## Label-free, Real-time Molecular Interaction Analysis

With GCI biosensor

With WAVEchip

With waveRAPID

### Benefits

High Sensitivity
Sample Robustness
Ease-of-use
Save your time and costs

WAVE δ

# creoptix
## sensors

# wave system

Next-generation bioanalytical
instruments for drug discovery.

Label-free, Real-time Molecular Interaction Analysis

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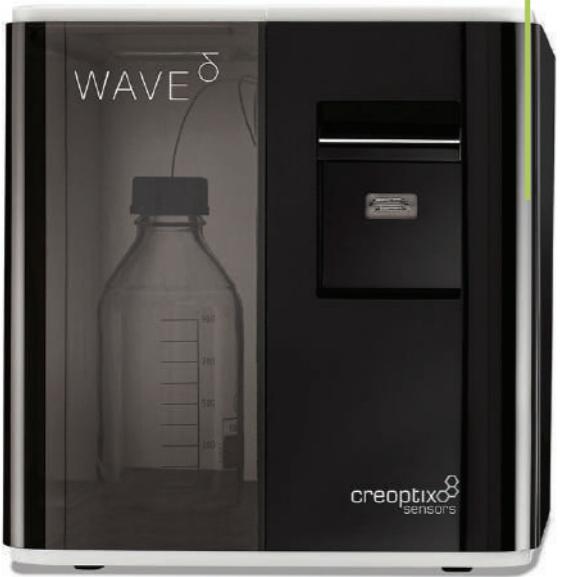서울 : 08507 서울 금천구 가산디지털1로 168 우림라이온스밸리 A동 606B / 02-2105-7020
대전 : 34025 대전 유성구 테크노2로 187 (용산동 미건테크노월드2차 B동 111호)/ 042-862-9636
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# The wave of the future in kinetics

## WAVE core
Proprietary sensor technology for highest sensitivity

## WAVE sampler
Temperature-controlled autosampler for plates and vials
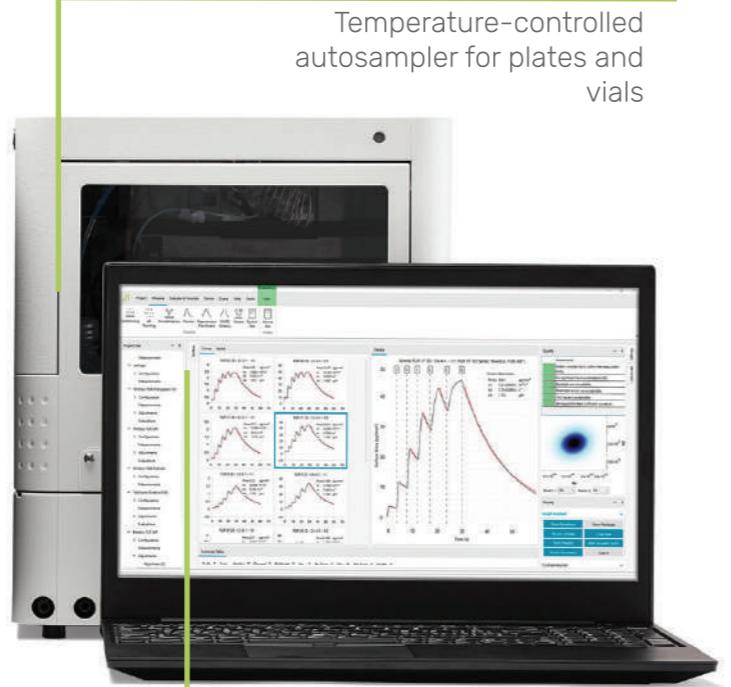
## WAVE chip
Microfluidics and sensor chip in one consumable

## WAVE control
Intuitive software for instrument control and automated data evaluation

# High performance and flexibility

# Main Features

| High Sensitivity | Sample robustness | Automated data evaluation |
| --- | --- | --- |
| — | — | — |
| GCI biosensor | WAVEchip | waveRAPID |

### High signal-to-noise ratio for high sensitivity

Engineered around a proprietary Grating-Coupled Interferometry (GCI) technology, the Creoptix WAVE system builds on waveguide interferometry to achieve superior resolution in signal and time. With low limits of detection, the WAVEsystem generates accurate kinetic rates, affinity constants, and concentrations of label-free biomolecular interactions, even at low analyte abundance, with no loss of definition.

