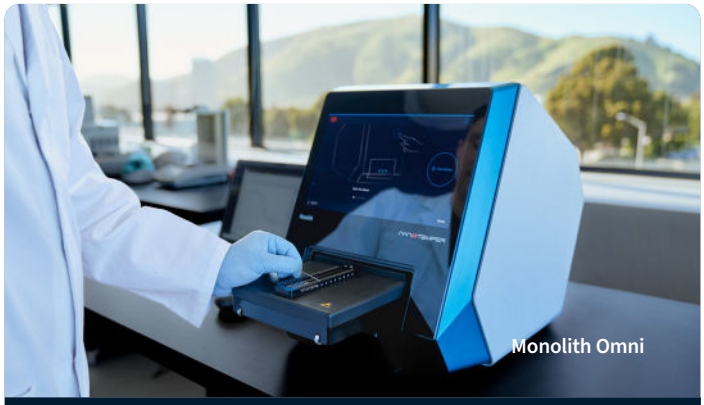
Monolith™ Omni

Affinity, kinetics, stability. One workflow.

Monolith™ Omni is a single biophysical platform for multi-parameter characterization of biomolecular interactions, in solution, using orders of magnitude less sample. Combining affinity, kinetics, thermodynamics, and qualitative protein stability analysis without surface immobilization, Monolith Omni enables researchers to generate high-quality interaction data across diverse modalities including proteins, nucleic acids, small molecules, and molecular glues across academia and industry with straightforward assays and software.


Monolith Omni

Key benefits

In-solution kinetics: Determine affinity constants and rate constants in solution to obtain a kinetic profile of candidates without surface immobilization artifacts.

Multi-parameter characterization: Combine affinity, kinetics, and qualitative stability analysis in one workflow to generate broader interaction data using only 10 µL of target sample - orders of magnitude less than other techniques.

Versatility: Generate actionable data for diverse target classes, including membrane proteins, intrinsically disordered proteins, and nucleic acids.

System components

The Monolith Omni system includes a benchtop instrument and laptop equipped with intuitive software for streamlined data acquisition and analysis. Capillaries containing 10 µL of sample volume are loaded via a capillary tray gate in the front; this easy-to-load capillary-based system minimizes system maintenance and user error by eliminating the need for fluidics.

Characterization technology

Monolith Omni is powered by four biophysical characterization technologies to quantify molecular interactions between a fluorescently labeled biomolecule (target) and an unlabeled binding partner (ligand): Spectral Shift, Temperature Related Intensity Change (TRIC), nano Temperature Alteration Kinetics (nanoTAK), and nano Laser Induced Stability Analysis (nanoLISA).

Combining four complementary technologies in the same instrument enables characterization of binding affinities, kinetics, thermodynamics, and stability. With Monolith Omni, a single workflow provides broad, comprehensive analysis of biomolecular interactions - all free in solution.

Spectral Shift

Spectral Shift detection quantifies molecular interactions between one binding partner that is labeled with a specific fluorophore optimized to report subtle environmental changes, and another unlabeled binding partner. Spectral Shift detects ligand induced changes in the hydrophobicity of the target biomolecule's surface by measuring picometer shifts in the fluorescence emission at two wavelengths, 650 nm and 670 nm. A ratiometric signal of the labeled target as a function of ligand concentration is measured to obtain a dose-response curve. As a rapid, isothermal measurement, it is non-destructive, permitting sample re-analysis, temperature-dependent studies and investigations of fragile molecules that destabilize quickly. The highly sensitive and robust detection allows work with small amounts of labeled target and suboptimal samples containing aggregation or precipitation.

Additional technologies powered by Spectral Shift:

nanoTemperature Alteration Kinetics (nanoTAK)

nanoTAK measures binding kinetics (k_{on}, k_{off}) of an interaction by applying a rapid temperature step to pre-equilibrated samples in capillaries. The perturbation drives the system out of equilibrium, and the subsequent re-equilibration is monitored in real-time via Spectral Shift.

