Malvern Panalytical
a spectris company

PEAQ-ITC Systems

MicroCal Technology

Understanding biomolecular interactions

PEAQ-ITC in action – proven versatility

Thousands of citations in reference databases illustrate the diverse applications of Malvern Panalytical PEAQ-ITC (MicroCal Technology) systems. They are used to determine the binding affinity and thermodynamic properties of any biomolecular change that can influence recognition between binding partners.

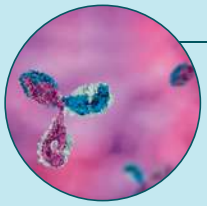
When combined with structural information, PEAQ-ITC data provides deeper insights into structure-function relationships and the mechanisms of binding. While the following examples provide a snapshot, you can find a wealth of detailed applications information at: **www.malvernpanalytical.com**

With isothermal titration calorimetry you can:

- Verify target activities prior to screening.
- Resolve binding into affinity, the number of binding sites, enthalpy, and entropy.
- Gain a deeper understanding of binding mechanisms for any biomolecular interaction.

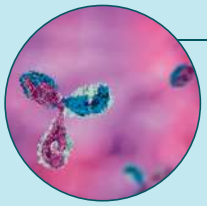
Key applications

Used widely in life sciences and drug discovery



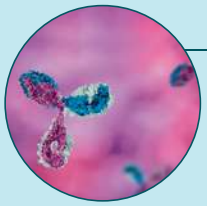
Optimizing enzyme kinetics

Traditional methods such as biochemical assay with endpoint measurements by HPLC, were complicated and prone to systematic error. Baumann and coworkers developed a system to measure xylanase kinetics with PEAQ-ITC. The ITC method was also found to offer greater sensitivity and used less material.



Predictive power and productivity in fragment-based drug discovery

In an early drug discovery program for treatment of drug resistant tumors. Data from an automated PEAQ-ITC was used to validate hits from a primary screen and to accurately rank the affinities of the fragments so that only the strongest binders were selected for co-crystallization attempts and structure based drug discovery program.



Zinc-induced dimerization of a chaperone

UreG is a molecular chaperone that activates urease by delivering two nickel ions. Conflicting evidence suggests that UreG can exist as a monomer or as a dimer.

Since UreG is unstructured in solution, Zambeli and coworkers used ITC to understand the role of disordered regions of UreG, from Helicobacter. ITC measurements of the stoichiometry indicated that UreG could exist in either form depending on the species of metal ion.

Characterizing biomolecular interactions, to:

- Confirm binding and activity
- Determine stoichiometry and thermodynamic parameters
- Study structure activity relationships

Studying the interaction of any two biomolecules including:

- Proteins, nucleic acids, lipids, drugs and inhibitors

Drug discovery for:

