Advances in Biosensor Technologies



SensiQ - providing biosensors for label-free screening

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sensíQ

SensíQ Technologies Inc

Introduction



Tom Jobe
Chief Operating Officer

Mr. Jobe has managed the Oklahoma City-based SensiQ site since February 2005.

Mr. Jobe spent 11 years in the energy business as an instrument developer, and the past 25 years as a developer and manager for medical diagnostic instruments with Organon Teknika/BioMerieux (OT/BMX), and subsequently for life science instruments with SensiQ Technologies

Mr. Jobe holds a BS degree in Electronic Engineering Technology and MS degree in Engineering and Technology Management from Oklahoma State University.

Today's Presentation

- SensiQ's role in biosensors
- Biosensor Overview
- Biosensor Transducer Technologies
- The Biomolecular Interaction Analysis portion of Biosensors
- Surface Plasmon Resonance
- New SPR Platform for Drug Discovery
- Questions

The SensiQ Story

The innovation leader in SPR











2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Collaboration with TI		*First SensiQ instrument launched*	*Discovery instrument launched*		*Pioneer instrument launched*		Key OneStep discovery		**NIH Award** **GSK & Roche collaborations**	**Pioneer AE Launched** Pioneer FE Launched		

Current Products



Pioneer Fragments Edition (FE)
High-throughout, small molecules-Pharma



Pioneer
Automated higher throughput



Pioneer AE
Automated
Academic Edition

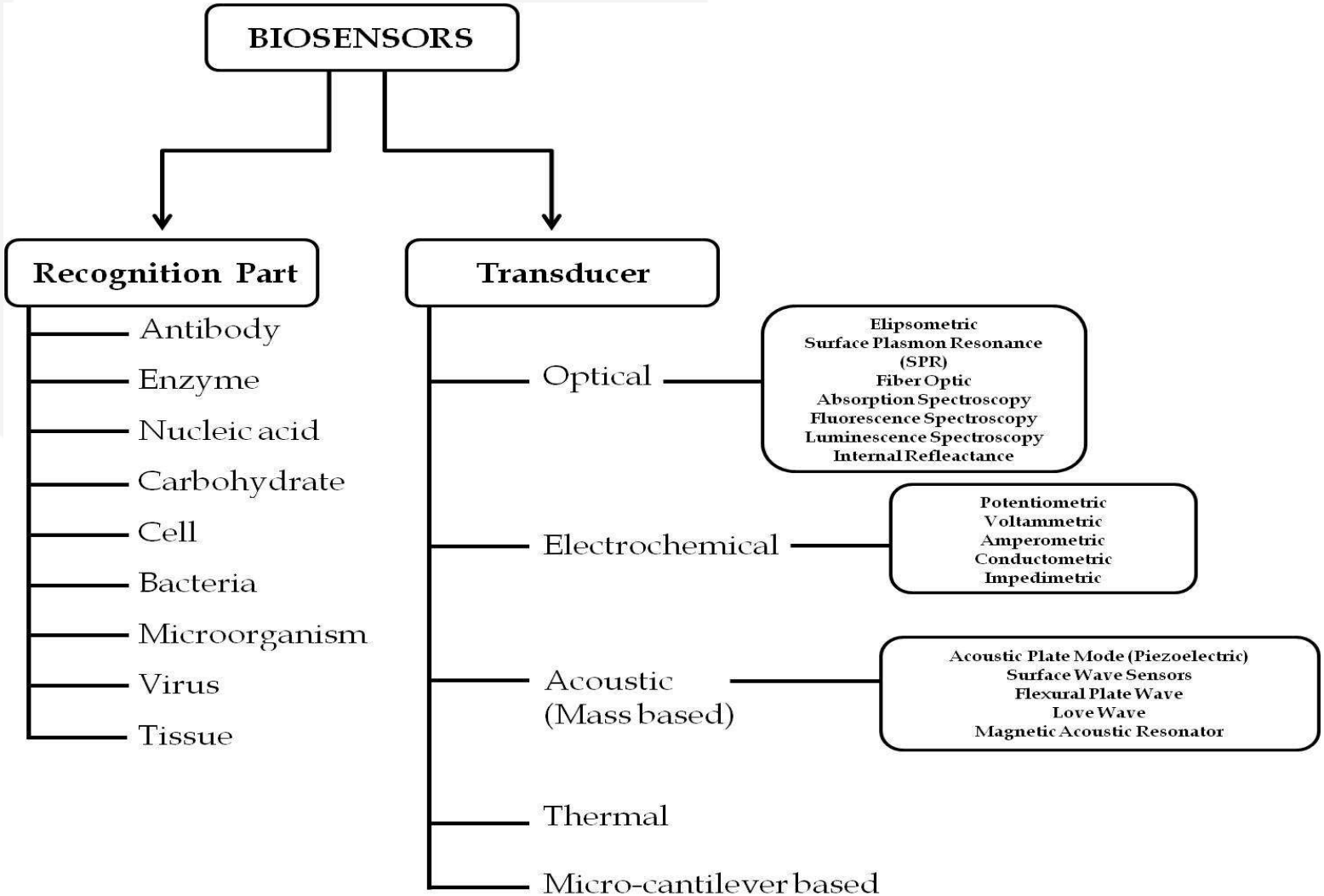


SensiQ
Low throughput-
Academic Research



Discovery
Academic Teaching Tool

Biosensor Overview



Reference: Bora Garipcan, Mustafa Caglayan and Gokhan Demirel (2011). New Generation Biosensors based on Ellipsometry, New Perspectives in Biosensors Technology and Applications, Prof. Pier Andrea Serra (Ed.), ISBN: 978-953-307-448-1, InTech, DOI: 10.5772/16256. Available from: http://www.intechopen.com/books/new-perspectives-in-biosensors-technology-and-applications/new-generation-biosensors-based-on-ellipsometry

Sample of Biosensor Transducer Technologies

Electrochemical

Fluorescence

Impedance Spectroscopy

Biolayer Interferometry

Surface Plasmon Resonance

Quartz Crystal Microbalance

Surface Enhanced Raman Spectroscopy

Optical Ring Resonantors

Scanning Probe Microscopy (AFM, SPM)

Dual Polarization Interferometry

Ion Channel Switch

Antibody/DNA probes

Carbon Nanotubes

Calorimetric (ITC, DSC)

MEMS Based

Commercial Biosensor Applications

Drug Discovery and Development

Biosecurity Monitoring/Analysis

Environmental Monitoring/Analysis

Biomedical Instrumentation

Medical Instrumentation

Medical POC

Diagnostics Instrumentation

Diagnostics Assays/test kits

Food Analysis/QC

Biofuels/Biopolymers

Biomolecular Interaction Analysis & the Label-Free Market Segment

BIA is also referred to as the Binding Affinity market segment, which includes affinity, kinetics and can include other parameters.

A historical approach to BIA would include assays relying on a reporter molecule (radio-isotope, fluorescence, chemiluminscence), while a more modern approach eliminates the need for a reporter molecule - “Label-Free” methods.