Work with low immobilization levels

Work with large ligand-to-analyte molecular weight (MW) ratios

### Innovative microfluidic cartridge

Innovative design and patented microfluidic cartridge to support crude samples, pathogenic samples, harsh solvents, and large particles up to 1000 nm normally only achieved with plate-based assays for kinetic analysis not possible before

No-clog for crude samples

Chemical-friendly for harsh solvents

No valves for fast transitions
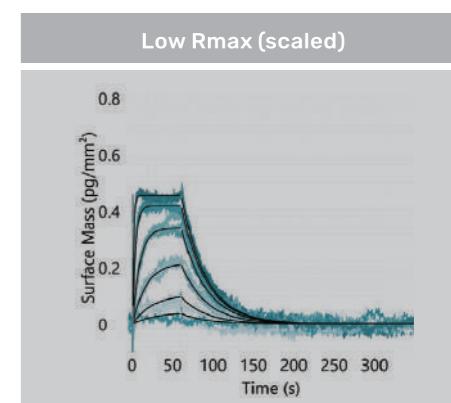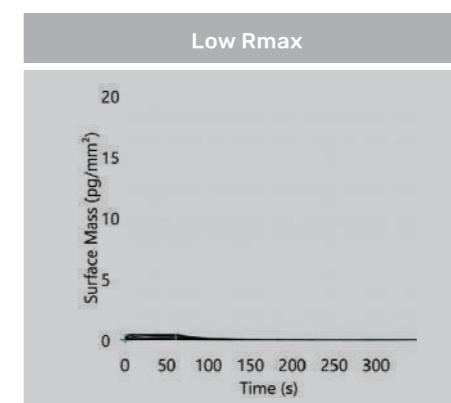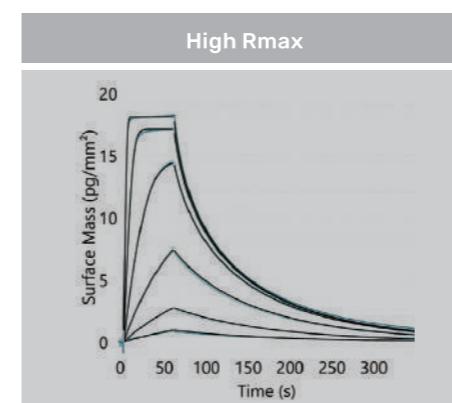
### Automated software

Move seamlessly moves from sample to data in a simple stepwise process, generating outputs at the touch of a button. The intuitive workflow and software wizards guide the user through experimental set up, kinetic evaluation and report generation, with open access formats supporting both LIMS integration and export of data files.

waveRAPID-Kinetics(on-rate, off-rate, affinity and Rmax) from a single well

DIrect Kinetics - automated data evaluation

## Small molecules can't hide anymore

**With the industry's fastest kinetics and utmost sensitivity, the WAVEsystem offers a whole new level of previously unattainable interaction data.**

Ligand: CAII (29kDa) at two different immobilization levels
Analyte: Acetazolamide (222.25 Da)

# Grating-Coupled Interferometry (GCI)

## High Signal to Low Noise
## High Sensitivity
## High Signal Stability for Strong Binders
## High Time Resolution
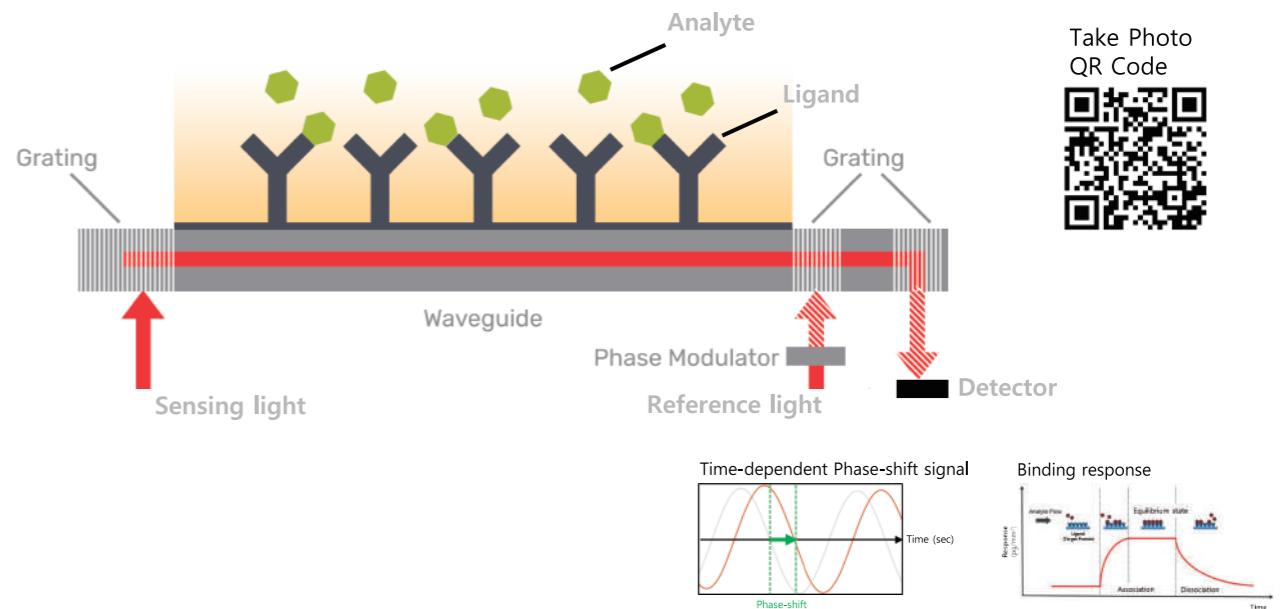
## Unrivalled flexibility and high sensitivity



Take Photo
QR Code

Grating-Coupled Interferometry (GCI) is a surface-based, label-free biosensing technique.