- Hit validation and characterization
- Lead optimization
- Mechanism of action

Measure multiple binding parameters in a single experiment

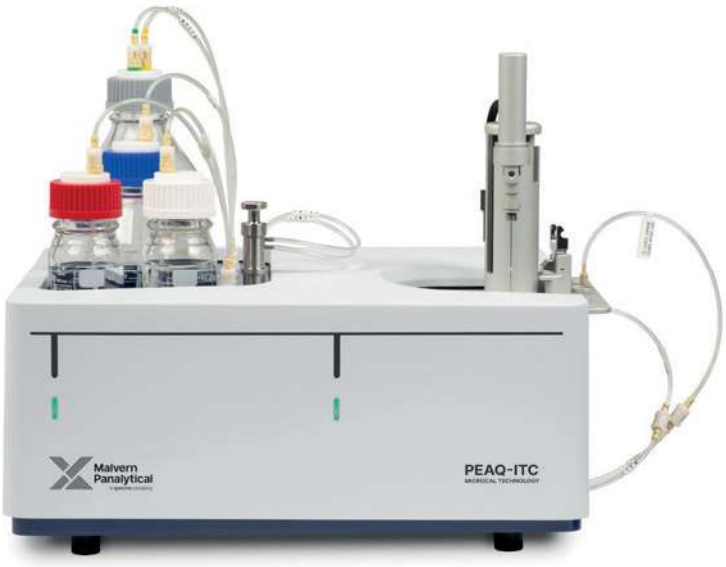
Isothermal titration microcalorimetry

Isothermal titration microcalorimetry (ITC) is an essential tool in drug discovery and the study in drug discovery and IN the study OF regulation of protein intercation. Having been developed specifically to meet the needs of life scientists working in these fields, Malvern Panalytical's PEAQ-ITC calorimeters deliver the exceptional performance and outstanding quality data needed in these application areas.

PEAQ-ITC (MicroCal Technology) systems. directly measure the heat released or absorbed during a biomolecular binding event. The result is a direct, label-free measurement of binding affinity, stoichiometry and thermodynamics in a single experiment. They deliver comprehensive information for studying a wide variety of biomolecular interactions.

Offering high sensitivity, a wide affinity range, reduced sample consumption and options for highER throughput. with walk-away automation, PEAQ-ITC microcalorimeters fully meet the demanding requirements of today's research laboratories. They also provide the security associated with a product portfolio based on MicroCal's 40 year+ experience in microcalorimetry.

This is supported by tens of thousands of scientific papers that confirm the value of these technologies in research and development.



Key benefits of Malvern Panalytical ITC systems

PEAQ-ITC Isothermal titration calorimeters all allow direct, label-free in solution measurement of measurement of reaction heat and thermodynamics in a single experiment, enabling the accurate determination of binding constants (K_D), reaction stoichiometry (N), enthalpy (ΔH) and entropy (ΔS).

This provides a complete thermodynamic profile of the molecular interaction. ITC goes beyond binding affinities and can elucidate the mechanisms underlying molecular interactions.

A range of systems to suit your requirements.

PEAQ-ITC delivers exceptional sensitivity and high quality data with low sample consumption. User-friendly guided workflows with embedded help videos give any level of user the ability to generate high quality data.

PEAQ-ITC Automated combines the high sensitivity of the PEAQ-ITC with walkway automation to meet the productivity needs of busy research and drug discovery laboratories.

Understanding biomolecular interactions

Model	Sample volume	Sample cell size	Operation	Throughput
PEAQ-ITC Automated	370 µL	200 µL	Fully automated	Up to 42 per 24 h (SIM)
PEAQ-ITC	280 µL	200 µL	Manual	8 - 12 per 8 h day

Introduction to isothermal titration microcalorimetry

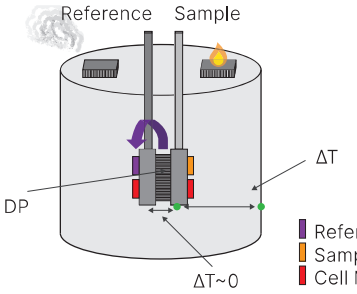
Isothermal titration microcalorimetry (ITC) measures the binding affinity and thermodynamics of biomolecular interactions, helping to understand why interactions occur. The technique is based on the measurement of heat evolved or absorbed when complexes are formed between molecules. It has the advantage of determined, all binding parameters in a single label-free, in-solution experiment, including binding affinity (K_D), reaction stoichiometry (N), enthalpy (ΔH), and entropy (ΔS). This reveals thermodynamic data, the forces that drive complex formation, enabling function and mechanism to be described at a molecular level.

The benefits of ITC

- Label-free measurement - ensures analysis of unaltered biomolecules in their native state giving a true picture of behavior.
- Broad dynamic range - measurement of molecules in solution preserves biological relevance and the sensitivity of the technique accommodates a wide range of affinities.
- Information rich data: all relevant parameters – affinity, stoichiometry, enthalpy and entropy – are measured in a single experiment.
- Ease of use – quick to first result with minimal assay development, no labelling, no immobilization and no molecular weight limitations.
- Broad range of applications - measurements can be made under a wide variety of solvent and buffer conditions.

Theory into practice

How do they work?



