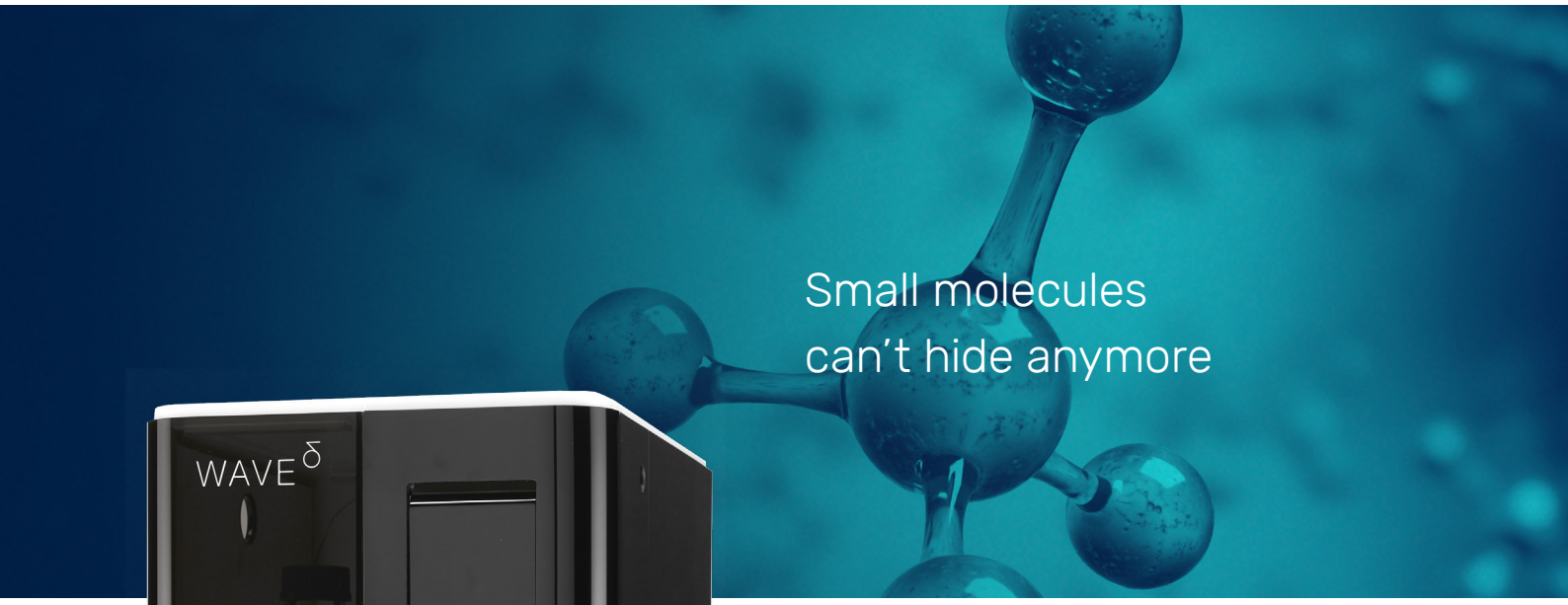
creoptix sensors

TechNote 1

Sensitive kinetic analysis of small molecules binding to large drug targets

Creoptix® WAVEsystem





In this TechNote we show how the WAVEsystem can be used to accurately monitor binding kinetics of large target-to-analyte molecular weight (MW) ratios (>300:1), thanks to the expanded sensing field over which the Grating-Coupled Interferometry (GCI) technology measures for high sensitivity

Summary

Real-time, label-free analysis of interactions between small molecules and drug targets provides valuable information to guide the drug discovery process and identify promising drug candidates. However, weak binders and large target-to-analyte molecular weight (MW) ratios can make kinetic characterization extremely challenging, as they often require high sensitivity and the ability to confidently measure fast off-rates (k_{off}).

