



PROTEOMELAB XL-A/XL-I

MACROMOLECULE AND NANOPARTICLE CHARACTERIZATION SYSTEM

Native-condition protein characterization



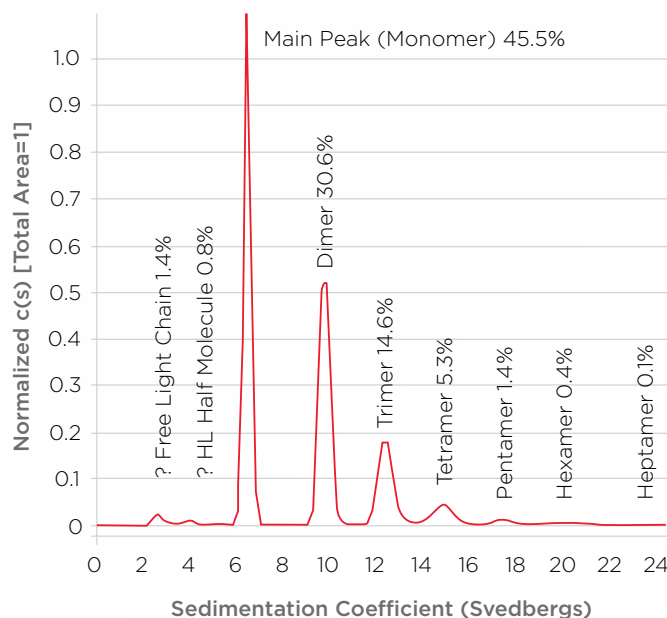
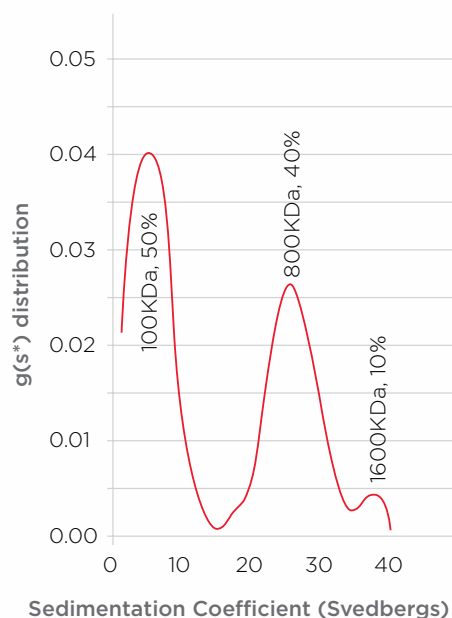
BRILLIANCE
at every turn.



By measuring proteins as interacting elements instead of in isolation, the ProteomeLab XL-A/XL-I accelerates the development of diagnostic markers and therapeutic targets, and delivers a unique system for protein characterization in solution.

PROTEIN HETEROGENEITY

The ability to characterize sample heterogeneity is an important part of process development, formulation and QA/QC. The accompanying graphs are distribution plots with heterogeneity visually indicated by peaks. The position of each peak indicates the sedimentation coefficient, while the area gives the amount of that species. The graph (left) uses the $g(s^*)$ -distribution method to resolve three non-interacting proteins. Levels of <10% by weight can be quantified. For more in-depth analysis, third party software is available for enhanced application versatility and sensitivity. The graph (right) is a distribution plot of a highly stressed monoclonal antibody sample, with heterogeneity visually indicated by higher resolution peaks. Use of the more sophisticated $c(s)$ distribution method provides enhanced resolution by removing the effects of diffusion. Aggregates or other variants can be quantified at levels well below 1% by weight.



Source: J. S. Philo Ph.D., Alliance Protein Laboratories

By analyzing proteins as interacting elements instead of in isolation, the ProteomeLab XL-A/XL-I more closely approximates true physiological conditions by considering the protein's conformation (folded or unfolded), assembly reversibility (interacting systems), stoichiometry (associative state), and heterogeneity (aggregation).