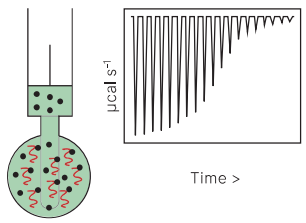
The DP is a measured power differential between the reference and sample cells to maintain a zero temperature between the cells

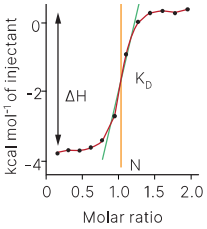
Reference Calibration Heater
Sample Calibration Heater
Cell Main Heater

DP - Differential Power
ΔT - Temperature difference

Basics of ITC experiment

Universal technique based on heat detection





Integration of heats are used to extract affinity (K_D), stoichiometry (N) and binding enthalpy (ΔH) using appropriate binding model

Isothermal titration microcalorimeters measure the heat change that occurs when two molecules interact. Heat is released or absorbed as a result of the redistribution and formation of non-covalent bonds when the interacting molecules go from the free to the bound state.

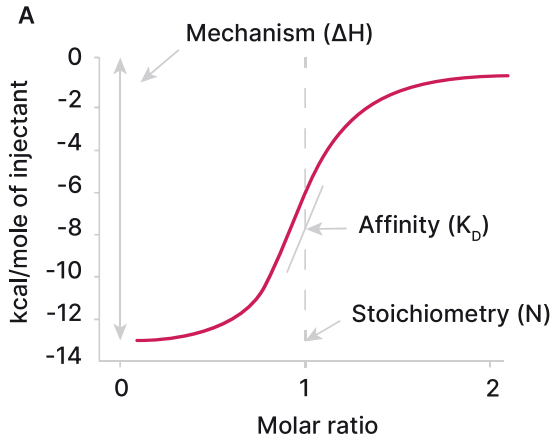
ITC monitors these heat changes by measuring the differential power, applied to the cell heaters, required to maintain zero temperature difference between the reference and sample cells as the binding partners are mixed.

The reference cell usually contains water, while the sample cell contains one of the binding partners (the sample, often but not necessarily a macromolecule) and a stirring syringe which holds the other binding partner (the ligand).

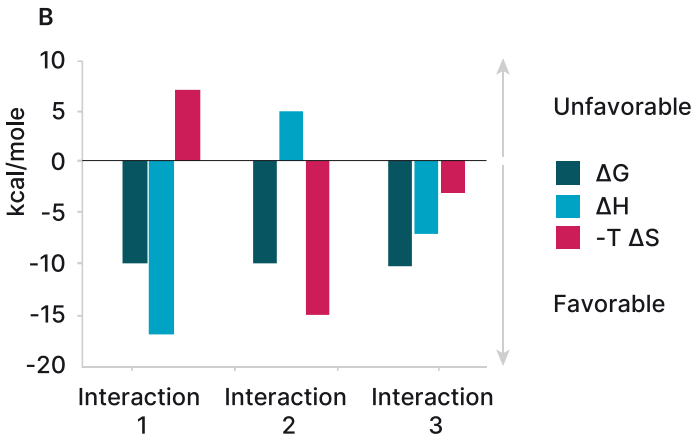
The ligand is injected into the sample cell, typically in 0.5 to 2 µL aliquots, until the ligand concentration is two- to three-fold greater than the sample. Each injection of ligand results in a heat pulse that is integrated with respect to time and normalized for concentration to generate a titration curve of kcal/mol vs molar ratio (ligand/sample). The resulting isotherm is fitted to a binding model to generate the affinity (K_D), stoichiometry (N) and enthalpy of interaction (ΔH).

The power of ITC

Isothermal titration calorimetry determines thermodynamic properties that tell you why interactions occur. Thermodynamic data reveal the forces that drive complex formation to describe function and mechanism at a molecular level.



A. ITC determines thermodynamic properties including: the stoichiometry of the interaction (N), the affinity constant (K_D), change in enthalpy (ΔH).