When target molecules (e.g. proteins) are attached to the sensor surface, binding of analytes leads to an increase in mass and hence to a change in the refractive index within the evanescent field near the surface.

In GCI, refractive index changes on a sensor surface are measured as time-dependent phase-shift signals. The long light-to-sample interaction length of the waveguide provides intrinsically high signal-to-noise levels

## General specification sheet

| item | spec |
|---|---|
| Noise | < 0.01 pg/mm$^2$ @ 1 Hz |
| Drift | < 0.3 pg/mm$^2$/min |
| Readout Frequency | 1, 10 and 40 Hz |
| Association Rate Constant ($k_a$, M$^{-1}$s$^{-1}$) | Small molecules: 1 x 10$^2$ – 5 x 10$^7$<br>Large molecules: 1 x 10$^2$ – 3 x 10$^9$ |
| Dissociation Rate Constant ($k_d$, s$^{-1}$) | 10$^{-6}$ – 10 |
| Equilibrium Constant ($K_D$) | 1 pM – 1 mM |

# WAVEchip

No-clog Microfludics design
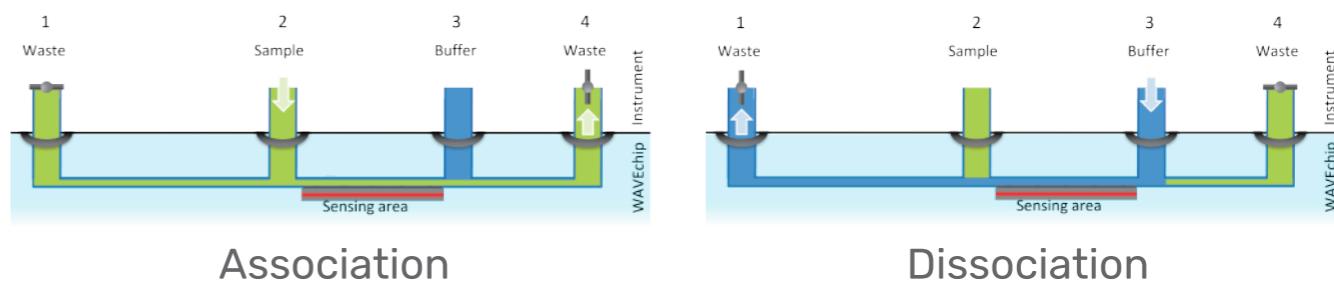Crude sample available
Fast Transition for Weak Binders
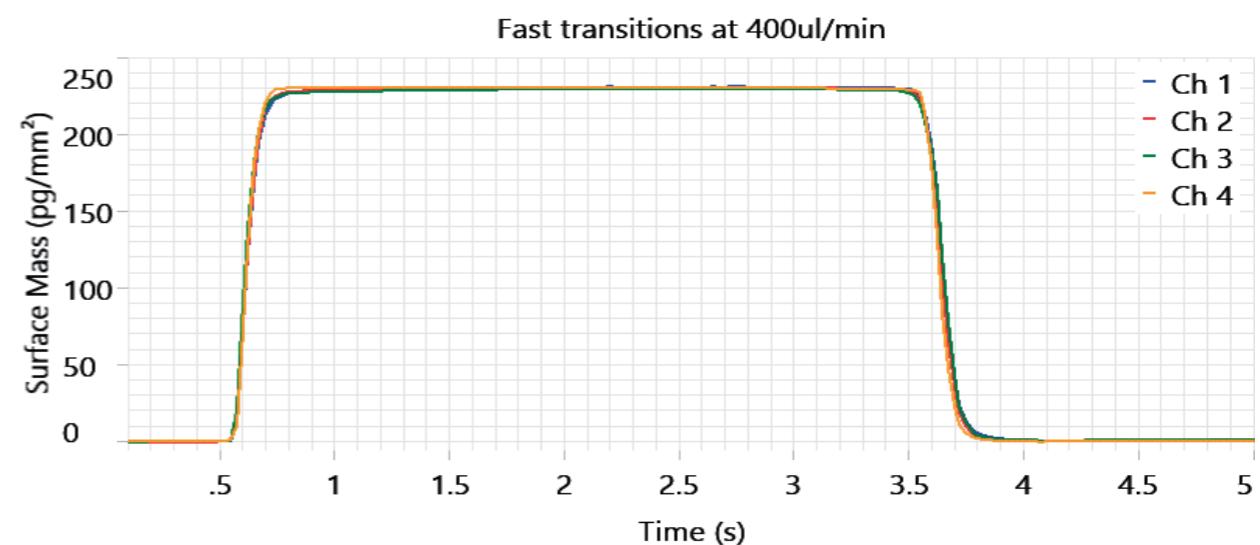
## No-clog Microfluidics and Fast-Transition



