

KEEPING KINETICS REAL

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A NEW LEVEL OF PERFORMANCE AND FLEXIBILITY IN DRUG DISCOVERY

By bringing together modern label-free technology, application development know-how and sophisticated software, Creoptix offers a unique optical biosensor tool for binding kinetics. Engineered around our proprietary Grating-Coupled Interferometry (GCI)¹ technology, the Creoptix WAVEsystem delivers high-quality kinetic data across a broader range of samples than traditional SPR equipment.

Assess drug performance in undiluted biofluids for reliable kinetic profiling in conditions closer to real life

Quantify binding affinities (K_d) from low pM to high μ M with confident kinetic analysis

Analyze multiprotein complexes and even larger particles like VLPs and crude membranes

GRATING-COUPLED INTERFEROMETRY (GCI)



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 for improved sensitivity.

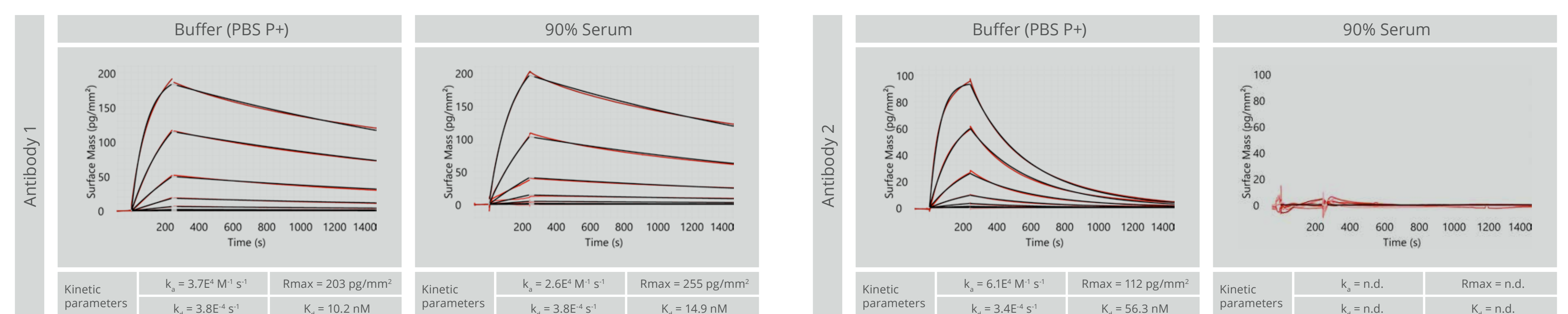
The Creoptix® WAVEsystem combines GCI with innovative no-clog microfluidics, allowing the study of interactions even between very small ligands and large complexes. The system uses a robust microfluidic sensor, the WAVEchip®, where (membrane) proteins,² antibodies, VLPs, peptides or other molecules can be immobilized using various chemistries.



ANTIBODY PROFILING IN BIOFLUIDS

The robust sensor and microfluidics of the WAVEsystem allows the kinetic characterization of molecular interactions in almost pure serum or plasma. Binding proteins developed for diagnostic applications can therefore be directly profiled in great detail within the respective crude matrix.