A definition of Label-Free BIA method:

> “ *A Label-free biosensor must detect a whole biologically active molecule in real time*”
>
> (Andrew Shaw –Univ of Exeter)

BIA Vendors/Suppliers

































Sapidyne Instruments

CORNING

IBIS TECHNOLOGIES



The SPRi-Array Company®

HORIBA



Binding Affinity Vendors

Surface Plasmon Resonance

- SensiQ - GE Healthcare/Biacrore -Reichert -KSV
-Biosensing Instruments - BioNavis
-BioRad -Bioptix - Sierra Sensors

Surface Plasmon Resonance Imaging

-GWC -Genoptics/Jobin Yvon -IBIS/Wastach -Horiba

Quartz Crystal Microbalance

-Q-Sense -Sierra Sensors

Other Label-Free Detection

-ForteBio -Creoptix -Sapidyne (Kinexa) - NanoTemper -Dynamic Biosensors
- Silicon Kinetics

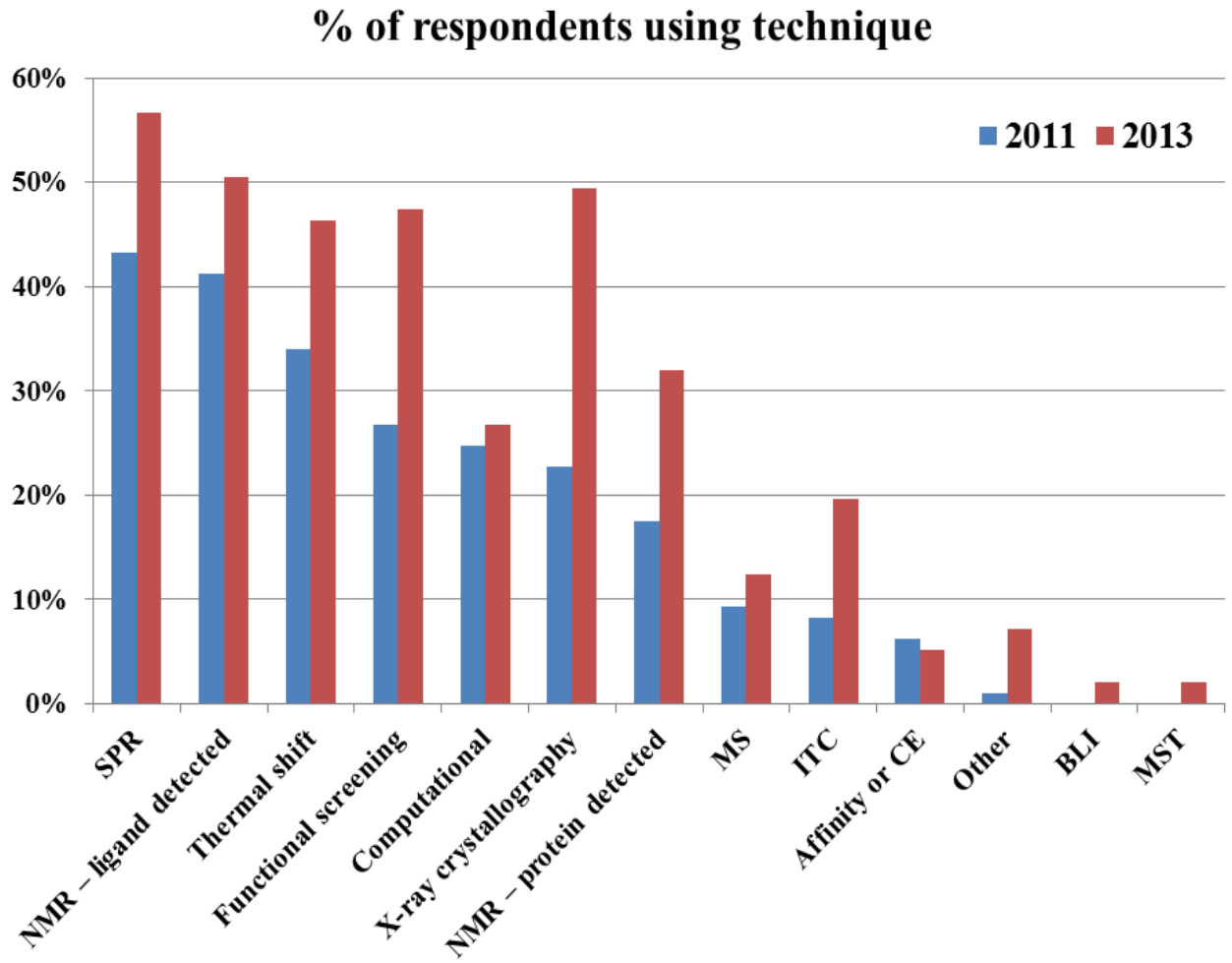
Biosensors in Drug Discovery

What are the measured targets in Drug Discovery ?

In the Biotherapeutics drug discovery pipeline, antibodies/antigens are the measured targets

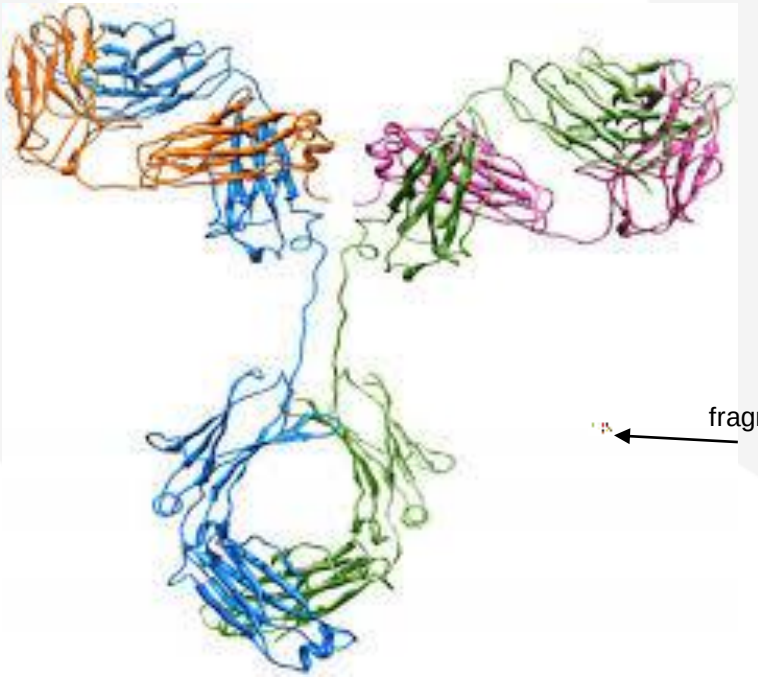
In the Small Molecule Drug Discovery pipeline, protein fragments are the measured targets

What biosensors are used in Drug Discovery ?

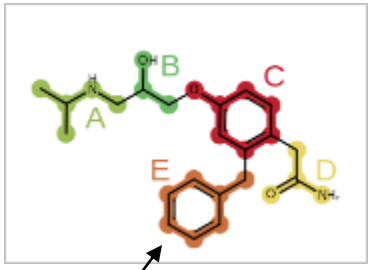


Graphic courtesy of www. practicalfragments.blogspot.com

Fragment Screening vs Antibody Screening



fragment size relative to size of a mAb



Fragment

Typical Antibody (mAb) MW ~ 150kDa
Typical off-rate: 10 minutes
Typical affinity range: xuM-xxpM
Typical Library size: 5K- 25K

Typical Compound Fragment: MW ~ 0.3KDa
Typical off-rate: 20 secs
Typical affinity range: mM-xxuM
Typical Library size: 1K-6K