B. Shown are thermodynamic signature plots of three interactions that have the same binding energy (ΔG). The binding energy is related to the affinity. Binding affinity is a combined function of the binding enthalpy (ΔH) and the binding entropy (ΔS). Binding enthalpy reflects the strength of the interaction due to hydrogen bond formation and van der Waals interactions. Binding entropy is a combination of the change in entropy from desolvation and conformational charges upon complex formation.

Delivered by PEAQ-ITC systems

Minimum preparation, maximum results, high productivity

- All binding parameters (affinity, stoichiometry, enthalpy and entropy) in a single experiment
- Measure sub-millimolar to picomolar diassociation constants (10^{-2} to 10^{-12} M) using direct or competitive binding techniques
- Outstanding sensitivity and data quality gives confidence in results
- Perform a label-free, in solution investigation of any biomolecular interaction using as little as 10 µg protein
- Get first results fast with no assay development needed
- Coin shaped cell optimizes sample mixing
- Nonreactive Hastelloy for chemical resistance and compatibility with biological samples
- Compatible with non-aqueous solvents
- Automate for the highest productivity

PEAQ-ITC range at a glance

PEAQ-ITC

PEAQ-ITC (MicroCal Technology) is designed for ease-of-use and exceptional sensitivity. The wide affinity range enables analysis of weak to high affinity binders, with excellent reproducibility. PEAQ-ITC analysis software offers experiment design simulation, batch evaluation of large data sets, automated assessment of data quality and a streamlined user interface that guides the user to final figures and presentation quality graphs quickly and easily. PEAQ-ITC is an essential tool for any research laboratory studying biomolecular interactions where high sensitivity and fast results are paramount.

Features:

- User-friendly guided workflows with embedded video tutorials give any level of user the ability to generate high quality data
- High signal to noise gives more confidence in accessing data quality and relevance of generated affinity and thermodynamic parameters
- Automated washing with detergent of the sample cell and titration syringe assists in producing high quality reproducible data
- Analyses all binding parameters (affinity, stoichiometry, enthalpy, entropy) in a single experiment
- Quick to first result with minimal assay development and no labelling
- Sensitive enough to investigate biomolecular interaction using as little as 10 µg protein
- Directly measures sub-millimolar to nanomolar affinities)
- Measures nanomolar to picomolar disassociation constants using competitive binding (10^{-9} to 10^{-12} M)
- PEAQ-ITC analysis software
  - Open multiple experiments in a single session
  - Automated fitting models (One-Site, Two-Site, Sequential, Competitive, Enzyme Kinetics, Dissociation)
  - Automated assessment of data quality
    - Good quality data - Binding
    - Good quality data - No binding
    - Poor quality data - Check data


DURAN
100 ml
Made in Germany
PEAQ-ITC
MICROCAL TECHNOLOGY
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PEAQ-ITC range at a glance

PEAQ-ITC Automated

Combining exceptional performance of the PEAQ-ITC with full automation and unattended operation, the PEAQ-ITC Automated is a valuable asset for any busy research laboratory. User-friendly software ensures efficient experimental design while automated data analysis delivers fast, reliable results. The automation and throughput it offers make it a particularly good choice for drug discovery applications such as hit validation where productivity is crucial.