Van't Hoff Thermodynamics:

The temperature dependence of binding can be used to derive thermodynamic parameters such as ΔH and ΔS. This adds thermodynamic context to affinity and kinetic measurements supporting a more complete understanding of molecular interactions.

nano Laser Induced Stability Analysis (nanoLISA)

nanoLISA detects unfolding and early aggregation by heating samples up to 95°C while monitoring spectral shifts. Unfolding alters the fluorophore's environment, producing a clear sigmoidal curve. Ligand binding shifts this curve, showing stabilization through covalent and non-covalent interactions. Comparing thermal melting profiles with and without ligand enables orthogonal hit confirmation and deeper insight into binding.

Temperature Related Intensity Change (TRIC)

TRIC also measures the interaction between the fluorescently labeled target and unlabeled ligand, using the same samples as Spectral Shift. TRIC detects ligand induced changes in the target's shape and structural flexibility by measuring the fluorophore response to a small temperature perturbation. Beyond K_d determination, TRIC is sensitive to aggregation or compound induced precipitation, providing additional insights into sample quality.

Software

The software consists of an integrated control and analysis module, designed with an intuitive user interface that minimizes the time required for experimental set up and analysis. Such a straightforward, single-platform system allows for installation and training to be completed in just one day, with extensive support information easily accessible at **support.nanotempertech.com.**

Monolith Control (MO.Control)

The software enables design and execution of binding affinity experiments. This includes assay setup, optimization, single-dose, or dose-response experiments with just a few clicks. The software allows users to test up to 6 different buffer conditions in less than 10 minutes.

Figure 2. Dose Response Curve: The Dose Response analysis displays concentration-dependent changes of Ratio 670/650 nm, which are used to calculate K_d or EC50 values. The signal of each capillary is plotted against the ligand concentration in the capillary.

MO.Control supports the user with step-by-step experimental planning, assay setup guidance, and immediate feedback on assay optimization. Data is easily exported, merged, and grouped for comparison, and automated analysis generates publication-quality outputs, including binding curves with error bars. Global fitting and Van't Hoff analysis enable extraction of kinetic and thermodynamic parameters such as ΔH and ΔS.

NanoTemper App Hub

The NanoTemper App Hub is a server-based platform that provides a collection of assay applications and analysis tools. It serves as a central workspace for transforming raw Monolith data into clear, actionable results with dedicated, easy-to-use apps. Continuously expanding with new applications, it evolves to streamline workflows and enhance data analysis.

The **nanoLISA app** analyses thermal unfolding profiles, calculates inflection points, and delivers stability and aggregation insights for binder validation.

The **nanoTAK app** evaluates temperature-induced fluorescence changes across the ligand concentration series and extracts kinetic rates k_{on}, k_{off}.

Services and training

Service contracts and user training are available to support consistent operation and effective use of the platform. Options include extended warranty and service coverage to minimize downtime, as well as training programs delivered online or onsite to ensure users gain proficiency in system operation, assay design and development. Extensive supporting information is provided online at: **support.nanotempertech.com.**

Consumables

Capillaries

Employing single-use capillaries provides several advantages and offers maximum flexibility for the Spectral Shift and TRIC measurements. Cross-contamination from re-use of sampling vessels or costly immobilization techniques is avoided and no cleaning is required; even highly viscous samples can be easily loaded into the capillaries for more challenging measurements in a variety of solutions or serums. Two different capillary types are available for use with Monolith Omni: Standard grade, made of borosilicate glass, and Premium grade, made of glass with a polymer coating to prevent protein adsorption.

Figure 3. Easy sample introduction with capillaries.

Capillaries chips

For convenient, rapid sample loading from 384-well microtiter plates, capillary chips with 24 individual capillaries mounted on a frame aligned to the well spacing can be used. For added convenience, a capillary chip filling station is also available.

Labeling kits

One of the binding partners, the "target", must be fluorescently labeled to measure the Spectral Shift and TRIC signals in the Monolith Omni. NanoTemper Technologies offers labeling kits with different coupling chemistries, such as covalent, affinity-based, site-specific, or amino acid-specific. The fluorophores used in the kits have been specifically engineered to detect subtle changes in the chemical environment, enabling sensitive and reproducible measurements.

