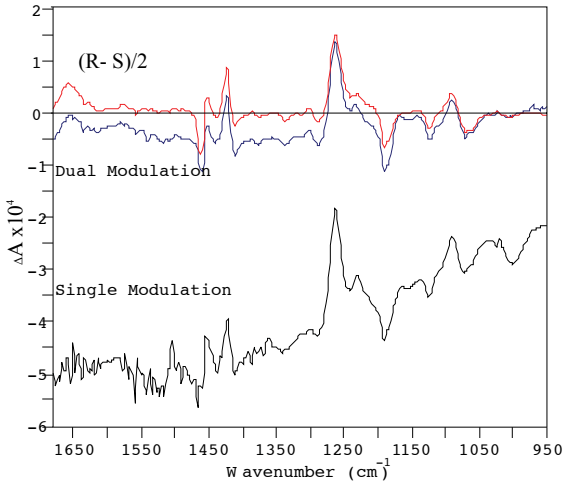
Dual*PEM*™ ACCESSORY BENCH FOR CHIRALIR-2X™

The Dual*PEM*™ is a patented technology of BioTools.

It is now available in two options: internal and external accessory bench

Performance of Dual*PEM*™

Baseline deviation from zero for the open sample compartment is less than ± 1 x 10^{-5} for any user-selected 500 cm^{-1} window in the spectral range 850 to 1800 cm^{-1}



ALSO AVAILABLE

*Sync*RoCell™ - Rotating stage for elimination of cell artifacts

*VCDμ*Sampl*IR*™ - Provides sampling of solid samples at 1mm^2 spatial resolution

TO UPGRADE YOUR EXISTING FT-IR SPECTROMETER TO VCD CAPABILITY, PLEASE CONTACT US

VCD Application Examples:
Chiral Drugs

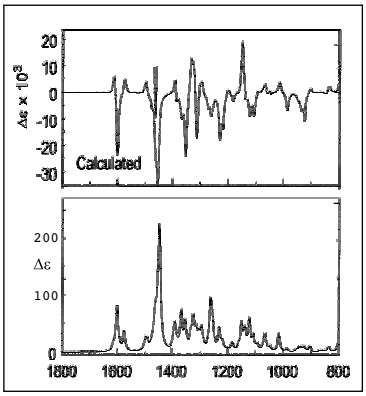
Since commercial introduction of VCD by BioTools thousands of compounds have been measured using this technology. It has become ***the-must-have-tool*** in the pharmaceutical and other industries , specifically for determination of absolute configuration.

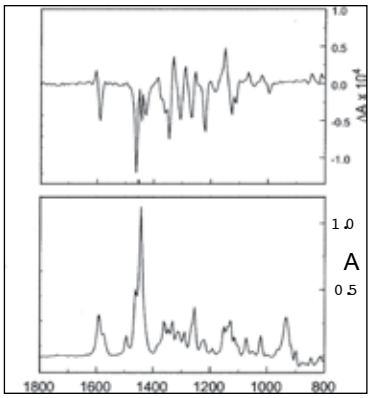
1) ABSOLUTE CONFIGURATION DETERMINATIONS

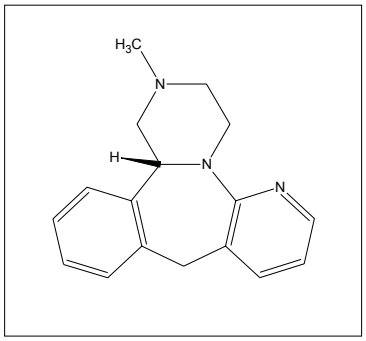
Step 1: Choose Configuration
e.g. (R) - Mirtazapine Configuration

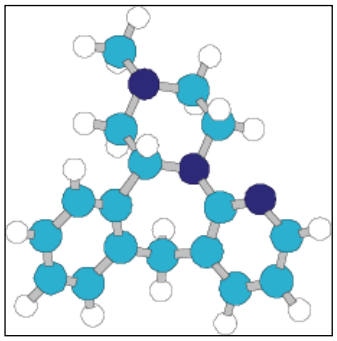
Step 2: Calculate IR (bottom) and VCD (top) spectra of (R) - Mirtazapine

Step 3: measure IR (bottom) and VCD (top) spectra of available enantiomer, e.g. (-) -Mirtazapine