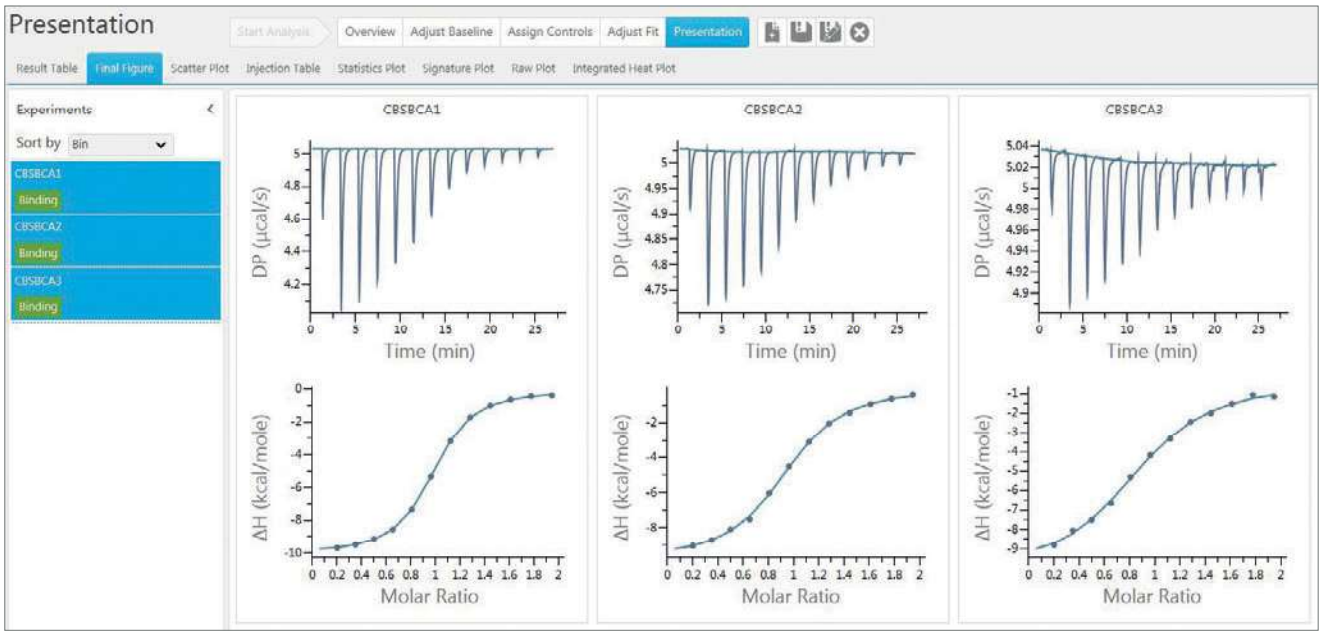
Features:

- Fully automated with capacity to run four 96-well plates unattended
- Optimized automation scripts for improved performance and assay reliability
- Software that streamlines workflows and improves data analysis consistence for confident decision-making
- Append new experiments ‘on the run’ to increase productivity
- Single syringe load for multiple titrations (i.e. 4 experiments of 10 uL)
- New simplified layout

User-friendly software for fast and accurate analysis

Instrument control software that takes you from experiment to final results:

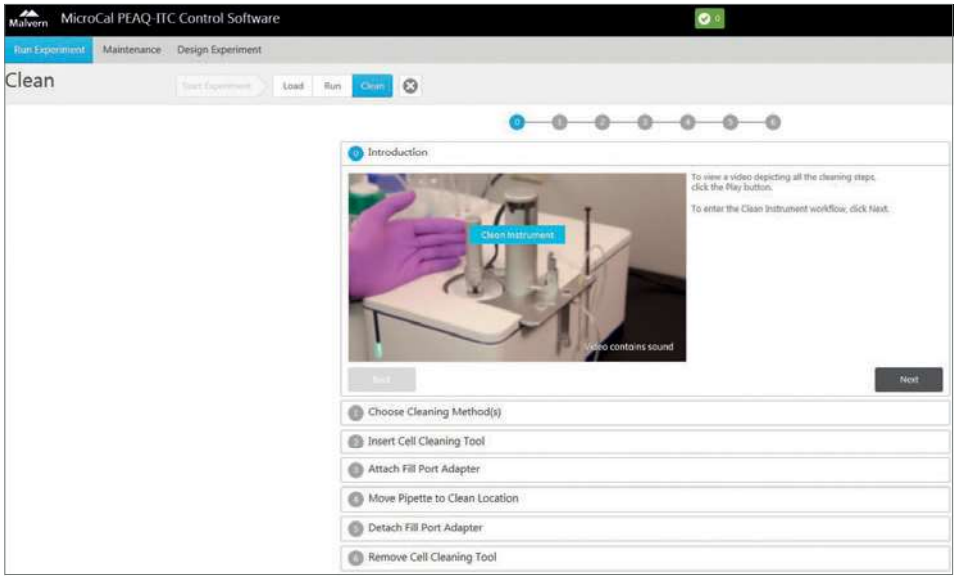
PEAQ-ITC instrument control software incorporates all the tools you need to go from experimental design to final results quickly and easily.