Traditional Non-Computational Approach to mAb Screening

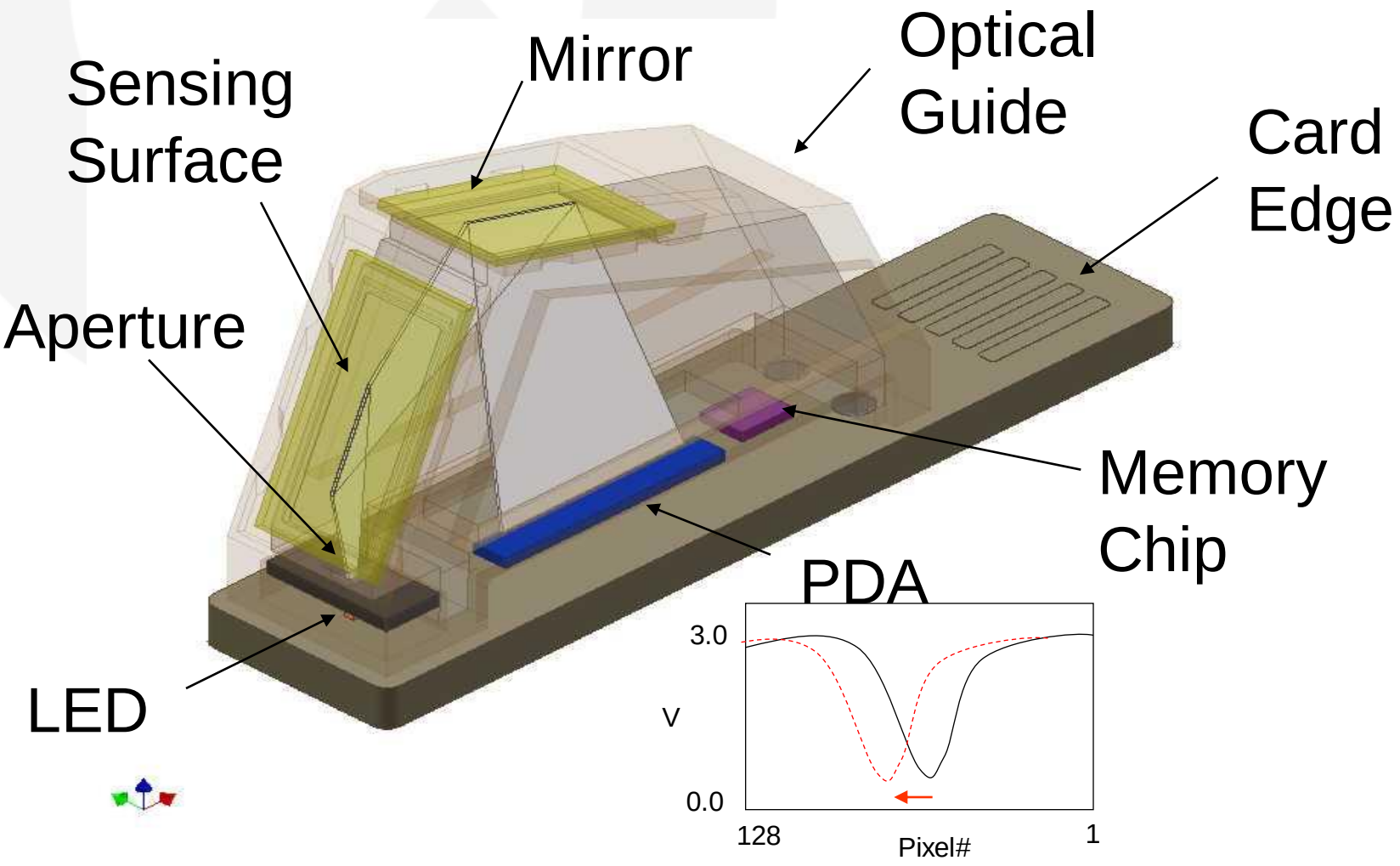
Typical Fragment Screening Approach

Surface Plasmon Resonance as a tool for Small Molecule Drug Discovery (SMDD)

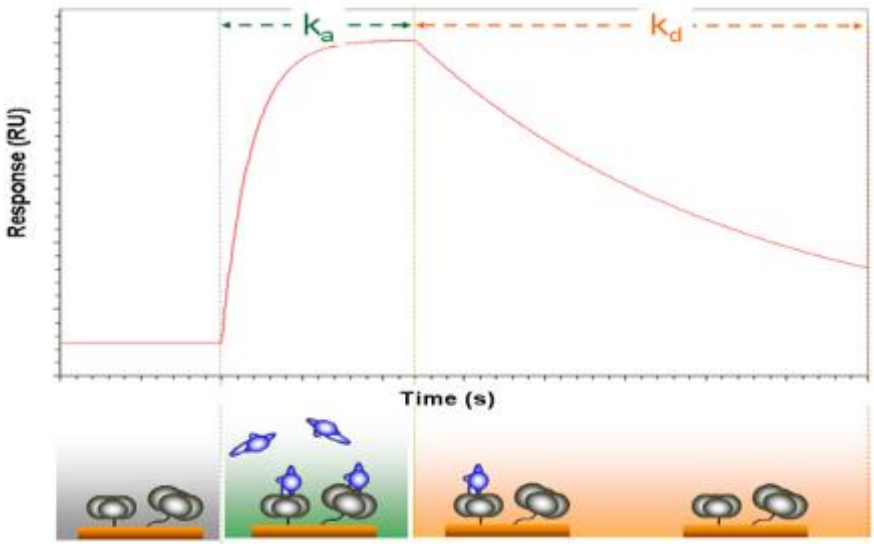
Why Use SPR ?

- **Real-time Sensing - movie vs. snap shot**
- **Direct feedback - enables rapid optimization**
- **Label Free – No reporter molecules**
- **Kinetic Analysis- some provide affinity only**
- **Truly Quantitative - 1 RU = 1pg/mm^2 over full range**
- **Requires low amount of precious reagent**
- **Can yield good data from impure samples**
- **Applications throughout drug discovery, development, and manufacturing.**

Basic SPR Sensor



How Does SPR Work?



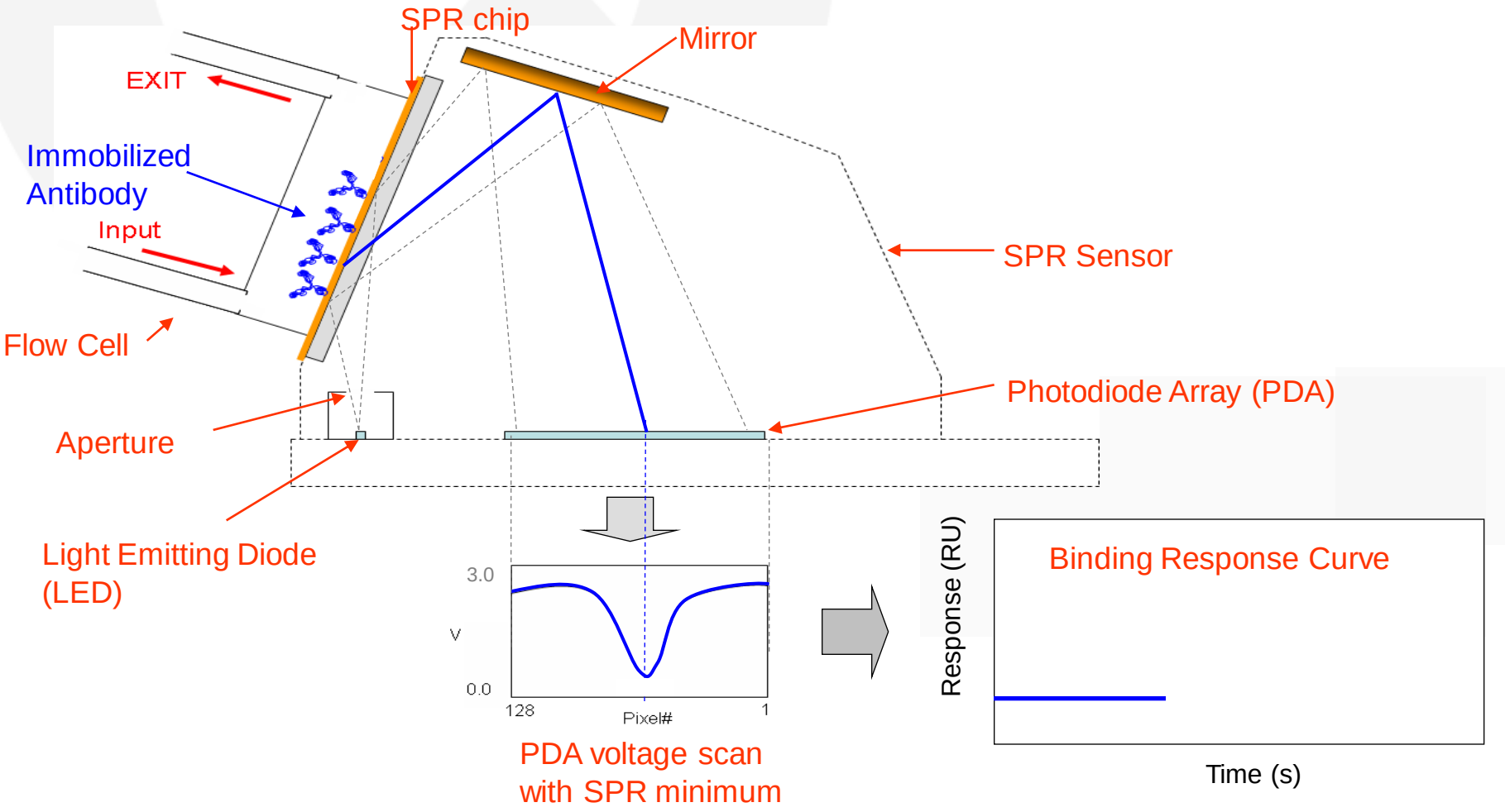
Ligand is first immobilized onto the surface giving a stable baseline.

