# Kinetic screening using grating-coupled interferometry (GCI) – highly sensitive biosensor-based assays enable the identification of weak fragment hits across a diverse set of challenging targets

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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 sensing 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 [1]. With high sensitivity and innate compatibility with high molecular weight ratios combined with an innovative, fast-transition fluidics architecture, the Creoptix® WAVEsystem can fully resolve extremely rapid binding kinetics [2].

GCI technology has a broad range of applications including fragment-based screening and kinetic analysis of small molecules, protein-protein, protein-peptide, and antibody-antigen interactions.

GCI is ideally suited for fragment-based drug discovery due to inherent sensitivity of the detection principle, and the ability to capture fast transitions. Here we show a collection of challenging target classes across a variety of fragment-based drug discovery projects where GCI was used to screen fragment libraries comprising of ~1100 compounds [3,4]. Hits were picked based on statistical errors and kinetic rate constants. Identified hits were subsequently validated via orthogonal methods including XRC and DSF, highlighting the robustness, reliability, and superior sensitivity of GCI.

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