Guided work-flows

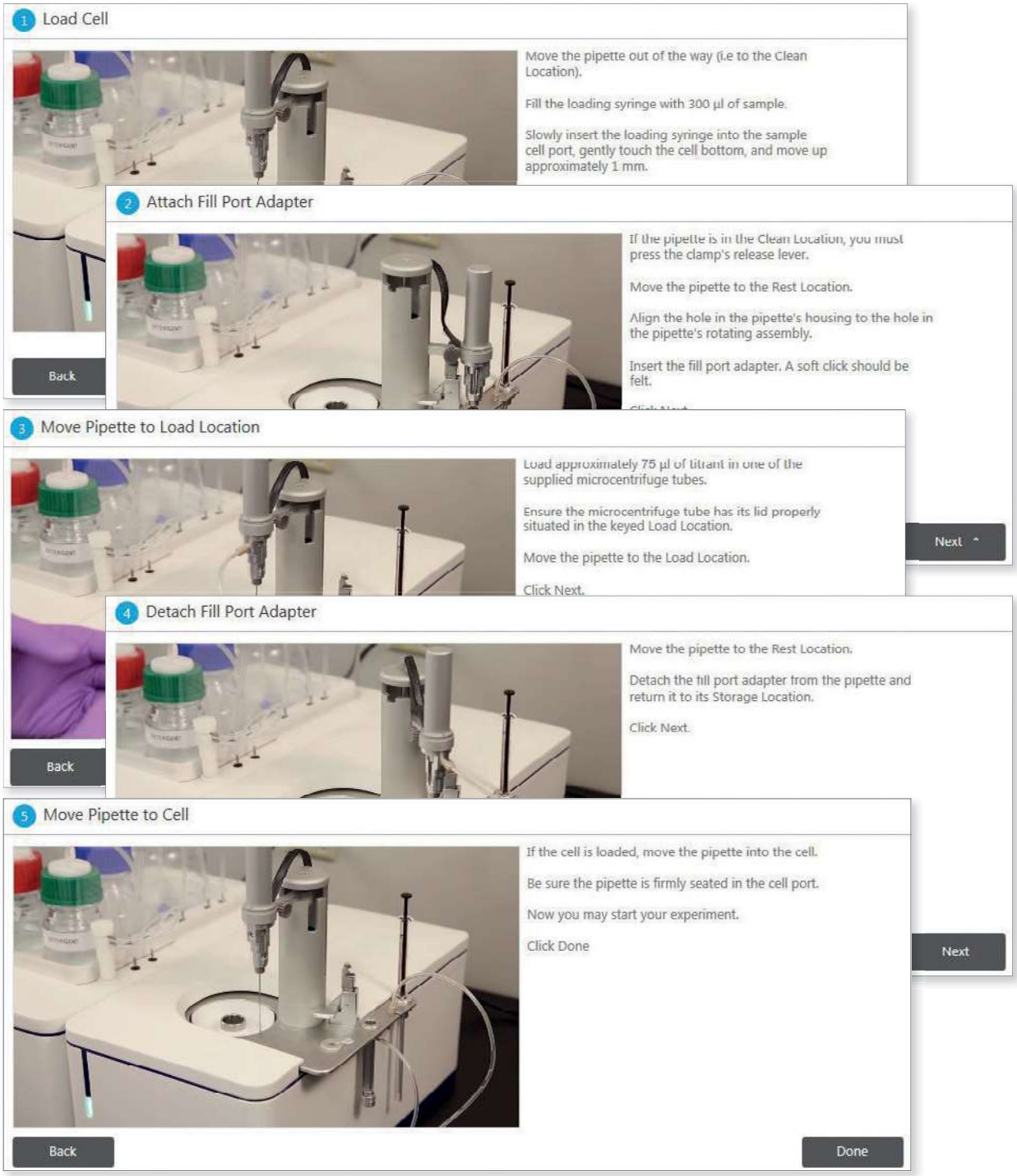
User-friendly guided workflows with embedded help videos give any level of user the ability to generate high quality data with the PEAQ-ITC.