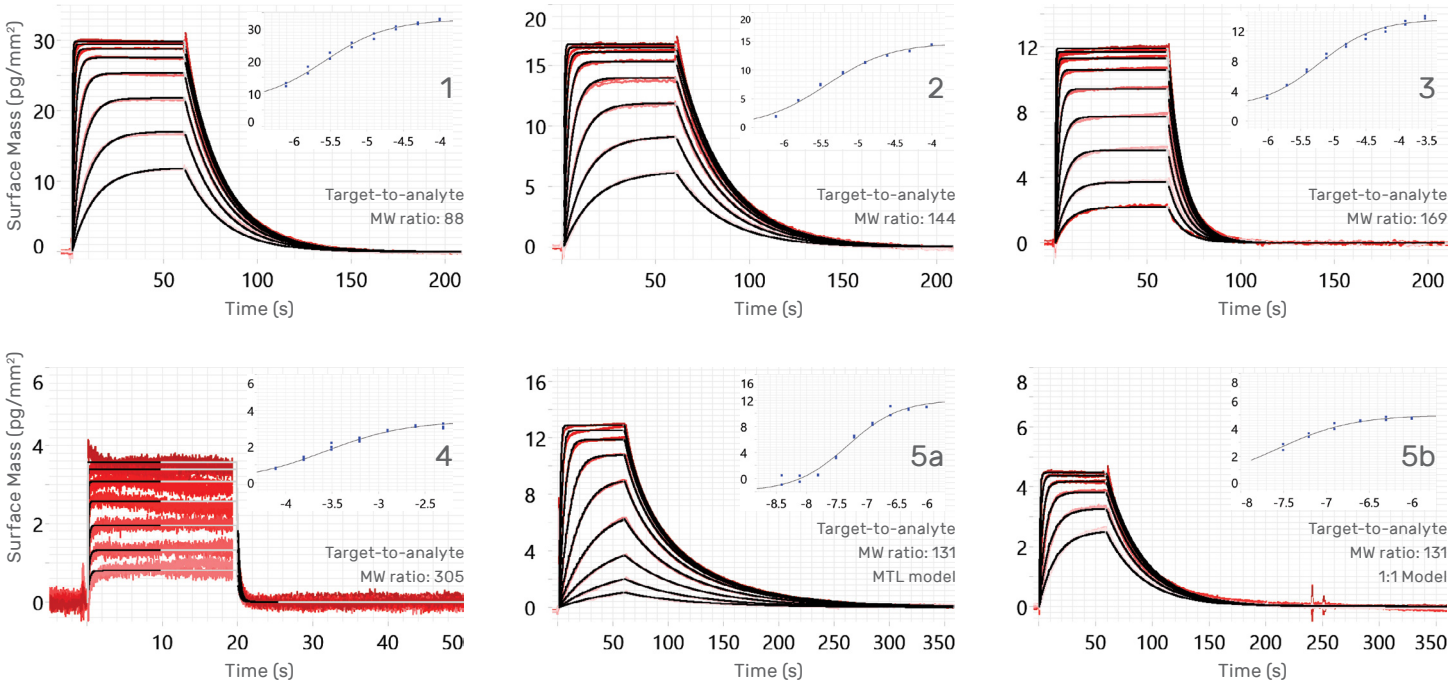
Using a proprietary Grating-Coupled Interferometry (GCI) technology, the Creoptix® WAVEsystem provides best-in-class sensitivity to allow highly accurate kinetic data to be generated at even low signal levels. Combined with robust microfluidic technology, GCI enables the characterization of molecular interactions in the presence of non-common solvents – such as acetonitrile or high concentrations of DMSO.

By measuring the binding kinetics of various small molecule inhibitors of Carbonic Anhydrase II (CAII), we show how the Creoptix™ WAVEsystem achieves outstanding resolution for small, weakly-binding drug molecules, for full kinetic characterization regardless of the target-to-analyte molecular weight ratio.

TABLE 1: Kinetic and equilibrium data of various small molecule inhibitors of Carbonic Anhydrase II (CAII)

	1 Furose-mide	2 4-Sulfa-moylbenz. acid	3 Sulfanil-amide	4 Methylsul-fonamide	5a Acetazol-amide	5b Acetazol-amide
MW (Da)	330.74	201.20	172.20	95.12	222.25	222.25
Immob. level (pg/mm^2)	6050	6050	6050	6150	6050	1450
Kinetic data						
k_{on} ($M^{-1}.s^{-1}$)	$3.75x10^4$	$2.98x10^4$	$2.67x10^4$	$1.15x10^4$	$1.31x10^6$	$1.22x10^6$
k_{off} (s^{-1})	0.051	0.040	0.180	3.37	0.038	0.031
k_m	-	-	-	-	$1.17x10^7$	-
R_{max} (pg/mm^2)	30.87	16.91	12.09	3.79	13.25	4.59
K_D (µM)	1.4	1.3	4.4	293	0.029	0.026
Equilibrium data						
R_{max} (pg/mm^2)	33.37	14.57	11.75	3.34	14.05	4.83
K_D (µM)	2.4	3.8	6	270	0.048	0.028

Figure 1: Binding kinetics of various small molecule inhibitors of Carbonic Anhydrase II (CAII)



MTL = Mass transport limitation
1 pg/mm^2 = 1 RU

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Keeping Kinetics Real

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