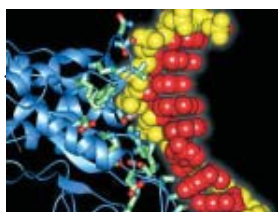
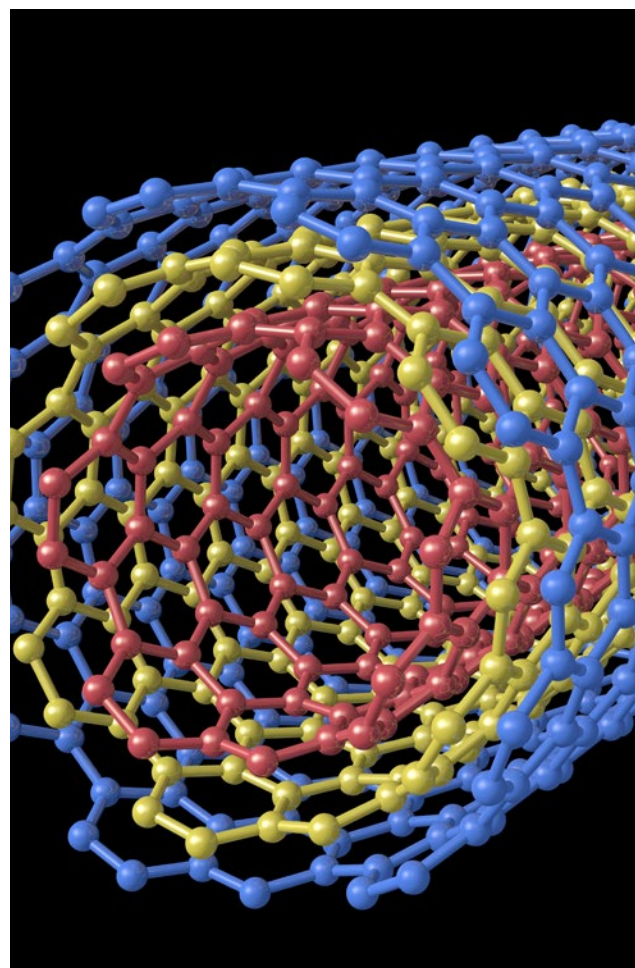
An important component of lead optimization is the ability to evaluate a drug candidate under concentrated "shelf-like" conditions before it moves into expensive preclinical or clinical trials. The ProteomeLab XL-A/XL-I functions over a wide range of concentration, temperature, ionic strength and pH, delivering more thorough characterization than other methods.

Our unique operating methodology measures the relative change in the distribution of molecular weights, providing an efficient way to measure heterogeneity, stoichiometry and self-associating systems.

Because the ProteomeLab XL-A/XL-I's measurements are based on the first principles of thermodynamics and hydrodynamics, no standards or calibrations are required. As a result, you spend less time on setup, and more time on discovery.

To ensure compatibility with the many additional capabilities and product support provided by third party software, all data is saved in standard ASCII format.

For easy sample preparation, inject as little as 15 μL to 120 μL of sample and reference solutions into opposing positions in the cell assembly, and place the assembly into the system. Up to 28 different sample/reference pairs can be studied in a single run, with each having a different set of solute/solvent conditions (pH, ionic strength, concentration). This provides data for accurate analysis in as little as three hours. Your sample can be retrieved for additional analysis.



A critical step in the proteomics process, characterization involves putting a protein's structure and function into context with all other interactions in a particular biological pathway.

"For monitoring protein aggregation and heterogeneity in many different projects, my XL-I is invaluable."