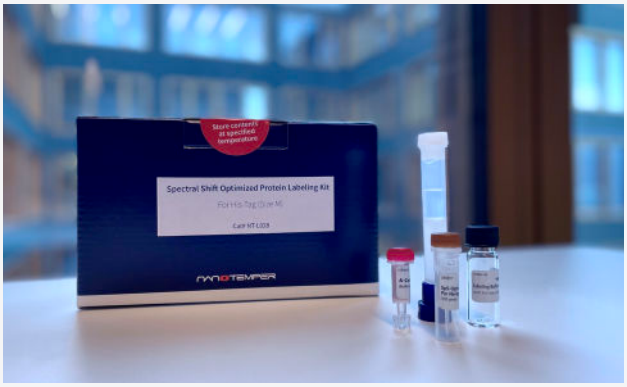


Figure 4. Easy-to-use labeling kits from NanoTemper support your success.

Applications

Monolith Omni is designed to measure a broad range of biomolecular interactions, detecting binding events in solution, at equilibrium, and in a manner that is mass-independent, eliminating complications associated with size differences between interacting partners. Integrating multiple Spectral Shift-enabled technologies into a single device enables the measurement of (i) isothermal affinity, (ii) kinetics, (iii) thermodynamics and (iv) quantitative stability all in one workflow and on the same sample. In addition, TRIC enables an orthogonal affinity readout and provides further insights into sample quality and aggregation detection. Combining all readouts establishes a comprehensive interaction profile for your ligand, covering a detectable affinity range from weak (mM) to tight (nM) binders and providing high-quality kinetics and stability information free in solution and with low sample consumption.

1. Isothermal binding studies of molecular interactions

Characterize interactions over a broad range of targets and ligands with Spectral Shift. Work with membrane proteins, transcription factors, nucleic acids and other difficult targets, and study binding of small molecules, peptides, proteins, degraders and more.

- Study binding of small molecules to any kind of target, including transcription factors and membrane proteins, across a broad and dynamic affinity range.
- Measure direct target engagement on nucleic acids, such as DNAs, various forms of RNAs and aptamers, binding to proteins, small molecules and antisense oligonucleotides.
- Work in the assay conditions that support your target and study membrane proteins in detergent, nanodiscs, or even in complex unpurified matrices.
- Investigate weak binders and assess low Dalton-sized compounds, e.g., fragments or ions, problematic for other biophysical methods.
- Measure covalent inhibitor binding at equilibrium via direct biophysical readout, eliminating surface regeneration issues.
- Analyze heterobifunctional degraders (molecular glues, PROTACs) for binary/ ternary complex affinities, cooperativity, and hook effects.

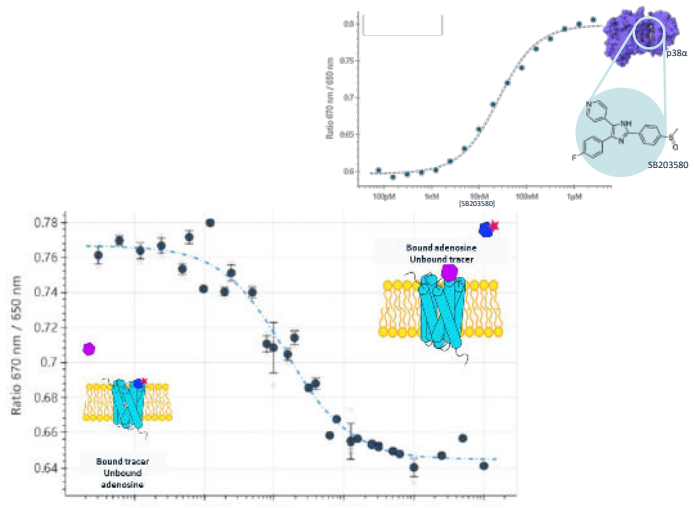


Figure 5. Exemplary isothermal measurements for different target classes and affinities. Top: Small molecule binding towards the kinase p38α, showing an affinity of 20 nM. Bottom: Displacement assay designed to study extracellular adenosine binding towards the membrane Protein A2A.