The analyte is then injected over this surface causing affinity complexes to form. This mass loading is then detected in the response.
1 RU ≅ 1 x 10^{-6} refractive index unit

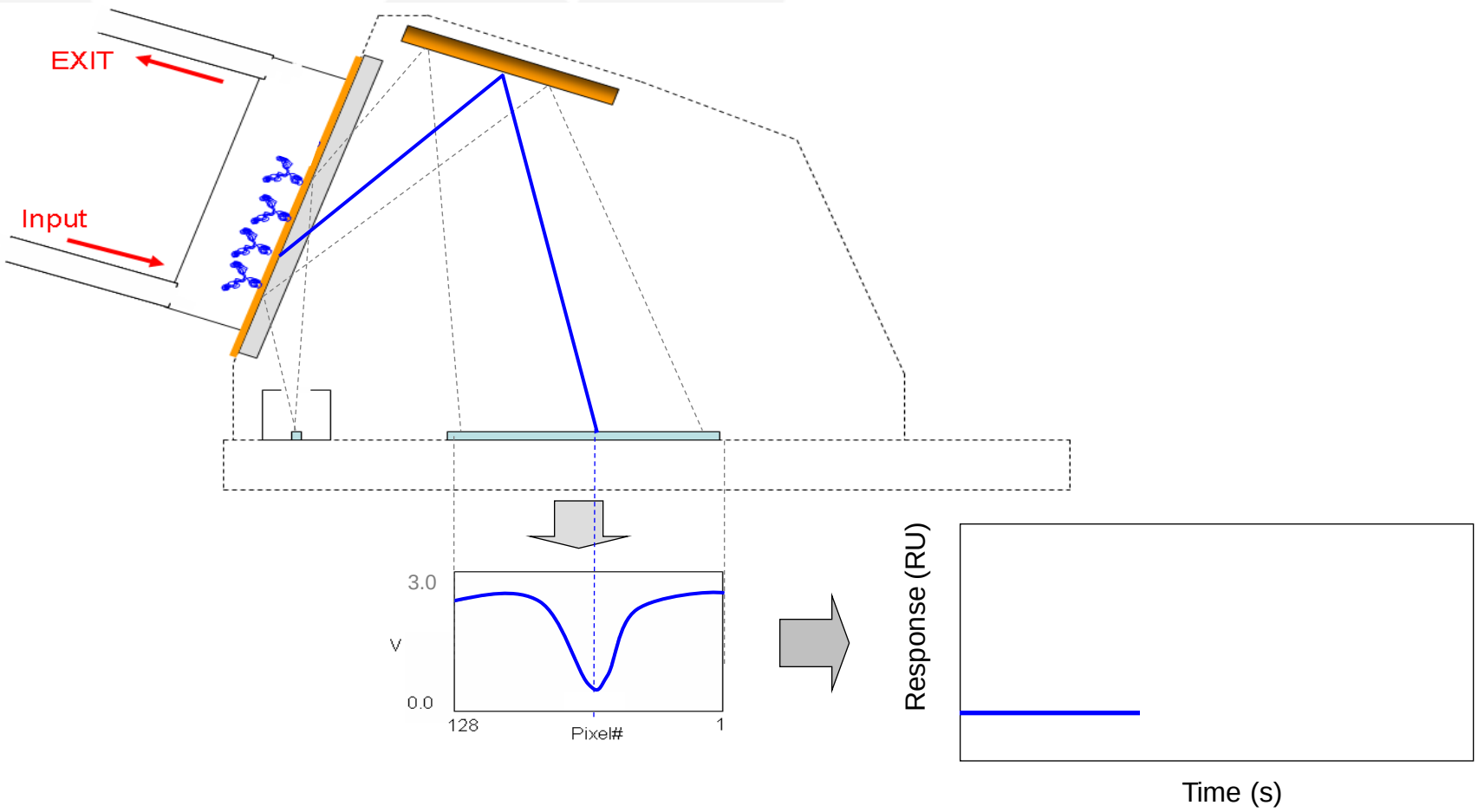
When the injection is complete the affinity complexes will dissociate causing a decrease in mass.

In the standard approach the kinetic interaction constants are obtained by fitting a binding interaction model to the association and dissociation phases of a number of these curves recorded at different analyte concentrations.