### No-Clog for Crude Samples

No-clog microfluidics accommodates of a broad range of sample types to preserve activity and biological context, saving time from detrimental purification steps and clogging that takes other systems
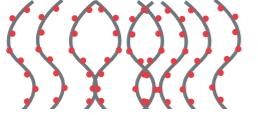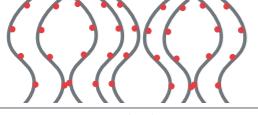


Association

Dissociation

### No Microvalves for Fast Transitions
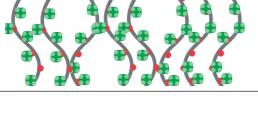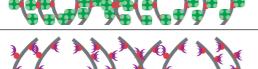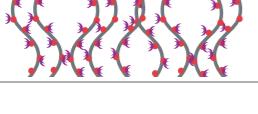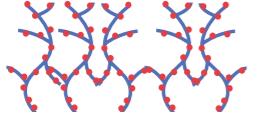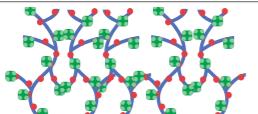
The cartridge design enables ultra-fast transition times of 150 msec for reliable determination of off-rates of 10 sec$^{-1}$ (half-life of 69 ms), enabling the kinetic study of weakly binding fragments.



Fast transitions at 400ul/min

### Compatibility

• 100% Serum & plasma & cell supernatant
• Non-traditional solvents, including high percentages of acetonitrile and DMSO
• Viscous detergents and additives to solubilize membrane proteins
• Cell membrane preps, partially solubilized, unpurified material
• Virus-like particles (VLPs), liposomes, or nanodiscs used as solubilization structures
• Large binding partners: nanoparticles and crude membrane preps

# WAVE chips QUICKGUIDE

| WAVE chip | Special Characteristics | Matrix | | Immobilization Modality | | | | Capacity | | Suggested Applications | Great for* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | PC | CMD | COV | BIOTIN | HIS | OTHER | HIGH | LOW | | |
| PCH | Thick hydrogel | ✓ | | ✓ | | | | ▲ | | Large ligand-to-analyte molecular weight ratio. General purpose. | |
| PCP | Quasi-planar | ✓ | | ✓ | | | | | ▼ | Large ligands and/or analytes such as proteo-/liposomes, viruses, VLPs. | |
| PCL | Thick hydrogel with reduced charges | ✓ | | ✓1 | | | | | ▼ | Complex matrices such as serum, culture supernatant. | |
| PCH-STA | Streptavidin-coated | ✓ | | | ✓ | | | ▲ | | Biotinylated ligands. General purpose. | |
| PCP-STA | Quasi-planar, streptavidin-coated | ✓ | | | ✓ | | | | ▼ | Large biotinylated ligands and/or analytes such as proteo-/liposomes, viruses, VLPs. | |
| PCH-NTA | NTA-functionalized | ✓ | | | | ✓ | | ▲ | | His-tagged ligands. General purpose. | |
| PCP-NTA | Quasi-planar, NTA-functionalized | ✓ | | | | ✓ | | | ▼ | Large His-tagged-ligands and/or analytes such as proteo-/liposomes, viruses, VLPs. | |
| PCP-PAG | Protein A/G-functionalized | ✓ | | | | | IgG | | ▼ | Antibody (IgG) ligands. | |
| PCP-LIP | Quasi-planar, lipid anchors | ✓ | | | | | Lipid | | ▼ | Hydrophobic ligands such as liposomes, membrane vesicles or fragments. Compatible with large ligands and/or analytes. | |
| PCZ | Zwitterionic polymer | ✓ | | | | | | | ▼ | Acidic protein and/or negatively charged ligands. Recommended for positively charged analytes. High non-fouling properties. | |
| DXH Upon request | Thick hydrogel | | ✓ | ✓ | | | | ▲ | | General purpose. | |
| DXH-STA Upon request | Streptavidin-coated | | ✓ | | ✓ | | | ▲ | | Biotinylated ligands. General purpose. | |

Legend: polycarboxylate(PC), carboxymethyldextran (CMD), covalent functionalization through -NH$_2$, -SH, -CHO, -OH and -COOH(COV), streptavidin/biotin coupling(biotin), His-tag/NTA-coupling (His)