- Kurt Drickamer, Ph.D., Department of Biochemistry, University of Oxford, UK

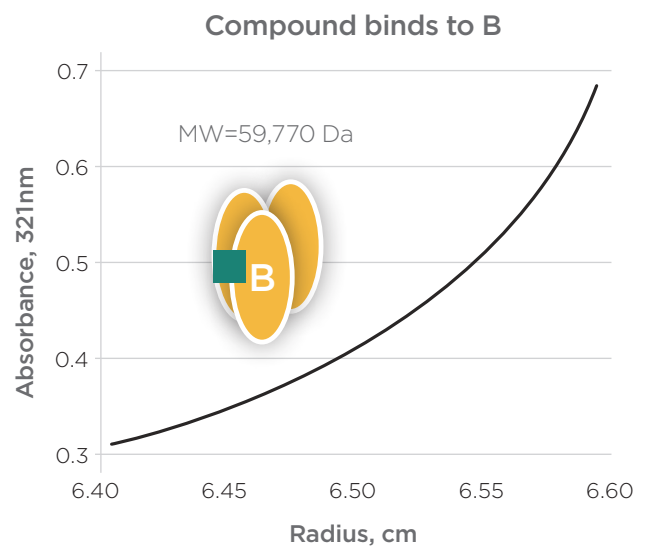
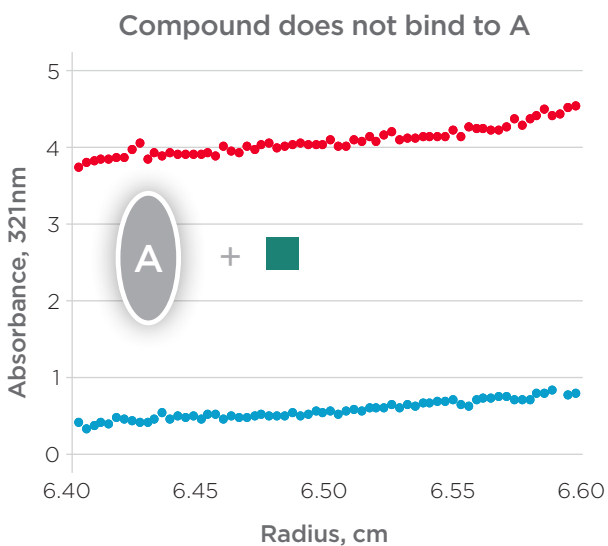


AN INTEGRATED SUITE OF EFFICIENT PROTEOMICS SOLUTIONS

All of Beckman Coulter's ProteomeLab offerings are designed to serve as an extension of your thinking, making it easier for you to do your best science, your way. As a result, you get a complete solution that puts meaningful, actionable information into your hands, quickly and easily.

INTERACTING SYSTEMS

The ProteomeLab XL-A/XL-I is adept at helping determine yes/no binding of a small molecule to a target protein. In the top-most example, a small-molecule inhibitor (the green square) of a hormone-receptor interaction could bind to either the receptor (A) or the hormone (B). The inhibitor uniquely absorbs at 321 nm and has a low molecular weight and therefore does not sediment. If it binds to a protein, however, the bound molecule will sediment with the apparent molecular weight of the protein at 321nm. The left-hand graph represents sedimentation equilibrium of an inhibitor, receptor mixture, with the absence of curvature for the inhibitor (red) indicating that the compound does not bind to the receptor. The right-hand graph shows a pronounced curve, indicating that the inhibitor binds to the hormone.



Source: Michelle Arkin Ph.D., Sunesis Pharmaceuticals, Inc.

MULTIPLE DETECTION SYSTEMS The ProteomeLab XL-A is configured with a scanning UV/Vis detection system, which provides sensitivity for low-concentration work and selectivity for optimizing detection based on the sample's maximum absorbance. The XL-I adds Rayleigh Interference Optics and the capability to measure the change in refractive index resulting from changes in sample concentration. This delivers increased accuracy and the ability to examine a greater concentration range with a wider selection of samples. The XL-I can collect data from both detection systems sequentially, to provide the broadest spectrum of data for protein characterization in solution.

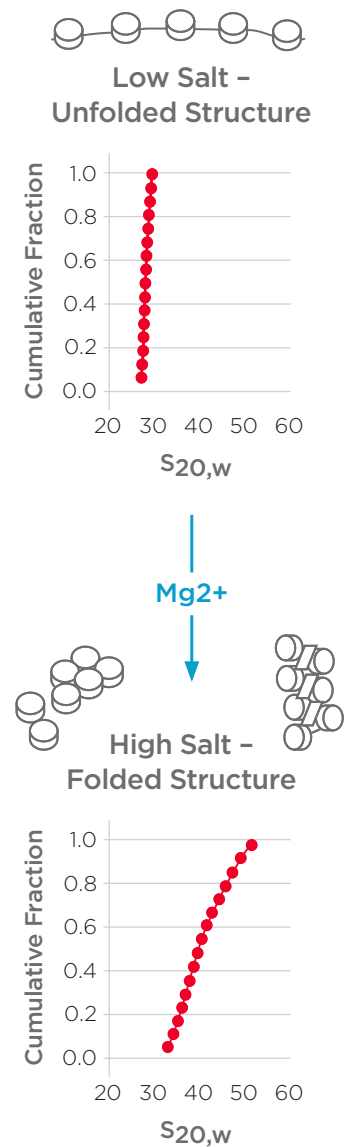
MOLECULAR CONFORMATION

The characterization of molecular conformation is a powerful quantitative method for proving to regulatory agencies that changes in manufacturing processes produce products with identical solution conformations. It's also used in preclinical studies to verify that recombinant proteins are properly folded, and as an aid in selecting mutants or engineered forms of a protein.