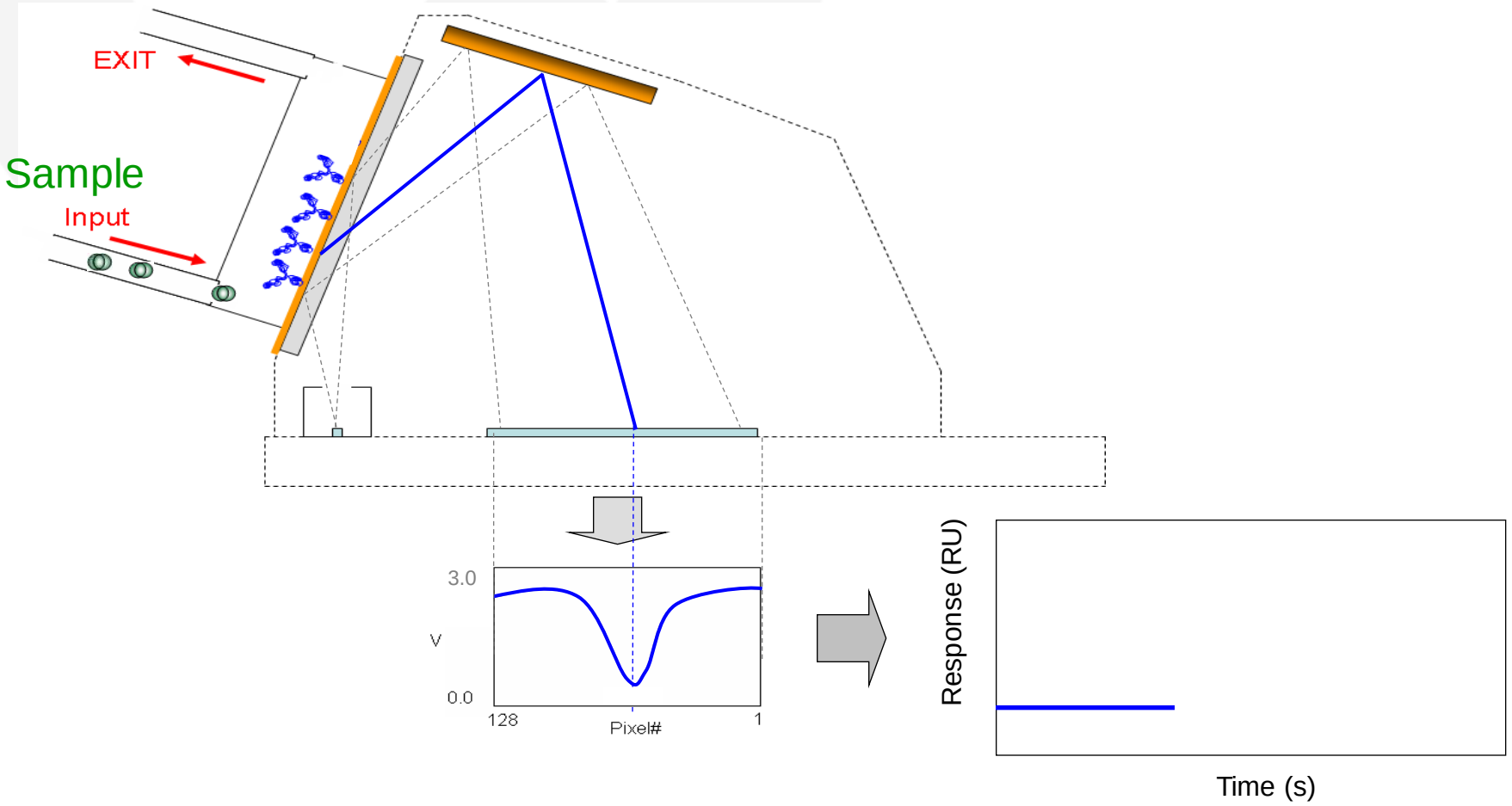
Tracking The SPR Response



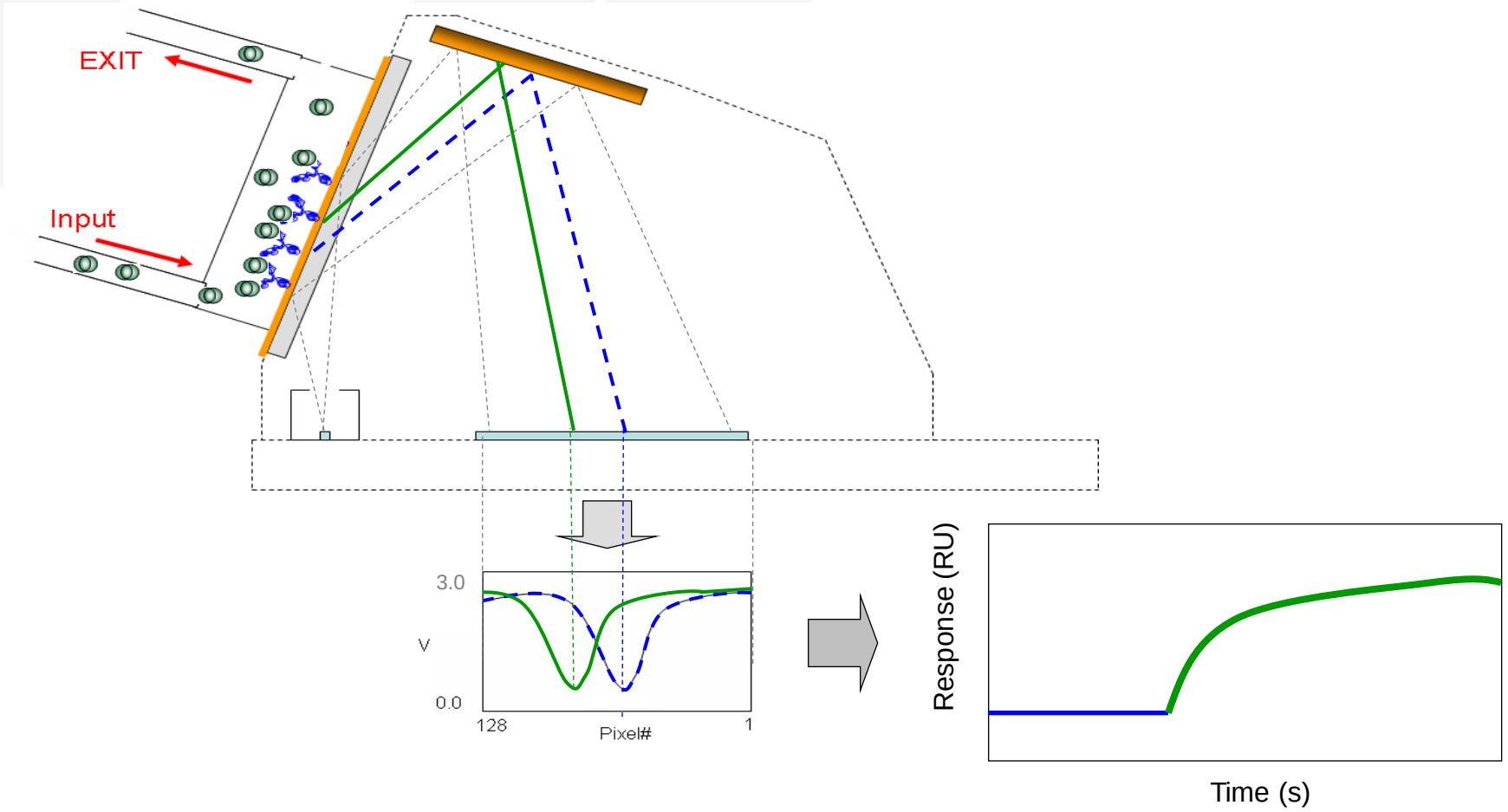
Tracking The SPR Response



Tracking The SPR Response



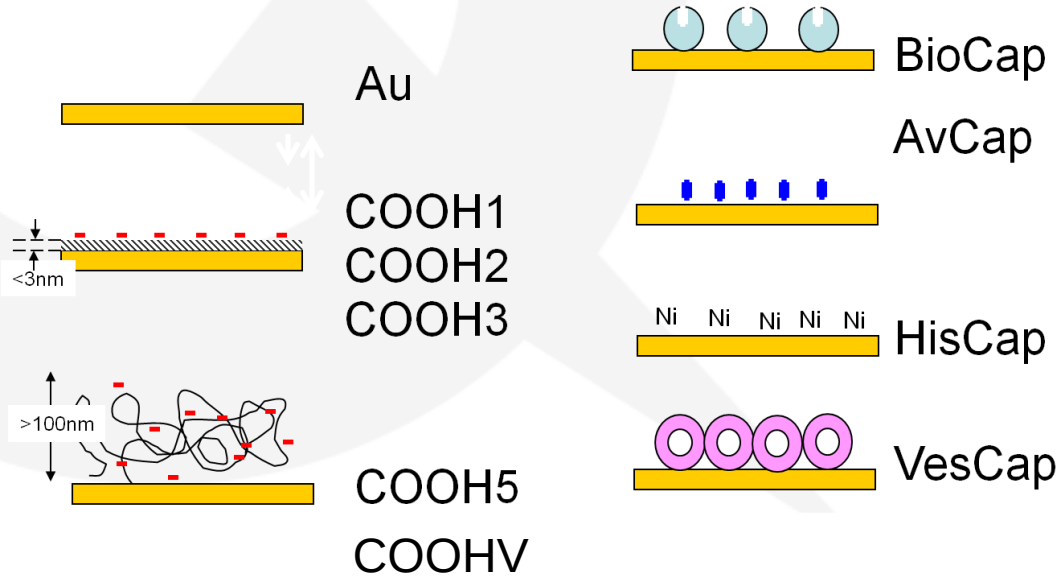
Tracking The SPR Response



Pioneer FE (Fragment Edition)



Surface Chemistries



A wide variety of surface chemistries and immobilization protocols are available to cater for the diverse range of applications that are possible.

Surface chemistries are developed and manufactured in-house.

Injection Types



Injections (uniform) have remained unchanged since the inception of the field limiting progress in the field.

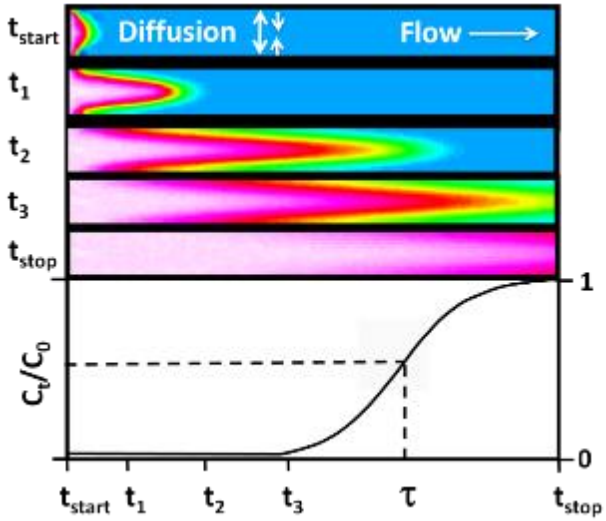
Gradient injections are practical and have substantial advantages that present opportunities to solve lingering problems.