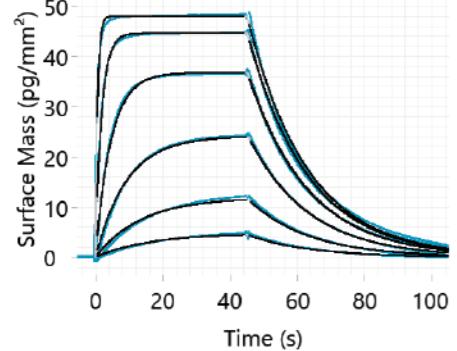*Applications: Small molecules/FBDS   Serology   Membrane proteins   Biologics

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For specific questions on our applications, contact us through support@creoptix.com

# waveRAPID technology

### Multi-Cycle Kinetics (MCK)
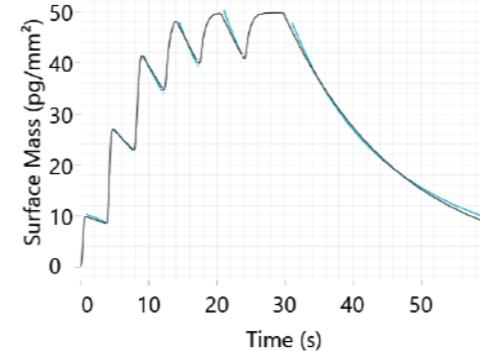


### waveRAPID



Prepare 6 dilutions per 1 sample
Inject 6 times, and Obtain 1 data set

Prepare 1 dilution per 1 sample
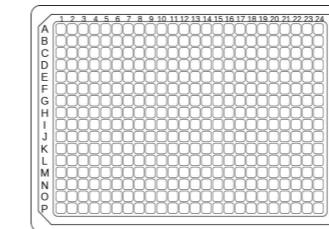Inject once, and Obtain 1 data set

Instead of relying on a titration series, **waveRAPID (Repeated Analyte Pulses of Increasing Duration)** injects a single concentration, pulsing the sample over the sensing surface at increasing durations, meaning kinetics can be derived from a single well.
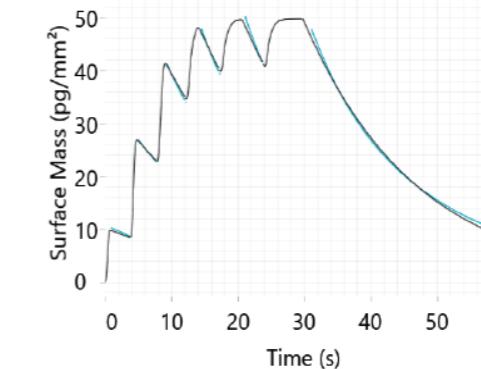
# Save your time and cost

### Sample Throughput Per Day



|  | WAVEdelta | Biacore T200 | Biacore 8K |
|---|---|---|---|
| Number of Targets | 2 | 2 | 2 |
| Number of Samples | 384 | 384 | 384 |
| Type of Assay | waveRAPID | Kinetics | Kinetics |
| Affinity Range | nM | nM | nM |
| Runtime (h) | 58 | 490 | 122 |
| Samples / 24h | 159 | 19 | 75 |

96 samples against 3 target proteins, traditional kinetics set up vs waveRAPID

Exemplary assay run times and sample throughput comparing waveRAPID on the WAVEdelta to state-of-the-art technologies (Biacore T200, 8k) for full kinetic characterization of 384 samples on 2 targets.

- Keep projects moving by getting your binding data sooner
- Skip serial dilution for sample prep (less samples/buffer)
- Get binding data sooner (waveRAPID is 10x faster than traditional kinetics)
- Analyze big dataset in 3-5 minutes with "1-click" analysis
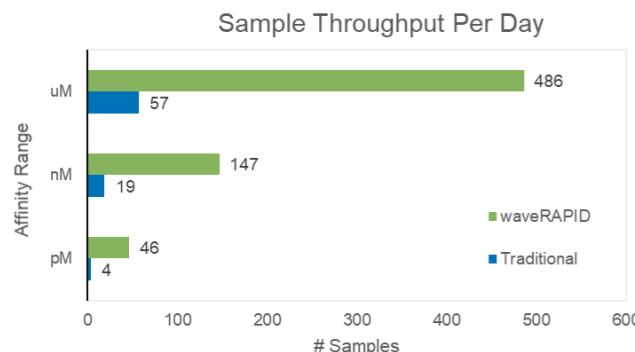
# Run more samples



*A full 384-well plate*          *384-measurements*          *384-datasets*

Analysis from a single well, not a titration series
Room on your plate for more samples