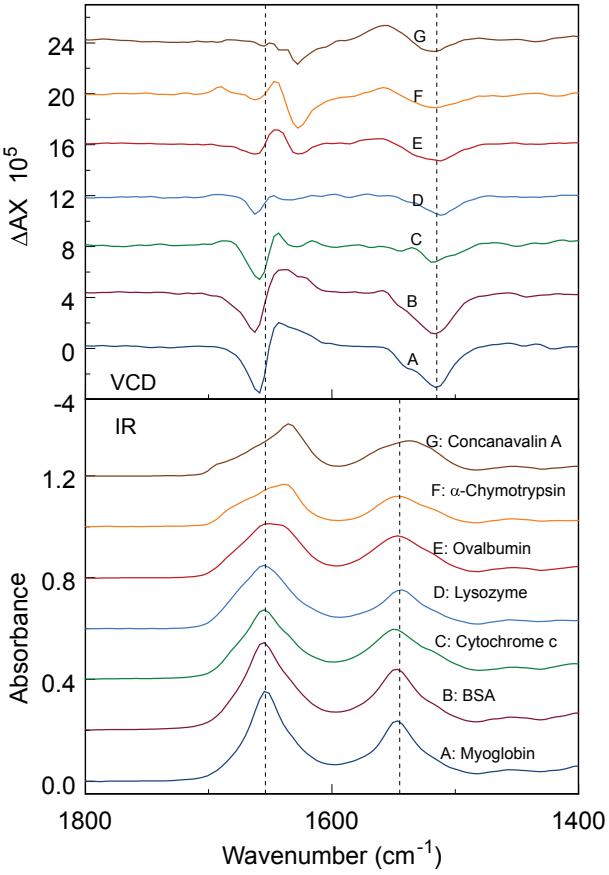


COMPARISON OF OBSERVED VCD SPECTRA (RIGHT) WITH CALCULATED VCD SPECTRA (LEFT) UNAMBIGUOUSLY DETERMINES ABSOLUTE CONFIGURATION (-)-(R)-MIRTAZAPINE AND CONFORMATION IN SOLUTION AS SHOWN ABOVE.

VCD Application Examples:
Proteins - Peptides - Carbohydrates - Nucleic Acids

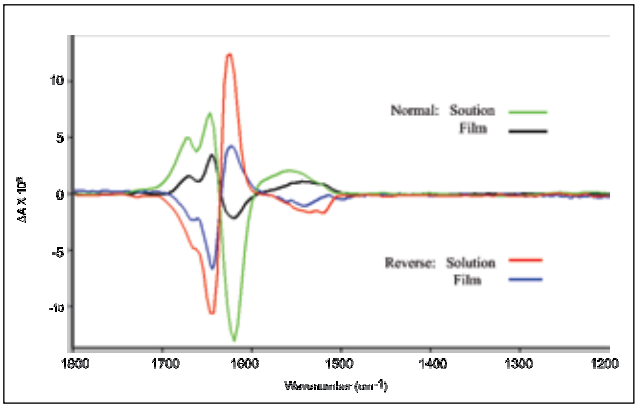
2) PROTEIN / PEPTIDE STRUCTURAL STUDIES

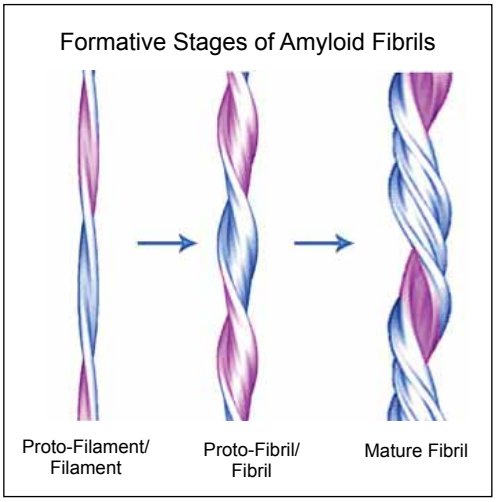
a) Secondary Structure



b) Characterization of Fibrils

VCD SHOWS A HIGH SENSITIVITY TO STRUCTURE OF FIBRILS





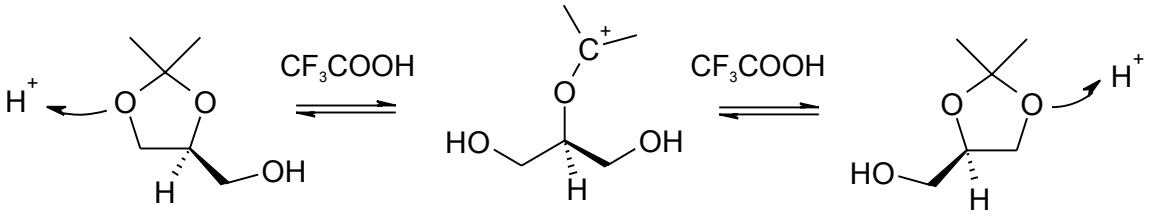
VCD PROVIDES AN ENHANCED SENSITIVITY TO SECONDARY STRUCTURE OF PROTEINS AND PEPTIDES. THE CHANGES IN VCD SPECTRA ARE OBSERVED IN BOTH THE AMIDE I AND II REGIONS. THE VCD SIGN OF AMIDE I BAND CHANGES FOR PROTEINS WITH THE TWO MOST COMMON MOTIFS - α-HELICAL PROTEIN MYOGLOBIN (LOWER SPECTRA) AND A PRIMARILY β-SHEET CONTAINING PROTEINS CONCANAVALIN A AND CHYMOTRYPSIN (UPPER SPECTRA).