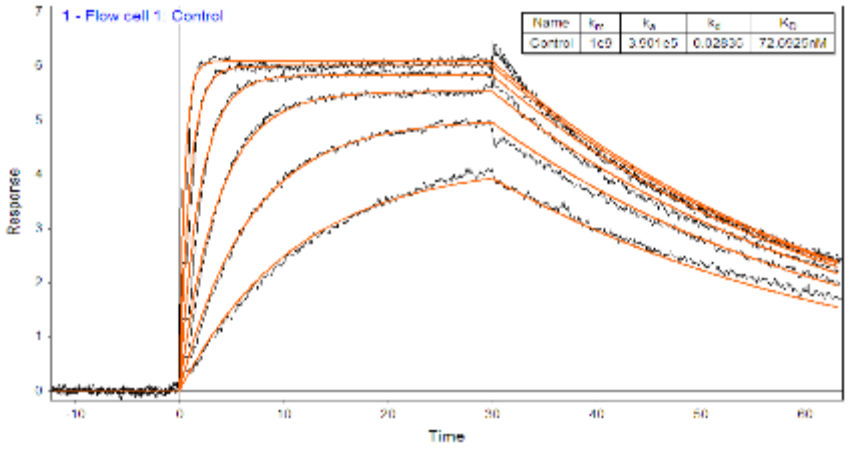
OneStep® Gradient Injections

sensíQ

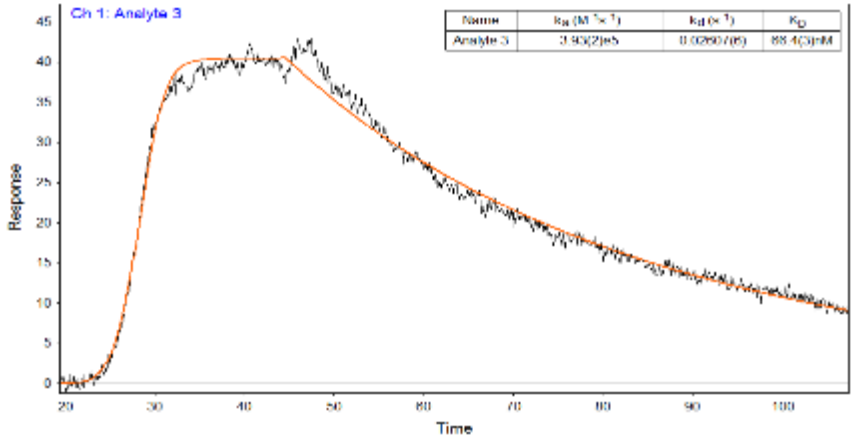
> **"*This is the first true innovation in SPR in 20 years.*"**
> a Key Opinion Leader in Pharma Drug Discovery.

OneStep® gives the same binding affinity data (K_D) as multiple fixed concentration injections (FCI) in a fraction of the time.





Six-Point FCI Assay



OneStep® Assay

Workflow comparison:
OneStep®-based Fragment Screening

Conventional SPR Workflow



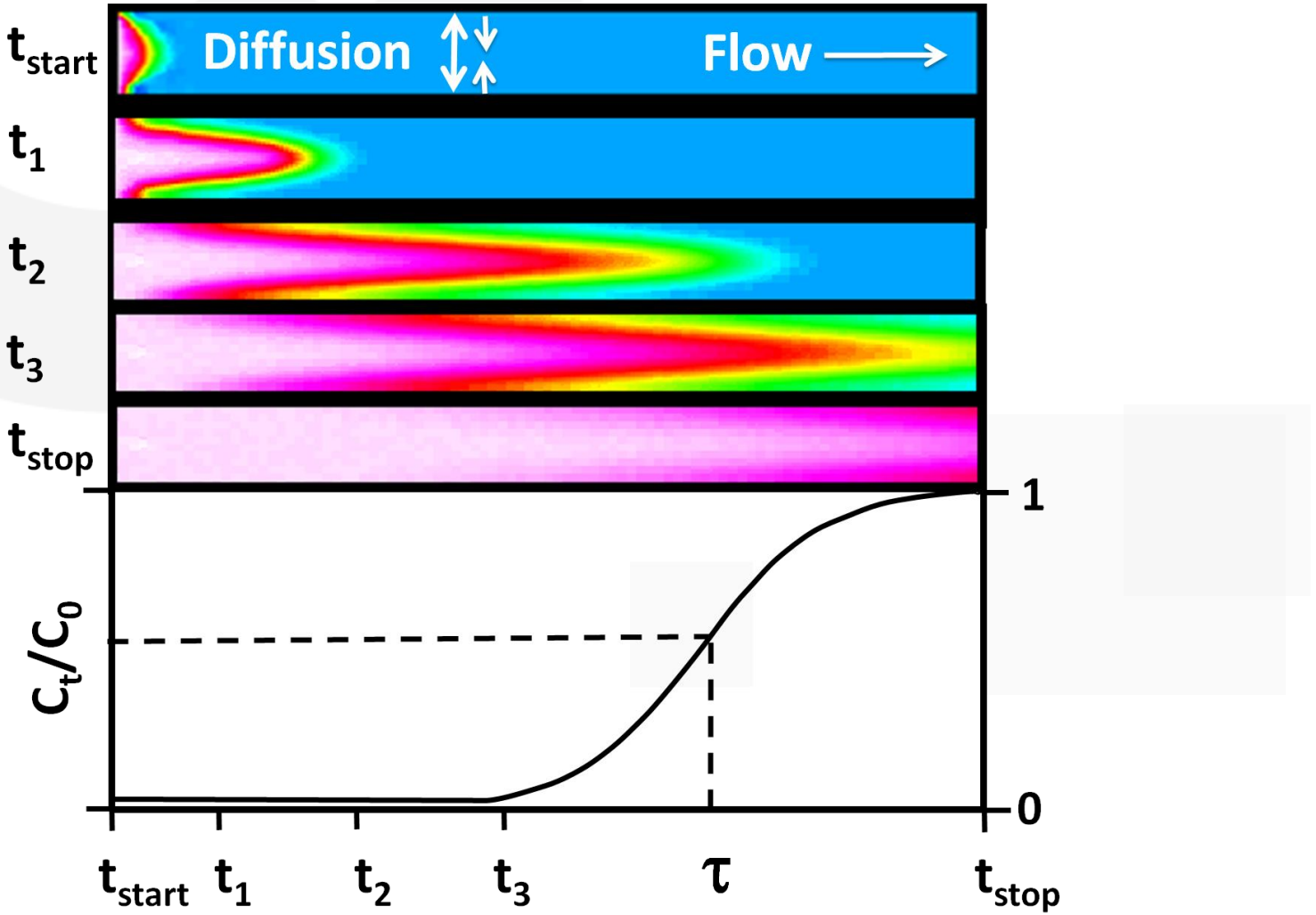
Optimized Workflow using diSPR®



OneStep® methods eliminate the need for secondary screening because primary screening contains kinetic/affinity information content.