# Get more insight



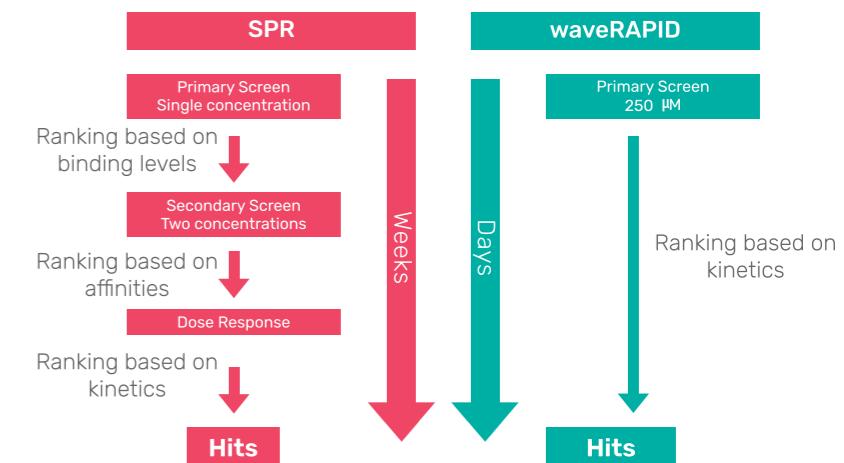Speeding up the early stages of drug discovery is crucial to getting new medicines to the patients faster. On the commercial side, accelerating R&D will improve the profitability of new therapies and shorten time-to-revenue.

Get more insight by using waveRAPID capacity to screen broad kinetic range

Built-in wizard available for pM – mM range interaction

Don't miss out on analytes with the desired kinetics

# CONFIDENCE IN KINETIC MEASUREMENTS

Real is measuring kinetics of biological interactions in relevant contexts. Only the WAVE innovative microfluidic cartridge tolerates native, physiological and harsh conditions, providing access to new data not possible before.
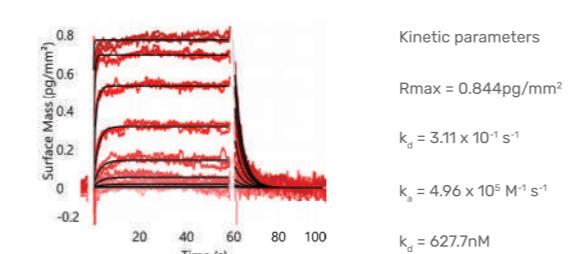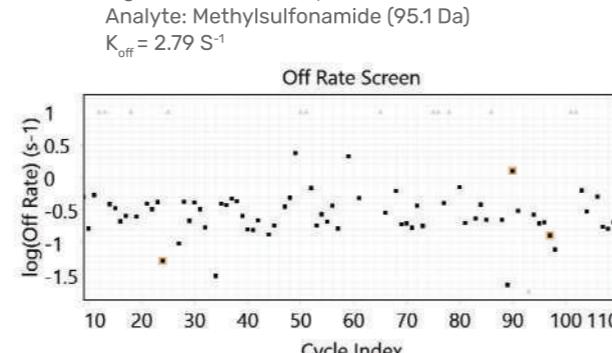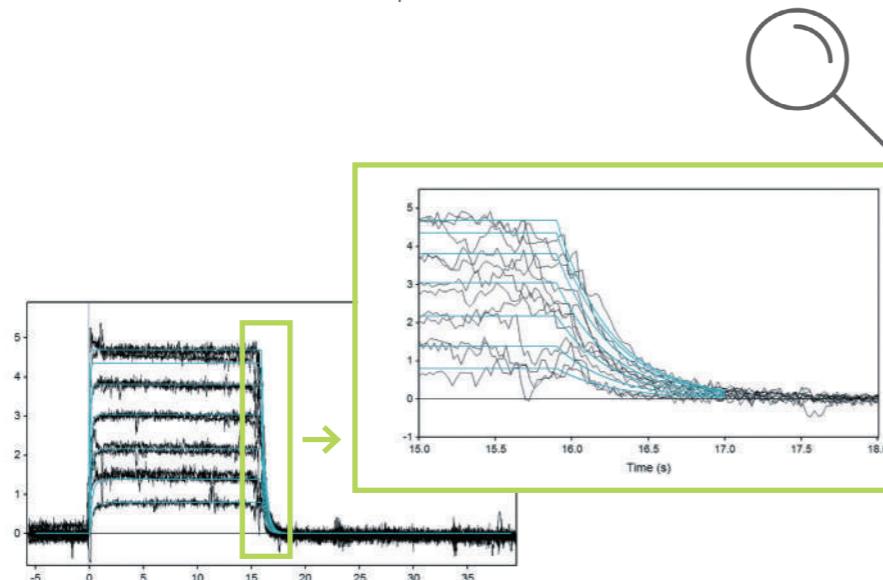
real is crude
## SMALL MOLECULE DEVELOPMENT

**Capture fast off-rates of weakly binding fragments and high-quality low potency leads for more successful drug discovery.**

• Separate binders from non−binders with off-rate kinetic analysis of crude reaction mixtures

• Resolve weak binders with off-rates as fast as 10 s⁻¹.