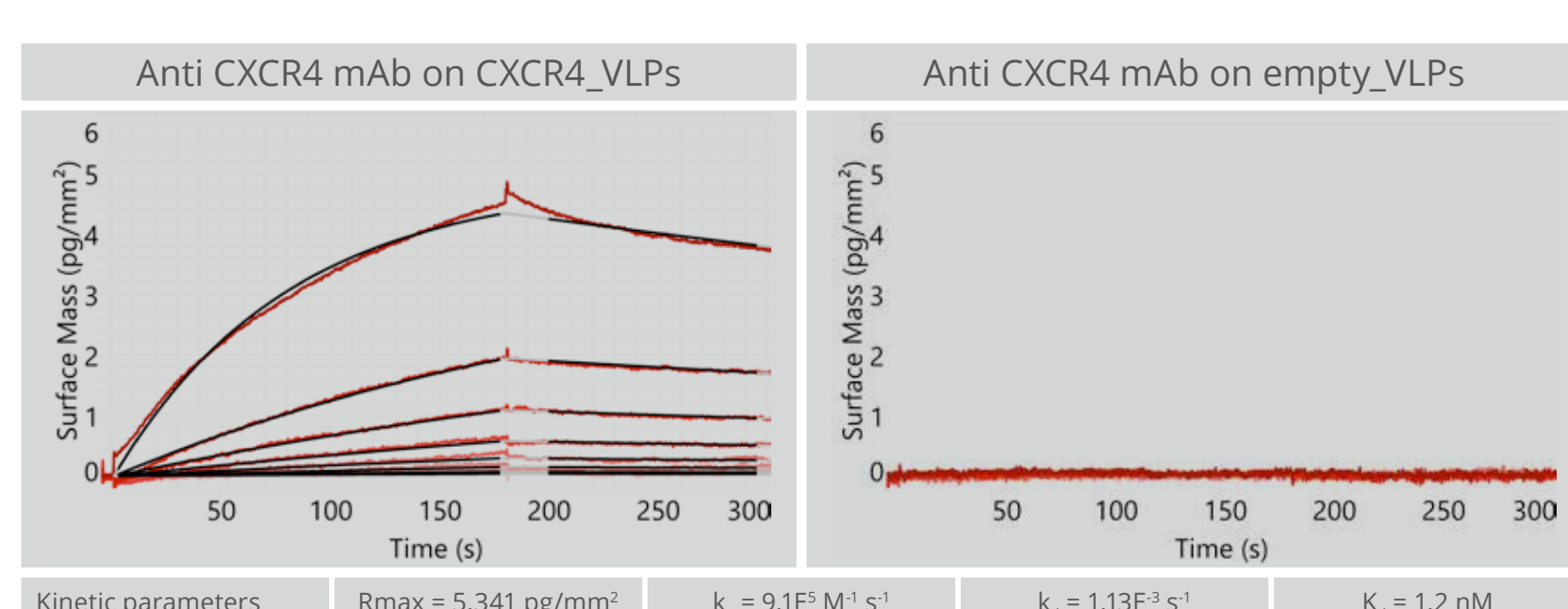
Here, a full kinetic interaction analysis acquired in the course of an antibody profiling study is shown. Two different antibodies were immobilized on a 4PCP WAVEchip via amine coupling. The respective antigen was injected in either buffer (PBS P+) or 90% human serum in a dilution series of eight (8) concentrations ranging from 137 pM to 300 nM at 95 μ l/min for 240s followed by 1200s dissociation. Raw data were double referenced and globally fit with a 1:1 binding model. For antibody 2 no binding was observed in serum.



KINETIC ANALYSIS ON MEMBRANE PROTEINS

The WAVEsystem allows for the kinetic characterization of analytes binding to membrane proteins (GPCR) embedded in VLPs.