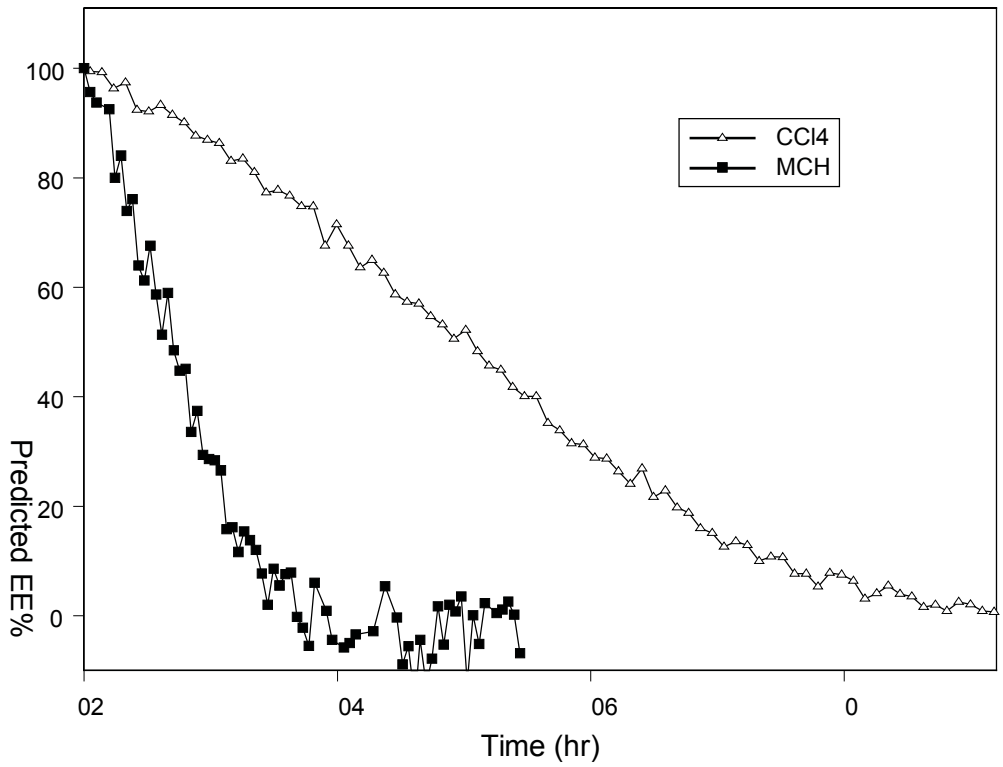
FEATURES

- The largest FT-VCD protein database available
- Dedicated software for protein data analysis

VCD Application Examples:
Reaction Monitoring

3) ASYMMETRIC REACTION MONITORING





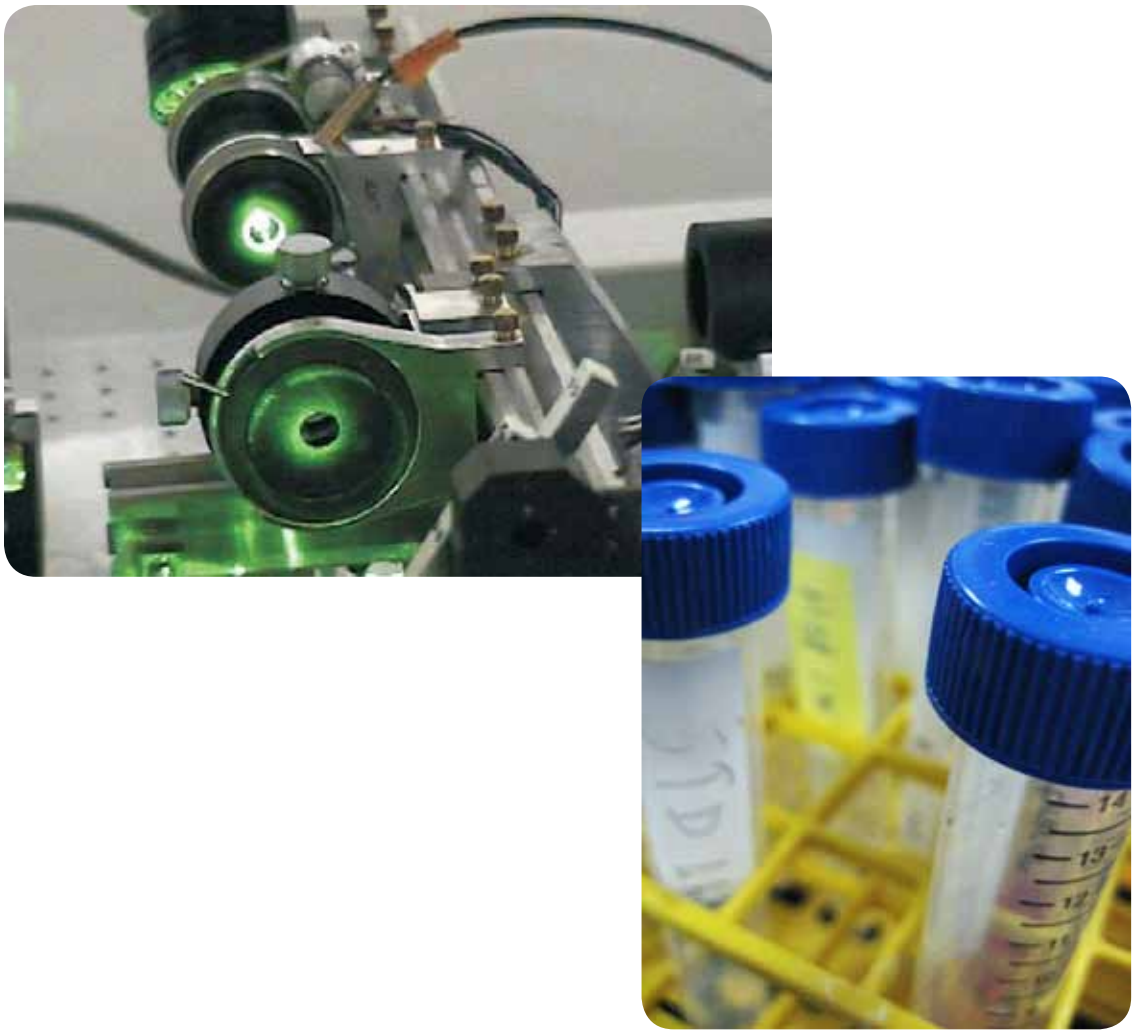
DURING A COURSE OF CHEMICAL STEREOSPECIFIC REACTION, THE COMBINATION OF *IR*, FOR DETECTION OF CHANGES IN MOLE FRACTION COMPOSITION, AND *VCD*, FOR COMBINED MOLE FRACTION COMPOSITION AND ENANTIOMERIC EXCESS (%EE), ENABLES ONE TO FOLLOW %EE OF EACH CHIRAL SPECIES AS A FUNCTION OF TIME. THE FIGURE ABOVE SHOWS EPIMERIZATION VERSUS TIME OF DDM WITH TRIFLUOROACETIC ACID IN TWO DIFFERENT SOLVENTS.