• Measure in non−traditional solvents, including high percentages of acetonitrile and DMSO.

• More space in the well plate to measure full kinetic data with only one injection using waveRAPID.

• Kinetic information in hours instead of



Ligand: carbonic Anhydrase II (29 kDa)
Analyte: Methylsulfonamide (95.1 Da)
$K_{off}$ = 2.79 S⁻¹



**Push the limits and generate high-quality binding kinetics with our sensitive GCI technology and resolve data at very low responses.**

• Kinetics analyses of molecules with dramatically different size ratios.

• Reliable kinetics at $R_{max}$ below 1 pg/mm².



Kinetic parameters

Rmax = 0.481 pg/mm²

$k_d$ = 3.38 x 10⁻² s⁻¹

$k_a$ = 8.52 x 10⁵ M⁻¹ s⁻¹

$k_d$ = 39.7 nM

Kinetic parameters

Rmax = 0.844pg/mm²

$k_d$ = 3.11 x 10⁻¹ s⁻¹
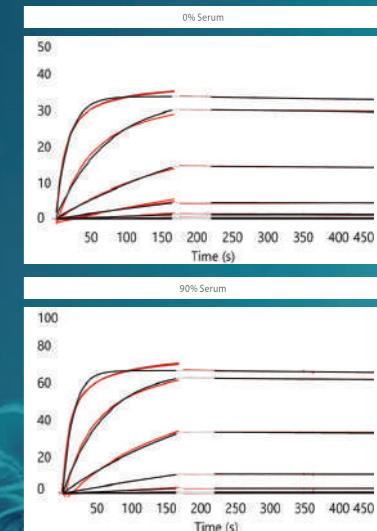
$k_a$ = 4.96 x 10⁵ M⁻¹ s⁻¹

$k_d$ = 627.7nM

real is (less) diluted

## SEROLOGY - SERUM, PLASMA AND MORE

Measure antibody kinetics in (un)diluted serum and plasma while reducing cross-contamination and potential clogging. Accurately measure binding kinetics in conditions closer to real life and **confidently characterize the tightest binders in:**

• 100% blood serum or plasma

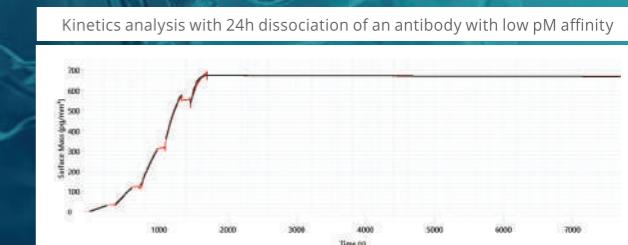• Cell extracts

• Cell culture supernatant



real is natural

## BIOLOGICS DEVELOPMENT

**Measure more than just affinity, even in the low pM range, while confirming and enrich ELISA data.**

• Slow off-rate analysis of high−affinity binders

• Detection of anti-drug antibodies (ADA) in the low ng/ml range

• Identify the most effective antibody pairs in diagnostic development



Kinetics analysis with 24h dissociation of an antibody with low pM affinity
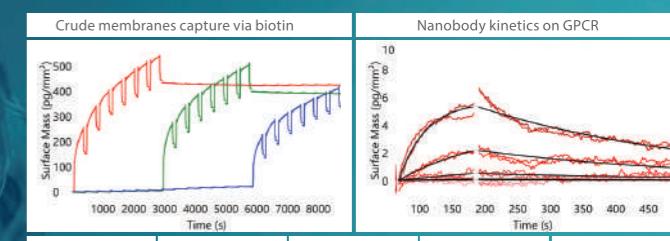
real is native

## MEMBRANE PROTEINS

Stay close to native state in cell membrane and study interactions with large binding partners. Study binding kinetics onto membrane proteins and retain their conformation and activity for more successful drug discovery
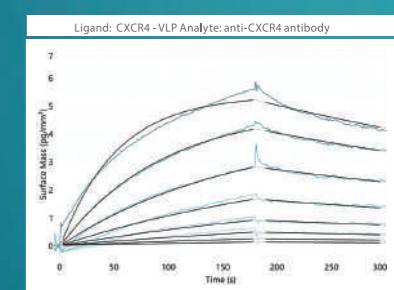
• Push the limits and generate high−quality binding kinetics and resolve data at very low responses

• Save time and precious samples by studing membrane protein pharmacology using only partially solubilized, unpurified material



| Crude membranes capture via biotin | | Nanobody kinetics on GPCR | |
|---|---|---|---|
| Kinetic parameters | Rmax = 6.435pg/mm² | $k_a$ = 7.1 x 10³ M⁻¹ s⁻¹ | $k_d$ = 2.87 x 10⁻³ s⁻¹ | $k_d$ = 406.7 nM |

**Virus-like particles, liposomes, and nanodiscs present unique challenges**

The resultant size of these structures – used to preserve membrane protein integrity and activity - combined with a tendency to aggregate, can cause microfluidics channels to clog. They can be run reliably and repeatedly on the WAVEsystem with no impact on performance or sensitivity to:

• Valveless microfluidics to analyze and characterize larger molecules.