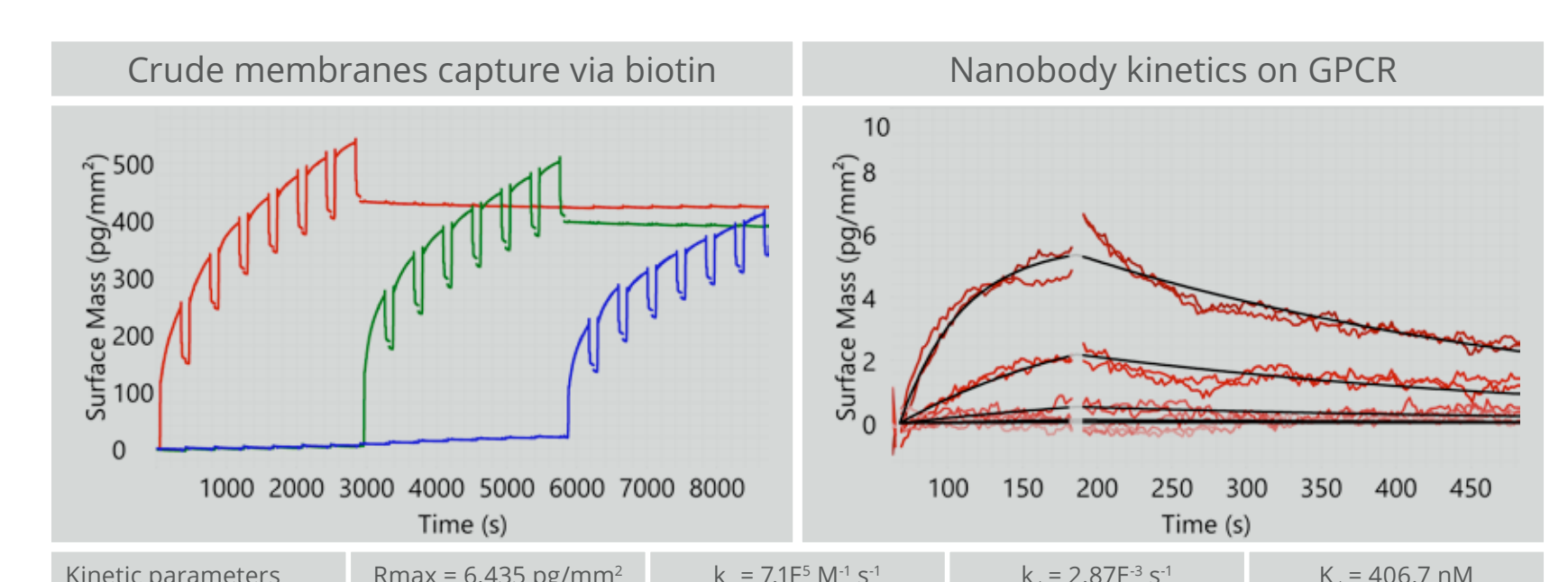
A 4PCP WAVEchip® was coated with Wheat Germ Agglutinin prior to injecting CXCR4_VLP and empty_VLPs (from Integral Molecular). Twelve (12) concentrations of the mAb anti-CXCR4 (ranging from 24 pM to 100 nM) were injected for 180s at 60 μ l/min. Raw data were double referenced and globally fit with a 1:1 binding model.



KINETICS ON GPCRS FROM CRUDE MEMBRANES

The WAVEsystem allows for the kinetic characterization of analytes binding to membrane proteins (GPCRs) captured from crude cell membrane extracts (centrifugation-sonication).

CHO cells crude membrane extracts (from Novartis) expressing: the Nt-AVI target GPCR (red), the Ct-AVI target GPCR (green) and the negative control Nt-AVI GPCR (blue) were injected onto a 4PCP-STA WAVEchip® at 10 μ l/min. Five (5) concentrations (0.96 nM - 3 μ M) of the anti-target-GPCR nanobody (scAb) were injected in duplicates for 180s at 45 μ l/min.



GCI IS FEATURED IN

NATURE Mechanistic basis for the activation of plant membrane receptor kinases by SERK-family coreceptors

PLANT PHYSIOLOGY The SERK3 elongated allele defines a role for BIR ectodomains in brassinosteroid signalling

NATURE COMMUNICATIONS Dynamics of human protein kinase Aurora A linked to drug selectivity

REFERENCES

1. P. Kozma et al., "Grating coupled optical waveguide interferometer for label-free biosensing", Sensors and Actuators B: Chemical, 156:446-450 (2011)
2. Hohnmann et al., "The SERK3 elongated allele defines a role for BIR ectodomains in brassinosteroid signalling", Nature Plants, 4:345-351 (2016)

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