Raman Optical Activity

RAMAN OPTICAL ACTIVITY (ROA) WAS FIRST MEASURED IN 1973

In 2004, BioTools commercialized the technology by introducing the Chrial *RAMAN*™. Chiral *RAMAN-2X*™, with the addition of a microscope, was introduced in 2010. We are proud to be the first and only company to present a stand-alone dedicated ROA spectrometer and to introduce its powerful applications in the fields of chemistry and biology.

ROA is a form of Vibrational Optical Activity (VOA) that is complementary to Vibrational Circular Dichroism(VCD) in the same way that Raman spectroscopy is complementary to IR spectroscopy. ROA is defined as the difference in Raman intensity for right (R)- minus left (L)-circulary polarized incident and/or scattered radiation in chiral molecules. It combines the structural specificity of vibrational spectroscopy with the stereo- sensitivity of chiral detection.



Chiral*RAMAN-2X*™ Instrument

UNIQUE ADVANTAGES OF THE CHIRAL*RAMAN-2X*™ SPECTROMETER

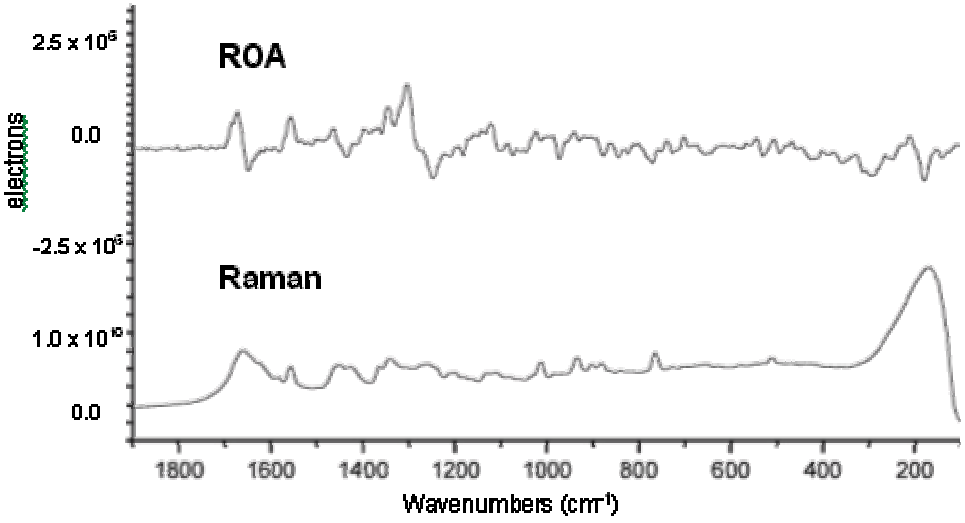
- Complete vibrational spectrum from ~100 to 2000 cm^{-1} is accessible in one measurement
- SCP configuration
- DCP form also possible
- Optional Olympus microscope IX71 or IX81
- Temperature control
- Water, an excellent media for studies of biomolecules, is not excluded as a solvent
- Only micrograms - milligrams of sample required
- Extremely *fast* collection Raman spectra, as fast as 150 msec

APPLICATIONS

- Determination of conformations of biological molecules such as proteins, nucleic acids, sugars and viruses
- Formulation of biologics
- Determination of absolute configuration without crystallization
- Direct measurement of enantiomeric excess without enantiomeric separation