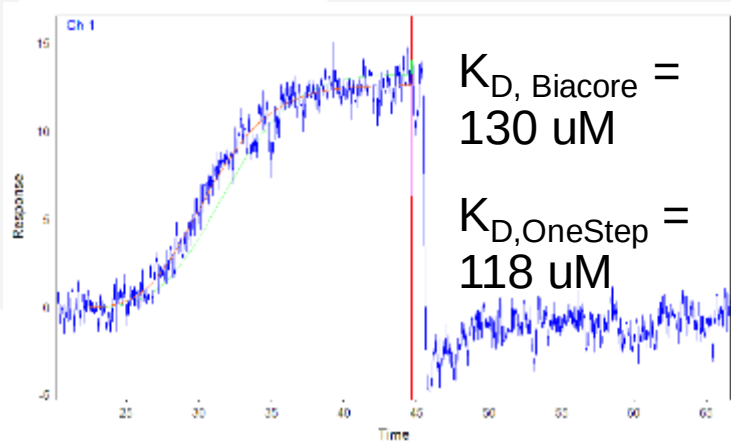
Dynamic Gradient Formation

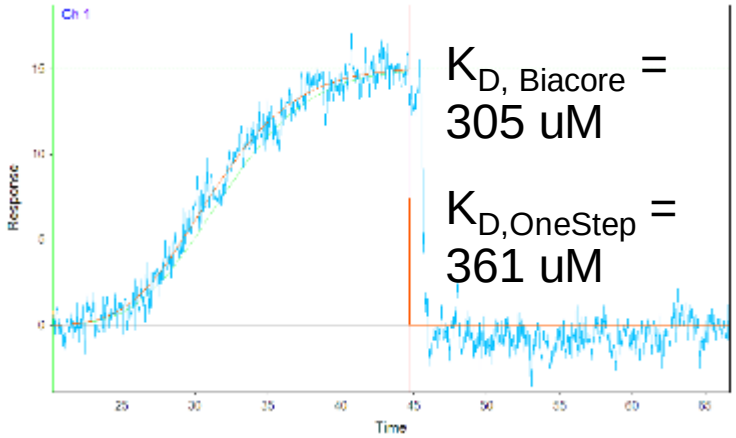
(b) Sigmoidal Taylor Dispersion

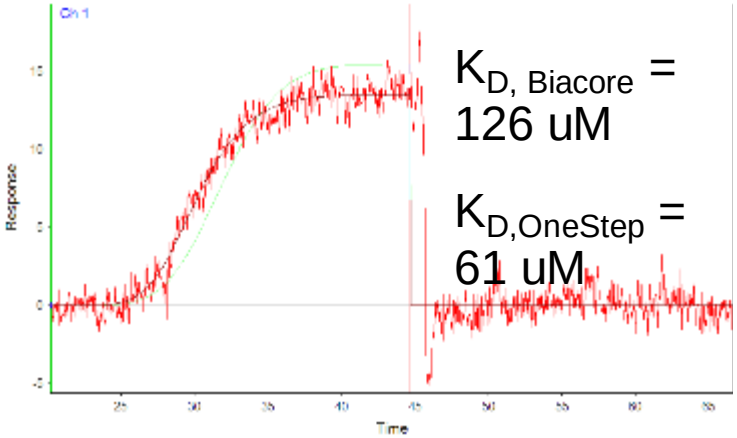


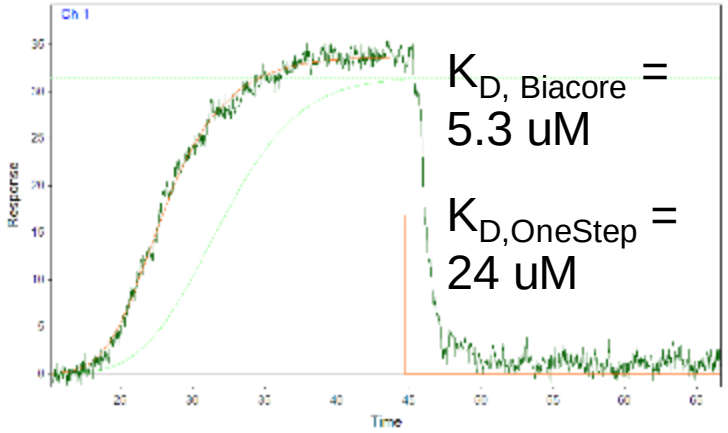
KDs from Primary Screen

- Examples from hits that gave crystal structures. Excellent fits with reasonable (unrestrained) parameters may be indicative of high hit quality



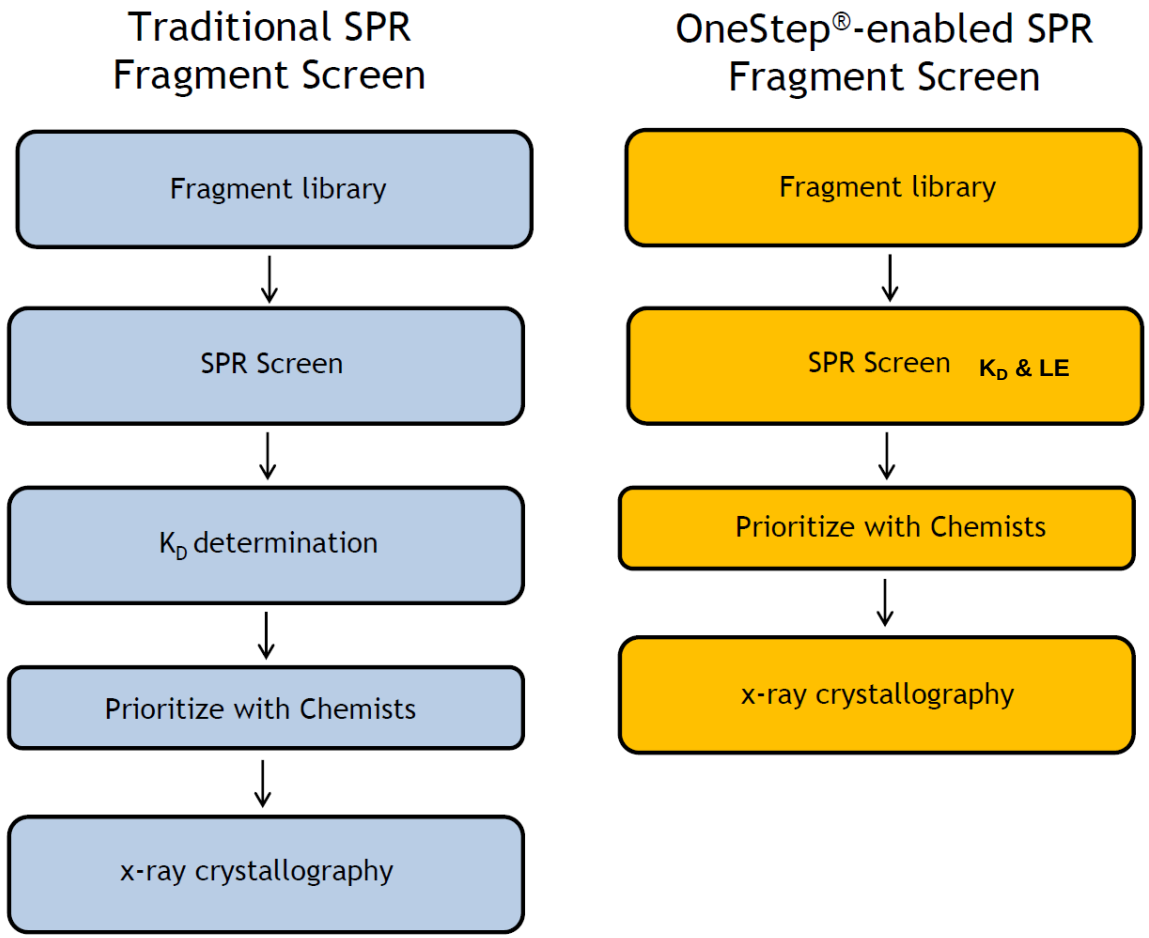






Data courtesy of Tony Giannetti of Genentech, Inc.

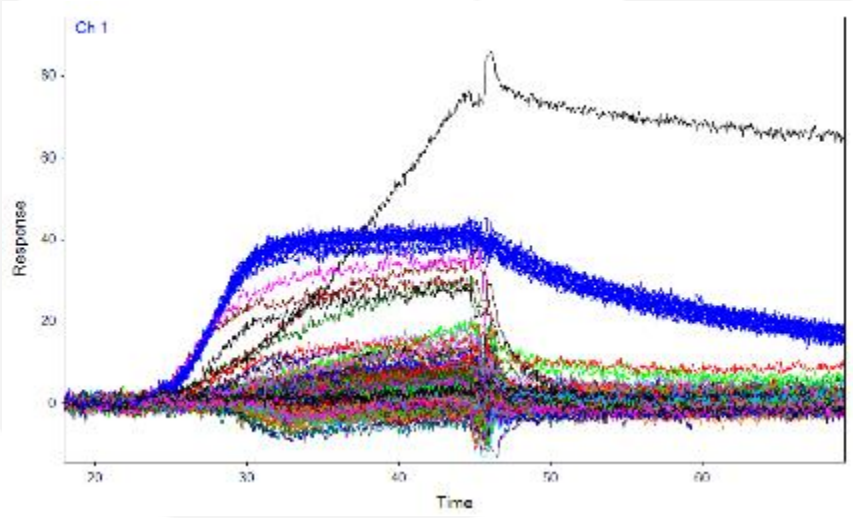
The SensiQ Advantage in SPR Fragment Screening