Maintenance has never been easier



User-friendly software for fast and accurate analysis

Experimental setup step-by-step




PEAQ-ITC AUTOMATED
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Specification comparison summary

	ITC	
Parameter	**PEAQ-ITC Automated**	**PEAQ-ITC**
Measurement parameter	Affinity (K_D)	Affinity (K_D)
Measurement parameter	Enthalpy ΔH	Enthalpy ΔH
Measurement parameter	Entropy ΔS	Entropy ΔS
Measurement parameter	Stoichiometry (N)	Stoichiometry (N)
Sample capacity	384 (four 96 well plates)	N/A
Sample tray temp range	4°C± 2°C at ambient	N/A
Sample volume	370 µL	280 µL
Cell volume	200 µL	200 µL
Injection syringe volume	40 µL	40 µL
Injection volume precision	< 1% @ 2 µL	< 1% @ 2 µL
Sample presentation	96 well plate	N/A
Throughput	Up to 42 per 24 h (SIM)	8-12 per 8 h day
Cell material	Hastelloy	Hastelloy
Cell configuration	Coin-shaped	Coin-shaped
Noise	0.15 ncal/s	0.15 ncal/s
Temperature Range	2°C to 80°C	2°C to 80°C
Temperature stability at 25 °C	± 0.00012°C	± 0.00012°C
Response time	8 s*	8 s*
Multiple feedback modes	Yes (passive, high gain, low gain)	Yes (passive, high gain, low gain)
Automated upgrade available	N/A	Yes
Operating Environment		
- Temperature range	10°C to 28°C	10°C to 28°C
- Humidity	0% to 70% RH, non condensing	0% to 70% RH, non condensing
Electrical ratings		
- Voltage	100 - 240 V	100 - 240 V
- Frequency	50/60 Hz	50/60 Hz
- Power	400 W	130 W
Weight	91 kg	13.6 kg
Dimensions (W x H x D)	63 × 77 × 35 cm	43 × 46 × 38 cm (calorimeter + wash station)

* The PEAQ-ITC Instrument Response Time is a true time constant. It is the time interval between the first deviation away from the baseline, and the point on the peak that is 63% of the maximum peak height.

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About Malvern Panalytical

We draw on the power of our analytical instruments and services to make the invisible visible and the impossible possible.

Through the chemical, physical and structural analysis of materials, our high precision analytical systems and top-notch services support our customers in creating a better world. We help them improve everything from the energies that power us and the materials we build with, to the medicines that cure us and the foods we enjoy.

We partner with many of the world's biggest companies, universities and research organizations. They value us not only for the power of our solutions, but also for the depth of our expertise, collaboration and integrity.

We are committed to Net Zero in our own operations by 2030 and in our total value chain by 2040. This is woven into the fabric of our business, and we help our employees and customers think about their part in creating a healthier, cleaner, and more productive world.

With over 2300 employees, we serve the world, and we are part of Spectris plc, the world-leading precision measurement group.

Malvern Panalytical. We're BIG on small™

Service & Support

Malvern Panalytical provides the global training, service and support you need to continuously drive your analytical processes at the highest level. We help you increase the return on your investment with us, and ensure that as your laboratory and analytical needs grow, we are there to support you.

Our worldwide team of specialists adds value to your business processes by ensuring applications expertise, rapid response and maximum instrument uptime.

- Local and remote support
- Full and flexible range of support agreements
- Compliance and validation support
- Onsite or classroom-based training courses
- e-Learning training courses and web seminars
- Sample and application consultancy

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