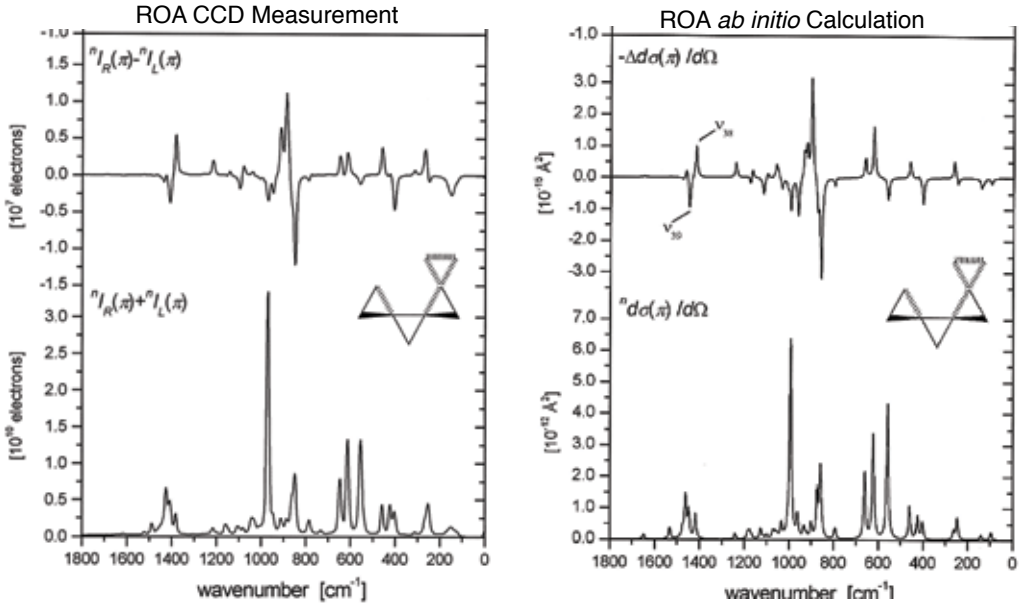
ROA Application Examples

1) PROTEIN CONFORMATIONAL STUDIES



ROA and Raman spectra of hen egg white lysozyme in water. Measurement time is 80 minutes; power 1.2 Watts at the sample.

2) ABSOLUTE CONFIGURATION DETERMINATION



COMPARISON OF EXPERIMENTAL (LEFT) AND THEORETICAL (RIGHT) ROA (TOP) AND RAMAN (BOTTOM) SPECTRA OF (-)-(M)-S -[4]HELICENE. DATA COURTESY OF PROFESSOR WERNER HUG.

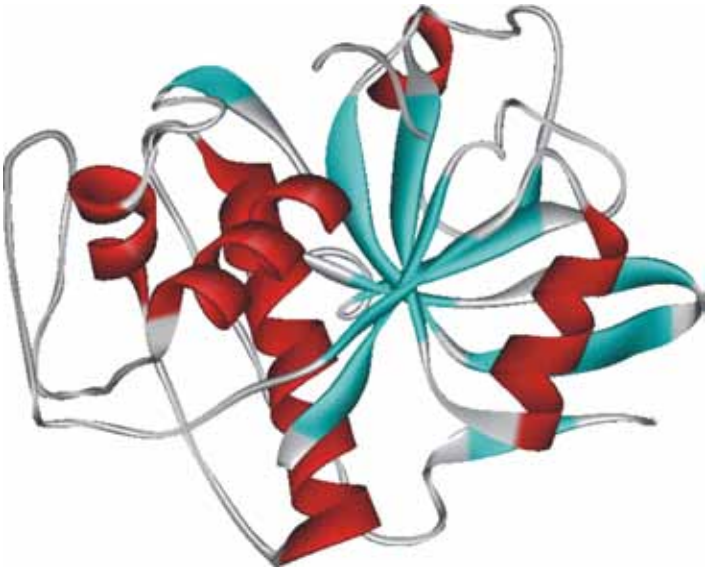
FT-IR Spectroscopy of Biologics

Bio*IR*™ is a family of dedicated solutions for the biopharmaceutical industry based on FT-IR instrumentation and comprised of specialized software and databases.

The first such system, PROTA™, was introduced in 1998 and has since rapidly become the industry's preferred choice. PROTA™ provides a fast, cost-effective and sensitive way to determine secondary structure of a protein or to follow structural changes due to perturbations. This turnkey system is designed to be used by both spectroscopists and non-spectroscopists. It's user-friendly, intuitive software guides users through data acquisition and analysis. PROTA™ includes all of the functions, in one integrated package, required to link IR spectral data and protein structure.

APPLICATIONS

- Formulation studies (liquids and solids) - effects of excipients, pH and buffers
- Determination of secondary structures of de novo proteins
- Conformational stability and dynamics
- Structure in aggregates
- Mutation studies
- Structural characterization upon environmental effects
- Stability studies (thermal and chemical)
- Drug delivery
- Protein-protein, protein-DNA/RNA and protein-drug interactions
- Crystallization condition screening



PROTA-2X™ Instrument

FT-IR SPECTROMETER SYSTEM

- ABB MB3000 FT-IR spectrometer consisting of:
  - Arid-Zone sample compartment with countercurrent purge flow in telescopic purge tubes
  - Non-hygroscopic ZnSe beamsplitter
  - High-sensitivity DTGS detector
- Resolution: 1 cm^{-1} - 128 cm^{-1}
- Spectral range: 6,500 - 500 cm^{-1}

ADDITIONAL HARDWARE

- Pre-loaded PC
- *Bio*Cell™ with CaF_2 windows
- Purge Control Kit

SOFTWARE

- Windows-based integrated software for data acquisition and data analysis
- Complete Grams A/I software
- Protein FT-IR databases
  - Transmission
  - ATR
  - Excipients