• Ensure more reliable data by protecting the sensor from inadvertent handling.



Ligand: CXCR4 - VLP Analyte: anti-CXCR4 antibody

## Creoptix WAVE



| GENERAL | |
|---|---|
| Noise (RMS) | <0.01 pg/mm² @ 1 Hz |
| Drift | <0.3 pg/mm²/min |
| Readout Frequency | 1 Hz, 10 Hz or 40 Hz |
| Association Const. Range | $k_a = 10^2 - 5 \times 10^7$ M$^{-1}$ s$^{-1}$ (small molecules)<br>$k_a = 10^2 - 3 \times 10^9$ M$^{-1}$ s$^{-1}$ (large molecules) |
| Dissociation Const. Range | $k_d = 10^{-6} - 10$ s$^{-1}$ |
| Analysis temperature range | 15°C – 40°C |
| Molecular Weight Limit | No lower limit |
| waveRAPID Functionality | No |

| FLUIDICS | |
|---|---|
| Flow Channels / Path | 2, parallel |
| Channel Referencing | 1–4 and 4–1 or 2–3 and 3–2 |
| Flow Cells | Sealed, disposable, integrated into disposable WAVEchip |
| Flow Rate | 1 – 400 µl/min |
| Crude Sample Robustness | Yes |

| SAMPLE HANDLING | |
|---|---|
| Sample Capacity | 2x microtiter plates (96 or 384 well, standard or deep well) or vial racks (48 positions of 1.5ml) |
| Buffer | 1 buffer |
| Degasser | Built-in |
| Injection Volume | < 450 µl, 100 µl typical |
| Sample Volume Required | Injection volume plus 15-50 µl (application dependent) |
| Sample Storage Temperature | Ambient or 4°C – 20°C regulated |
| Sample Recovery | Yes |
| Automation | 120h of unattended operation |

| DATA TREATMENT | |
|---|---|
| Information Provided | Kinetic affinity ($k_a$, $k_d$, $K_D$) |
| Graphs | Real-time curves, multiple curve overlays, fit, report point plots |
| Data Extraction | Curves, $k_a$, $k_d$, $K_D$ tables, graphs, reports |
| Data Analysis | Fully automated data evaluation |
| Kinetic Models | Predefined models including 1:1 interaction, mass transport, heterogenous ligand, conformational change and bivalent |
| Direct Kinetics | Yes |

## Creoptix WAVEdelta



| GENERAL | |
|---|---|
| Noise (RMS) | <0.01 pg/mm² @ 1 Hz |
| Drift | <0.3 pg/mm²/min |
| Readout Frequency | 1 Hz, 10 Hz or 40 Hz |
| Association Const. Range | $k_a = 10^2 - 5 \times 10^7$ M$^{-1}$ s$^{-1}$ (small molecules)<br>$k_a = 10^2 - 3 \times 10^9$ M$^{-1}$ s$^{-1}$ (large molecules) |
| Dissociation Const. Range | $k_d = 10^{-6} - 10$ s$^{-1}$ |
| Analysis temperature range | 4°C – 45°C (max 20°C below ambient) |
| Molecular Weight Limit | No lower limit |
| waveRAPID Functionality | Yes |

| FLUIDICS | |
|---|---|
| Flow Channels / Path | 4, parallel |
| Channel Referencing | Any combination of the 4 channels |
| Flow Cells | Sealed, disposable, integrated into disposable WAVEchip |
| Flow Rate | 1 – 400 µl/min |
| Crude Sample Robustness | Yes |

| SAMPLE HANDLING | |
|---|---|
| Sample Capacity | 2x microtiter plates (96 or 384 well, standard or deep well) or vial racks (48 positions of 1.5ml) |
| Buffer | Automatic switching between 4 buffers |
| Degasser | Built-in |
| Injection Volume | < 450 µl, 100 µl typical |
| Sample Volume Required | Injection volume plus 15-50 dependent) |
| Sample Storage Temperature | Ambient or 4°C – 20°C regulated |
| Sample Recovery | Yes |
| Automation | 120h of unattended operation |

| DATA TREATMENT | |
|---|---|
| Information Provided | Kinetic affinity ($k_a$, $k_d$, $K_D$) |
| Graphs | Real-time curves, multiple curve overlays, fit, report point plots |
| Data Extraction | Curves, $k_a$, $k_d$, $K_D$ tables, graphs, reports |
| Data Analysis | Fully automated data evaluation |
| Kinetic Models | Predefined models including 1:1 interaction, mass transport, heterogenous ligand, conformational change and bivalent |
| Direct Kinetics | Yes |