2. Kinetic profiling of lead candidates with nanoTAK

Use nanoTAK to analyze the kinetics of your biomolecular interactions in-solution and fluidics-free.

- Determine binding kinetics in solution and without the limitations of surface-immobilization techniques.
- Measure even the fastest kinetics with k_{on} values of up to 10^8 $M^{-1}s^{-1}$ and k_{off} of up to 2 s^{-1}, by avoiding mass-transport effects and fluidics.
- Compare the kinetic binding profile of your lead compounds and investigate how changes in the molecules impact binding behavior.
- Investigate degrader induced complex formation and evaluate the kinetic profile of binary and ternary complex formation.

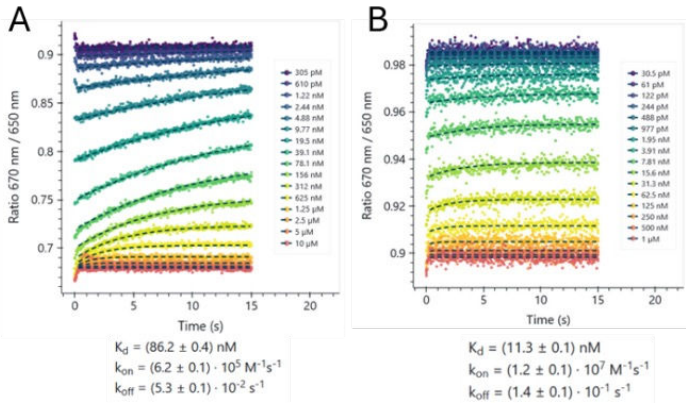


Figure 6. Interactions displaying kinetics on different timescales. A. DNA-DNA hybridization and B. protein – small molecule binding. Both samples were recorded for a temperature jump from 20°C to 25°C and kinetic traces were recorded for 15 seconds per concentration. A global fit was used to derive the kinetic parameters k_{on} and k_{off}, as well as the affinity at the final temperature.

3. Additional applications - basic research

Use a Van't Hoff analysis to investigate the thermodynamics of your biomolecular interactions and unfold your sample with nanoLISA in just 60 seconds and at nanomolar concentrations to get insights into stability.

- Optimize assay conditions and investigate target stability and foldedness.
- Orthogonally confirm binding of ligands to your target by monitoring a thermal shift in the nanoLISA unfolding profile.
- Characterize ligand induces stabilization effects and understand the concentration dependency by performing nanoLISA on a serial dilution.
- Determine the thermodynamic profile of your interaction to gain deeper insights into ligand binding from enthalpy and entropy changes.

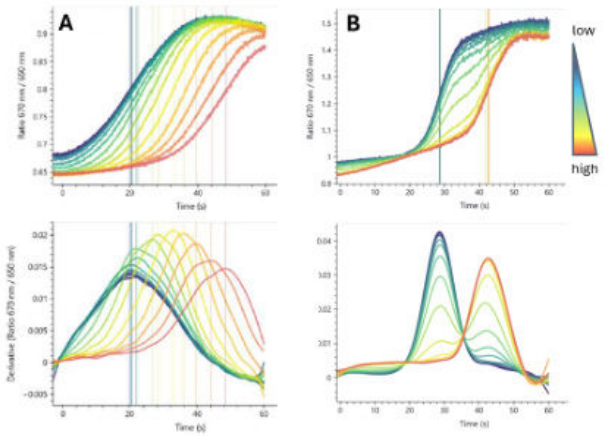


Figure 7. nanoLISA experiment for two biomolecular interactions with unfolding traces (top) and first derivative (bottom). A. Weak interaction between a DNA aptamer and AMP. Upon temperature increase the aptamer destabilizes and unfolds. AMP stabilizes the aptamer in a concentration-dependent manner, resulting in a gradual shift in the unfolding profile. B. Picomolar interaction of the kinase p38α with BIRB796. nanoLISA reveals a stochiometric population of unbound and bound state of p38α, resulting in two clearly distinct unfolding events. Concentration of the ligand is encoded in the color bar.