AFTER-SALES SERVICE

- Installation and training on FT-IR spectroscopy of proteins by experienced scientists
- BioTools combined service and technical protein application support for one year

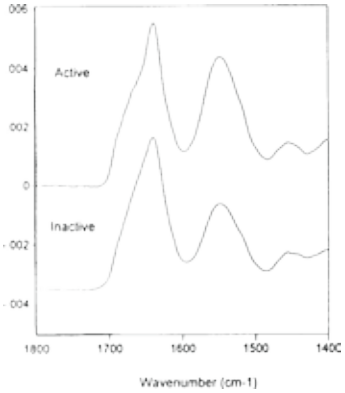
OPTIONS

- Variable Temperature cell and automatic temperature controller with computer interface
- KBr and ATR accessories
- Microscope
- A dry air purge supply is recommended to achieve optimal performance

PROTA™ Applications

APPLICATION EXAMPLES

1) Low Protein Concentration Studies



Protein samples with concentrations as low as 3 mg/ml in H_2O can be routinely measured with PROTA™. Conditions: 20 min. acquisition time, NO water vapor subtraction, buffer subtracted using the automated buffer subtraction function.

2) Formulation Studies

FT-IR derivative spectrum of 'intact' immunogenic antibody compared to a lyophilisate, that yields inactive, non- immunogenic form after reconstitution with water. Obvious differences are observed between the two spectra. These spectral differences identify structural changes that a protein undergoes upon lyophilization. This information may streamline and improve the formulation process.

3) Protein Secondary Structure Determination

Protein	% α-helix	% β-sheet	% bend	% turn	% other	sum
A-chymotrypsin	12	32	12	11	33	100
Carbonic Anhydrase B	14	33	14	13	26	100
Citrate Synthase	58	4	9	11	20	102
Carboxypeptidase	43	15	8	13	23	102
Catalase	44	11	11	12	24	102
Γ-chymotrypsin	12	35	12	13	26	98
Chymotrypsinogen	27	24	12	13	25	101
Concanavalin A	0	43	15	13	25	97
Other Proteins						

PROTA™ CAN BE USED TO DETERMINE QUANTITATIVE PROTEIN SECONDARY STRUCTURE USING FACTOR ANALYSIS, COMPARED TO THE 50-PROTEIN DATABASE. TYPICAL RESULTS ARE SHOWN ABOVE.

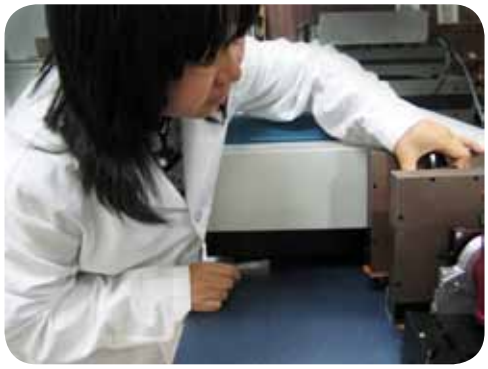
Lab Services

CHIRAL MOLECULES

- Absolute Configuration
- VCD Measurements
- *ab initio* calculations (VCD, ECD, ROA)
- VCD Consulting & Training
- Chiral Methods Development
- % Enantiomeric Excess
- Small Scale (~1g) Purifications

PROTEINS

- de novo Secondary Structure
- Formulation of Biologics
- Effects of Excipients
- Structure in Aggregates
- Effect of Environmental Changes - temperature, pH, storage
- Structural comparison of production lots

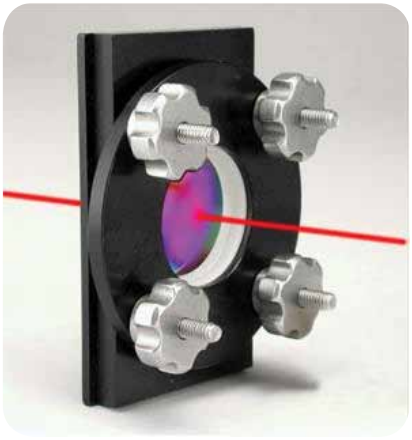


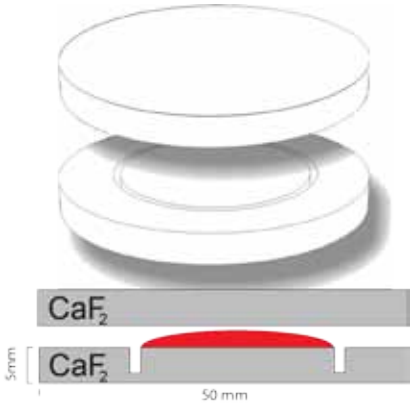
Accessories

*Bio*Cell™

The CaF_2 cell for IR/UV-CD spectroscopy is created between a perfectly flat, optically clear plate and another plate, the center of which is deepened to form a recessed parallel surface surrounded by a groove. This groove serves as a barrier between the sample area and the outer seal, keeping the sample from readily coming into contact with the outer seal. The seal is created by the “upper” flat plate pressing onto the outer ring of the “lower” plate

The cells are very easily assembled and disassembled, filled with solution, and washed between measurements. The seal of the cell prevents the evaporation of water for about 24 h at room temperature. The reproducibility of the cell path length after assembly / disassembly is 0.1 µm.