This example demonstrates molecular conformation under varying salt conditions. In TE buffer (top) an oligonucleosome structure was shown to have a sedimentation coefficient of between 27-30 S (visually indicated by a vertical distribution plot). In 1.8mM $MgCl_2$, the same oligonucleosome structure was shown to have a sedimentation coefficient of between 33-52 S (visually indicated by a non-vertical distribution plot). The solution's molecular mass of the oligonucleosome in these two salts' concentrations remained the same (demonstrated by sedimentation equilibrium), indicating that the oligonucleosome folded into a more compact conformation in the presence of salt.

“There are other bioanalytical instruments and methodologies for characterizing the behavior of proteins, but the XL-A/XL-I is often my first choice because of its unique ability to deliver quantitative information about heterogeneity, conformation and association state. Without it, we and our clients would waste a lot of time and material doing calorimetry, SPR, CD, and other procedures on bad samples.”

- John Philo, Ph.D., Alliance Protein Laboratories, Thousand Oaks CA, USA

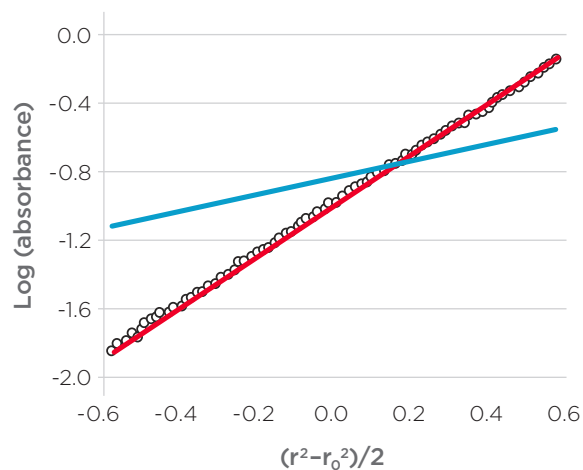
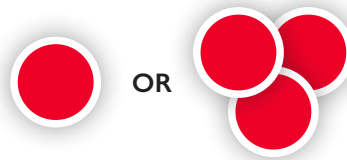
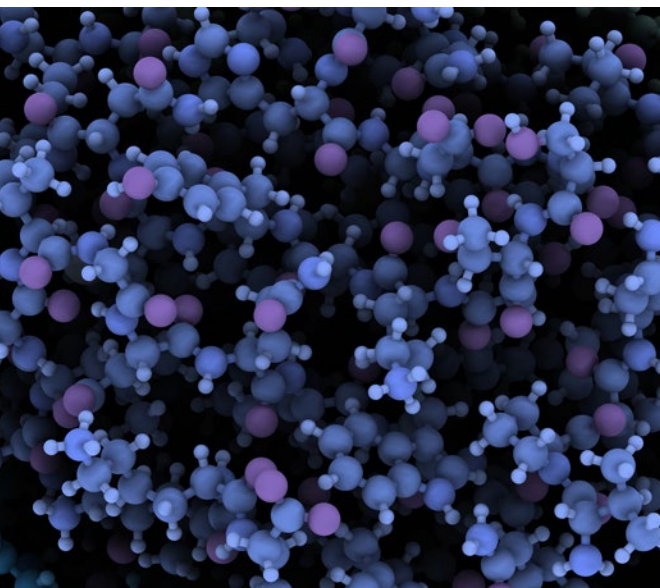


Source: Jeffrey C. Hansen, Ph.D., Dept. of Biochemistry, University of Texas, Health Science Center, San Antonio, Texas, USA.

THE PROTEOMELAB ADVANTAGE To provide researchers with the most comprehensive and efficient proteomics research solutions, we're integrating our leading-edge systems, software and chemistries with a targeted focus on protein research. By combining our many technological strengths, ProteomeLab delivers a system of complementary tools that are uniquely optimized for accelerating protein discovery.