Specifications

General specifications

Time it takes to K_d and kinetic rates	~ 5 min (fast reactions, koff~ 0.1-1.0 s-1) ~ 20 min (slow reactions, koff~0.001-0.1 s-1)
Dynamic range	K_d: 1 nM - mM k_{on} ~ 10^3 – 10^8 $M^{-1}s^{-1}$ k_{off} ~ 0.001 – 1.0 s^{-1}
Data export	JSON
Molecular weight range	10^1 -10^7 Daltons
Sample volume required (per capillary)	10 µL
Capillaries per run	Up to 24
Temperature control	20-40 °C ± 0.5 °C (isotherm, via tray) 20-40 °C ± 0.5 °C (kinetics, via temperature jump)
Fluorescence wavelengths	Excitation: 592 nm Emission: 650 & 670 nm
Dimensions	Width: 36 cm Height: 40 cm Depth: 58 cm
Weight	27 kg

Computer requirements

Operating system	Windows 11 24H2 Enterprise IoT LTSC, English Language.
CPU	Intel Core Ultra 5 125H vPro Essentials — 14 cores, 18 threads, up to 4.50 GHz, 28W TDP
Memory	16 GB (2 × 8 GB), DDR5, 5600 MT/s, non-ECC
Storage	256 GB M.2 2230, Gen4 PCIe NVMe SSD (Class 35)
Display	15.6" FHD 1920×1080, 60 Hz, 250 nits, non-Touch
Software	Microsoft.NET Framework 4.8.1
Network	Intel AX211, Wi-Fi 6/6E (802.11ax), 2×2 MIMO, 2400 Mbps, 2.4/5/6 GHz + Bluetooth

Compliance

Compliant with	CE, CB, NRTL/UL, CSA
Safety	IEC 61010-1:2010/AMD1 :2016 Part 1, IEC 61010-2-010:2019 Part 2-010, IEC 60825-1:2014, 21 CFR 1040.10 and 1040.11[1]
Electromagnetic compatibility (EMC)	IEC 61326-1:2012 EMC IEC 61000-3-2:2006 EMC IEC 61000-3-3:2008
Overvoltage category	CAT I
Laser classification	1920 x 1080 or better
Software	Laser Product Class I
Environmental	Pollution degree 2

Ordering information

Product	Code
Monolith Omni *incl. Dell Mobile Precision Workstation, SW MO.Control*	MO-G040
Standard capillaries	MO-G039
Standard capillaries	MO-K25
Premium capillaries	MO-MK025
Capillary chip filling station	NT-AT100
Spectral Shift Optimized Protein Labeling Kit — For His-Tag (Size M)	NT-L028
Spectral Shift Optimized Protein Labeling Kit — Lysine-Reactive (Size L)	NT-L021
Spectral Shift Optimized Protein Labeling Kit — Cysteine-Reactive (Size L)	NT-L024
Biotinylated Target Labeling Kit	NT-L020
His-Tag Labeling Kit RED-tris-NTA 2nd Generation	MO-L018
Protein Labeling Kit RED-NHS 2nd Generation	MO-L011
Protein Labeling Kit RED MALEIMIDE 2nd Generation	MO-L014
SNAP-Tag® Labeling Kit RED 2nd Generation	MO-L019
Human Fc Labeling kit	NT-L030

Note: all NanoTemper labeling kits are compatible with the Monolith Omni, Monolith X, Dianthus, and Dianthus uHTS.

Scan the QR code to open the Monolith product page.
nanotempertech.com/monolith-omni

For local office contact information, visit
nanotempertech.com/offices

[1] Exception: conformance with IEC 60825-1 Ed 3, as described in Laser Notice No 56, May 8, 2019.