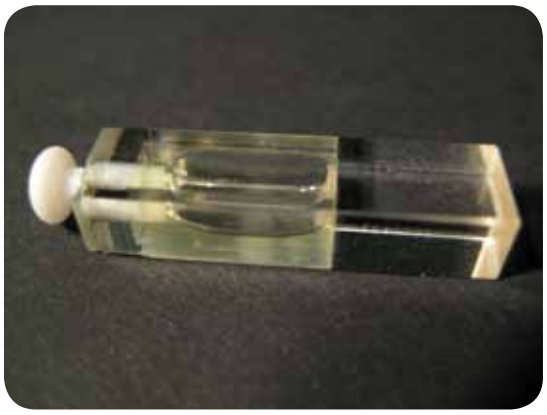
- Wide range of available path lengths: ~5-10, ~20, ~40, ~80 and ~120 µm
- 5 mm thickness x 50 mm diameter standard size. Cells with 4 mm x 40 mm dimensions are also available

*ROA*Cells™

Artifact-free sample cells for the Chiral*RAMAN-2X*™ instrument.

Available as:

- 3x4mm (100µL volume)
- 4x4mm (200µL volume)



Accessories (continued)
Temperature Control Options

*Temp*Con™

Pelltier based temperature controller

*Temp*Con™ temperature controller unit is designed for use in FT-IR spectrometers with two types of windows: large circular *Bio*Cell™ windows and rectangular windows. The controller can be controlled either manually or through computer interface.

The Ramp-Soak Control Interface allows for temperature studies that can be aligned with FT-IR scanning software and can be used in applications such as effect of temperature on protein conformation.

*Bio*Jack/T™

High precision cell holder (Thermostated available)

Features:

- Aluminum construction
- Threaded for tight seals
- High quality, low cost option for temperature control

*Accu*Tune™

Gear for BioJack for extreme precision and ease of use

Accessories (continued)

*CCD*sp™ Scientific Camera

Specifications

CCD:

» Pixel Size: 26 mm square

» Image Area: 26.6 x 6.7 mm

» Full Well Capacity: ~300,000 e-

» Dark Current: <1 e- / pixel / sec.

Electrical:

» Voltage: 110 V / 220 VAC (50 Hz / 60 Hz)

Cooling:

» Type: Thermo-electric -30˚C (from ambient 20˚C)

Communications:

» Ethernet: 10/100BaseT Serial: 115 kbps, RS-232, USB

Mechanical Dimensions:

» 4.58” L x 3.54” W x 3.54” H

» High-performance scientific camera

» Integrated digital signal processor (DSP)

» Designed for very low-light applications

» Thermo-electrically cooled to -30˚C

» Requires no computer interface card

» Flexible communication options

» Customizable

Software & Databases

VCD*base*™

We offer an online database of published VCD spectra. Spectra can also be downloaded for your use. Find your molecule at www.btools.com

View*VCD*™

ViewVCD software extracts IR and VCD intensities from Gaussian 09 output in ASCII XY ` format. It provides templates for comparison plots of observed and calculated spectra.

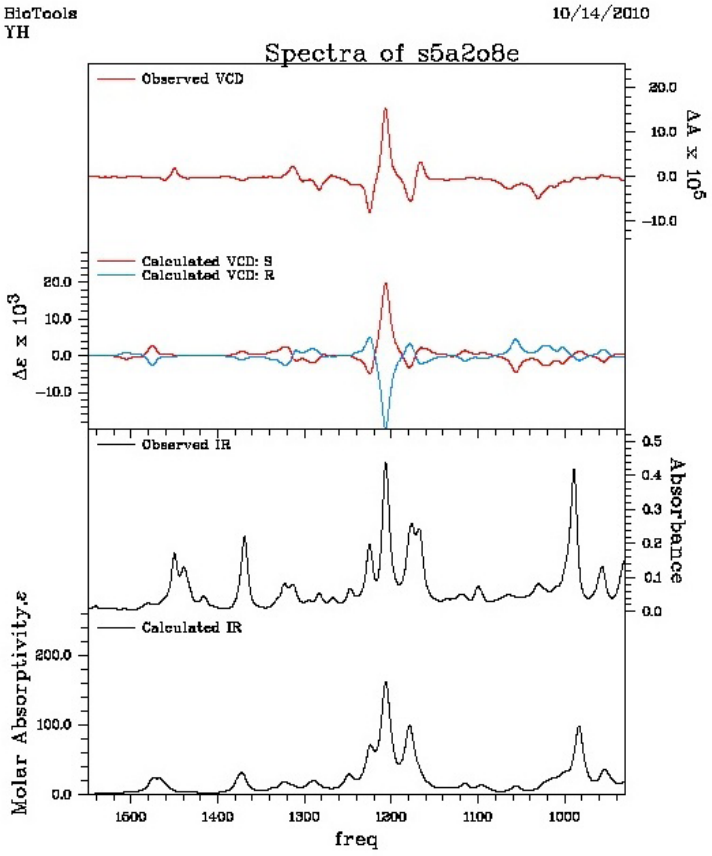
Protein Databases

(IR, CD, VCD, RAMAN & ROA)

The database of proteins in the liquid form, measured in transmission in water-based buffers, has now been extended. Databases of proteins in solid and liquid forms measured using ATR are also available. Also, same databases for CD, VCD, Raman, and ROA.