STOICHIOMETRY

Data describing a protein's stoichiometry can be useful early in drug development, and in providing characterization and comparability data to regulatory agencies. The data below is for a sequence homolog of a tumor necrosis factor, part of a family of proteins that are all trimers. Size exclusion chromatography indicated that this protein is a monomer, suggesting either that it is not a true trimer or that it was not properly folded after expression in *E. coli*. In this form of plot, a single species gives a straight line with a slope proportional to the solution mass. The blue line shows the slope predicted for a monomer, the red for a trimer. Clearly, this protein is indeed a trimer, as expected.



Source: J. S. Philo Ph.D., Alliance Protein Laboratories

“YES/NO” CHARACTERIZATION A simple “yes” or “no” answer is not only easy to obtain, many times it’s all that’s required— especially in initial experiments. While the ProteomeLab XL-A/XL-I family can accurately measure several decimal places, it also helps save time and effort by giving you the flexibility to get quick, top-level answers.

The ProteomeLab XL-A/XL-I is an important part of a broad continuum of Beckman Coulter products, including research automation, flow cytometry, centrifugation, cellular analysis, genomics products, and particle characterization.

Software resources Additional software and algorithms are actively being developed and are available as shareware to enhance your individual application needs. Third party software is available, including: Sedfit—Features the c(s) algorithm method for measuring heterogeneity at levels below 1% by weight; Sednterp—A utility program that provides information on amino acids, common salts and buffers and interpreted results on molecular conformation, molecular weights and sedimentation coefficients, and; Nonlin—An analysis program for measuring self-associating or interacting systems for up to five molecular species.

Customer training Our three-day course combines lectures with hands-on labwork to teach theory, operation and data analysis. One free training spot is available with each purchased instrument. You’ll leave knowing how to efficiently operate and maintain your instrument, optimize experimental design, save time and minimize sample use.

Service network As advances in life sciences yield phenomenal improvements, researchers face growing pressure to do more with less. That’s why Beckman Coulter has maintained its excellent reputation for service and support. As a result, thousands of our instruments are installed worldwide. All backed by our on-line, on-site and on-call support.

On-line searchable reference library See how your colleague is solving a problem. Explore new methods. Search over 400 references cataloged by author, reference, title or keyword with our valuable on-line reference resource library.



“The XL-A was unique in its ability to determine the bivalency of the Interleukin-6 (IL-6) dimer when binding to the IL-6 receptor in solution. This information is crucial in interpreting results from other techniques such as surface plasmon resonance, which require one of the components to be immobilized.”

- Dr. Geoff Howlett, Biochemistry & Molecular Biology,
University of Melbourne, Australia

WORKFLOW

IDENTIFY

- Flow cytometry
- Automated fluorescence microscopy
- Microarray technology
- Cell viability analysis

ISOLATE

- General purpose centrifugation
- High performance centrifugation
- Ultracentrifugation
- Centrifugal elutriation
- Automated liquid handling

FRACTIONATE

- High performance centrifugation
- Ultracentrifugation

CHARACTERIZE

- Protein characterization in solution
- Automated protein crystallization

EVALUATE

- Microarray technology
- Software solutions

DIAGNOSE

- Automated immunoassay
- Flow cytometry
- Immunochemistry
- Immunofixation

PROTEOMELAB XL-A/XL-I

ORDERING INFORMATION

Part No.	Description
969340	ProteomeLab XL-I (200-240 VAC, 60Hz) includes: An 50Ti (8 hole rotor), 3 assembled cells (sapphire windows), counterbalance set, torque stand, & accessory kit
969341	ProteomeLab XL-I (220-240VAC, 50Hz) includes: An 50Ti (8 hole rotor), 3 assembled cells (sapphire windows), counterbalance set, torque stand, & accessory kit
969342	ProteomeLab XL-A (200-240VAC, 60 Hz) includes: An 60 Ti (4 hole rotor), 1 assembled cell (quartz windows), counterbalance set, torque stand, & accessory kit
969343	ProteomeLab XL-A(220-240VAC, 50Hz) includes: An 60Ti (4 hole rotor), 1 assembled cell (quartz windows), counterbalance set, torque stand, & accessory kit
392773	Individual assembled cell (sapphire windows)
392772	Individual assembled cell (quartz windows)

SPECIFICATIONS

Height	120.7 cm (47.5 in.)
Width	94.0 cm (37 in.)
Depth	67.3 cm (26.5 in)
Weight	465 Kg (1025 lb)

For information on our comprehensive line of ProteomeLab systems, please contact your local Beckman Coulter representative or visit our web site at:

beckmancoulter.com