

ExtRA™ - Extended Rate Analysis

Kinetic analysis of slowly dissociating compounds

Beactica has developed a proprietary method for determination of slow dissociation rates. The method extends the range for which reliable k_{off} values can be determined, and has a lower limit of $\sim 10^{-7} \text{ s}^{-1}$. This corresponds to a residence time of >100 days.

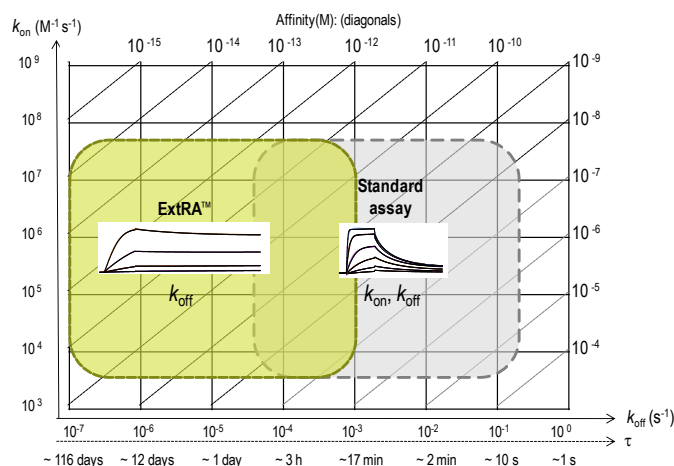
In the late stages of lead optimization, it is common that compounds dissociate very slowly from their target. For such interactions, steady-state approaches are not useful and standard kinetic methods can only reliably quantify dissociation rates faster than $\sim 10^{-4} \text{ s}^{-1}$ [1].

ExtRA™ deliverables

- Dissociation rate constants (k_{off})
- Residence times (τ)
- Interaction kinetic profiles
- Mechanistic interpretations

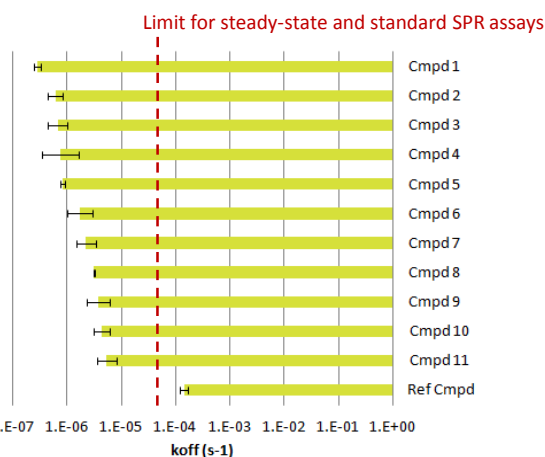
Case study

Eleven high affinity compounds in a late stage project were to be ranked and differentiated on the basis of dissociation rate constants (k_{off}). The ExtRA™ method enabled reliable determination of k_{off} for all compounds (figure below). The ranking correlated perfectly with results from an orthogonal cell-based assay, and the results allowed a SAR analysis and further optimization of the compounds.



ExtRA™ range for quantification of dissociation rate constants (k_{off}) or residence times (τ), compared to standard SPR-based assays.

The ExtRA™ method is based on a novel experimental design and analysis procedure and has been successfully applied in several partner projects.



All 11 compounds showed k_{off} values below the limit for steady-state and standard SPR assays, and could only be determined using the ExtRA™ method.

Reference: [1] Önell & Andersson, *J. Mol. Recogn.* 2005; **18**:307-317

Beactica – Interactions understood. Leads improved.

Beactica represents scientific excellence in Surface Plasmon Resonance (SPR) biosensor-based interaction analysis for small molecule drug discovery programmes. We offer expertise and services in the area of lead discovery and optimization using our proprietary drug discovery platform.

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