Custom Spectroscopic Databases

Let us create a database specialized to your needs



Compare*VOA*™

Confidence level algorithm for comparing VCD and ROA experimental and theoretical spectra.

Customers & Testimonials

WE PROUDLY SERVE HUNDREDS OF COMPANIES, UNIVERSITIES AND GOVERNMENT AGENCIES

AMGEN
Baxter
Millennium
Merck
Genzyme
AstraZeneca
Bristol-Myers Squibb
Pfizer
GlaxoSmithKline
MedImmune
Eli Lilly

WHAT OUR CUSTOMERS ARE SAYING

"In June, 1996, I attended the AIRS conference and had the honor of meeting Drs. Larry Nafie and Rina Dukor who introduced me to a beautiful new technique, Vibrational Circular Dichroism (VCD), which had at long last come of age, due in large part to the commercialization of their FT-VCD spectrometer. As a long-standing analytical chemist in pharmaceutical research with a focus on vibrational spectroscopy, I recognized the potential impact VCD could have on many aspects of big pharma. Four years later, in the summer of 2000, we purchased a BioTools ChiralIR (serial number 5). I made my first stereochemical assignment in the fall of that year and since then have successfully assigned the configurations of more than 600 exploratory drug molecules, providing an international service to research facilities in Europe and the United States.

We upgraded our ChiralIR to a dual-PEM system in 2004, allowing us to more reliably assign the configurations of single enantiomers. Our unit has been a real work-horse throughout the years. It has been used on a near-daily basis since its purchase in 2000, without requiring a single major repair. This instrument is truly robust, with a level of reliability well beyond other vendor's FT-IR instrumentation in my lab.

Would I purchase another BioTools ChiralIR FT-VCD spectrometer? Absolutely-we have one budgeted for fiscal year 2011. I consider this instrument to be world-class and a bargain for the price given its state-of-the art technology and incredible level of reliability. "

Dr. Douglas James Minick
Senior Research Investigator
GlaxoSmithKline

"Over the last several years, the Vibrational Circular Dichroism (VCD) technique has dramatically revitalized the utility and visibility of vibrational spectroscopy within pharmaceutical drug discovery. The ability of VCD to deliver absolute chiral assignments without the need for standards or crystallizations, renders the technology a vital complement to traditional pharmaceutical analytical technologies. "

Dr. Don Pivonka
AstraZeneca

Support & Service

CONSULTING

BioTools offers consulting services that bring our expertise in VCD, ROA and spectroscopy of biomolecules to bear on your applications and needs. Costs depend on the extent of the study and degree of urgency.

TECHNICAL SUPPORT AND MAINTENANCE

We strive to provide the best technical support to all our customers. Each instrument sold comes with a full one year warranty, and additional maintenance contracts can be purchased. E-mail based help desk is open 365/24/7 at *info@btools.com*.

FOR MORE INFORMATION, PLEASE CONTACT YOUR LOCAL REPRESENTATIVE

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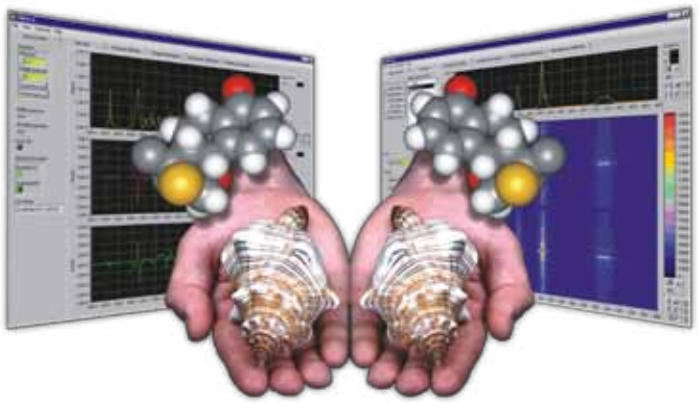
The European Centre for Chirality (EC^2) is based in Belgium at the University of Antwerp and Ghent University and is an exclusive alliance with BioTools Inc. Together, the three organisations are the European Centre for Chirality.

The European Centre for Chirality is a unique blend of scientific expertise using the considerable knowledge and know-how within EC^2 to provide analytical services for chiral molecules using techniques of Vibrational Circular Dichroism (VCD) and Raman Optical Activity (ROA).

Our service packages are designed to give you maximum choice and flexibility to meet your requirements and budget.



TOOLS FOR DISCOVERIES OF LIFE

At BioTools we have created a company that brings to life dedicated instrumentation that no one else has dared to create, such as Chiral*IR*™, Chiral*RAMAN*™ and Bio*RAMAN*™. We are here to help you solve some of life's most intriguing bio-problems.

Our slogan, Tools for Discoveries of Life, has a double meaning. We provide Tools to help scientists make discoveries in their Biographical Life, and, at the same time, these Tools can be used to discover new information about molecules that make up Biological Life as we know it. Hence, these are BioTools. We concentrate our efforts in the areas of proteins and chirality by specializing in two types of pharmaceuticals: Chiral-organic and protein-based drugs.

BioTools

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