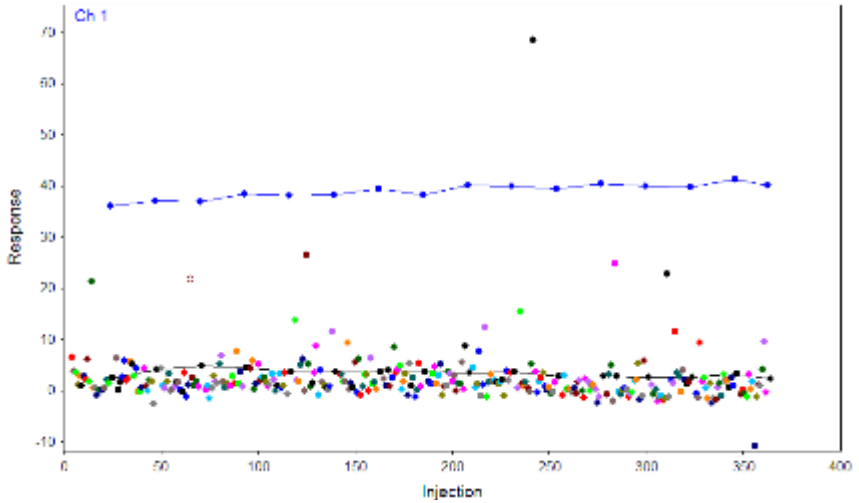


Fragment Screening via OneStep

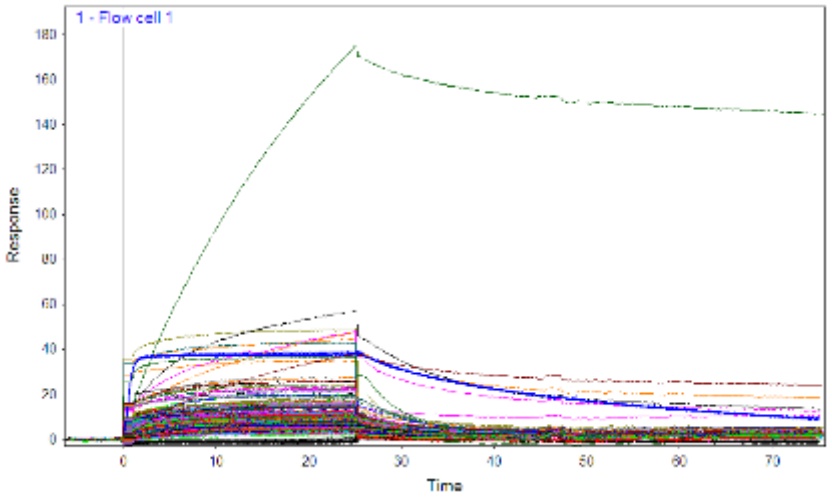
SensiQ can screen two 384 plates in 24 hrs

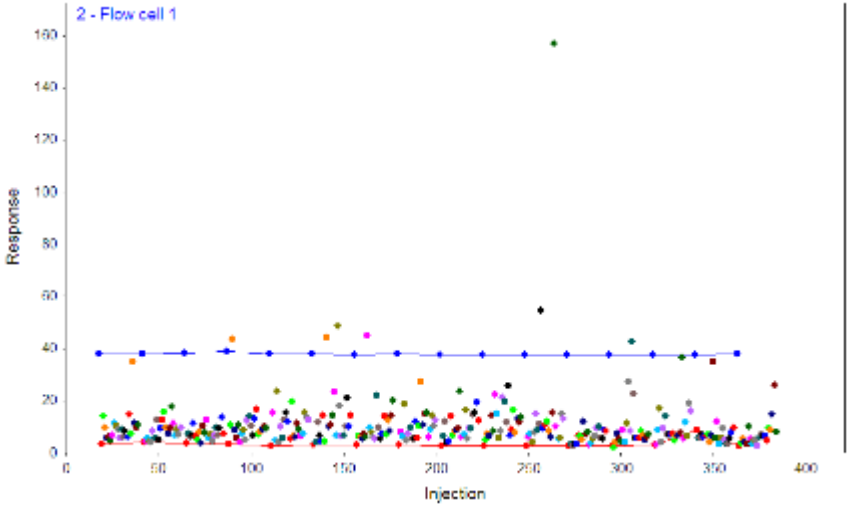
SensiQ





S51

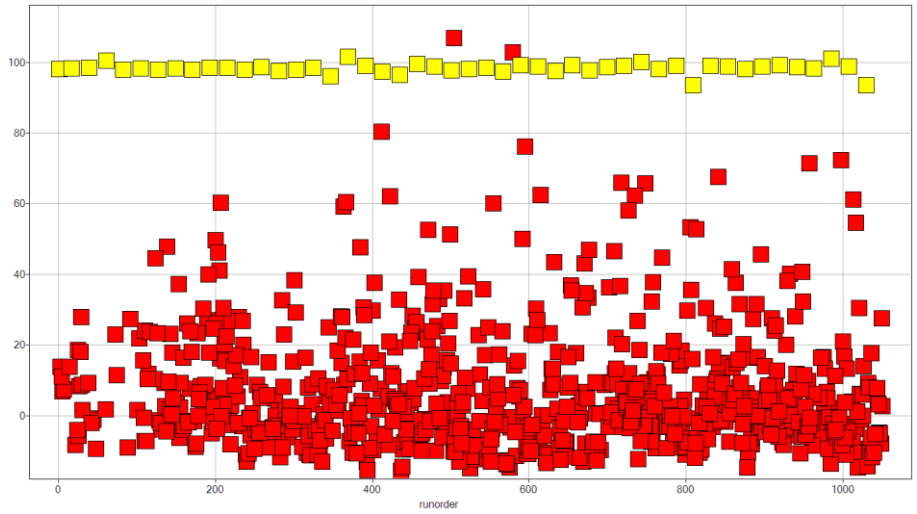


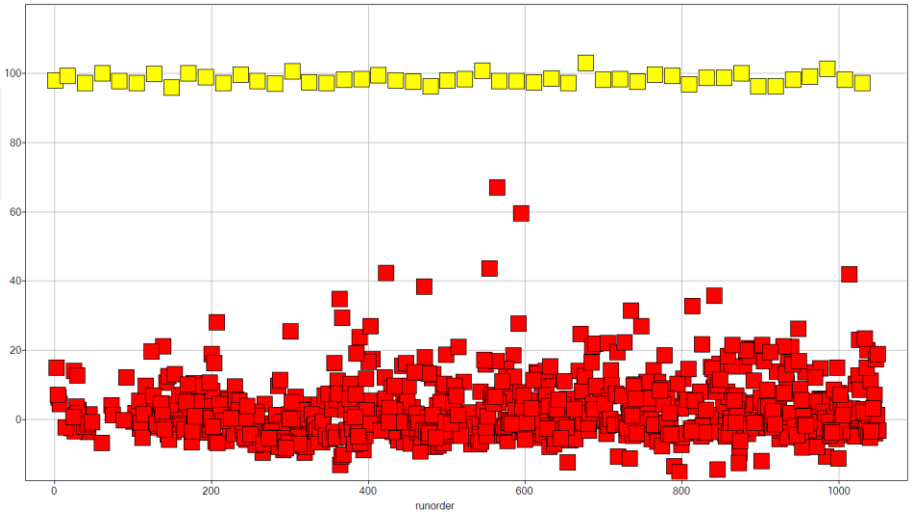


Data courtesy of Tony Giannetti of Genentech, Inc.

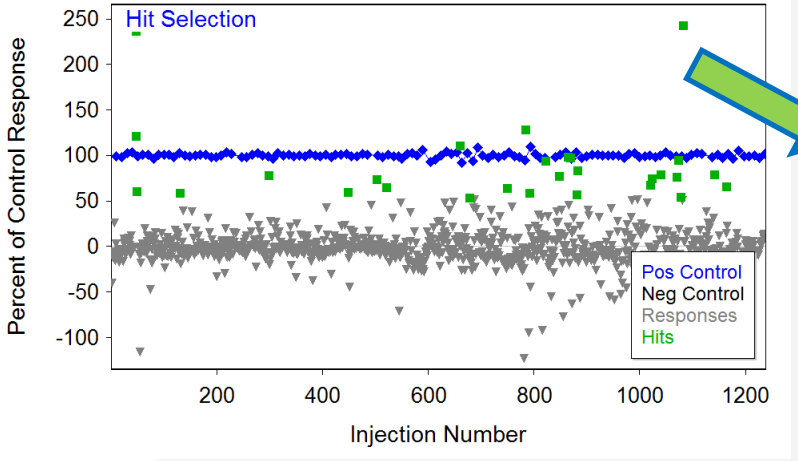
Mini Screen - FCI vs OneStep

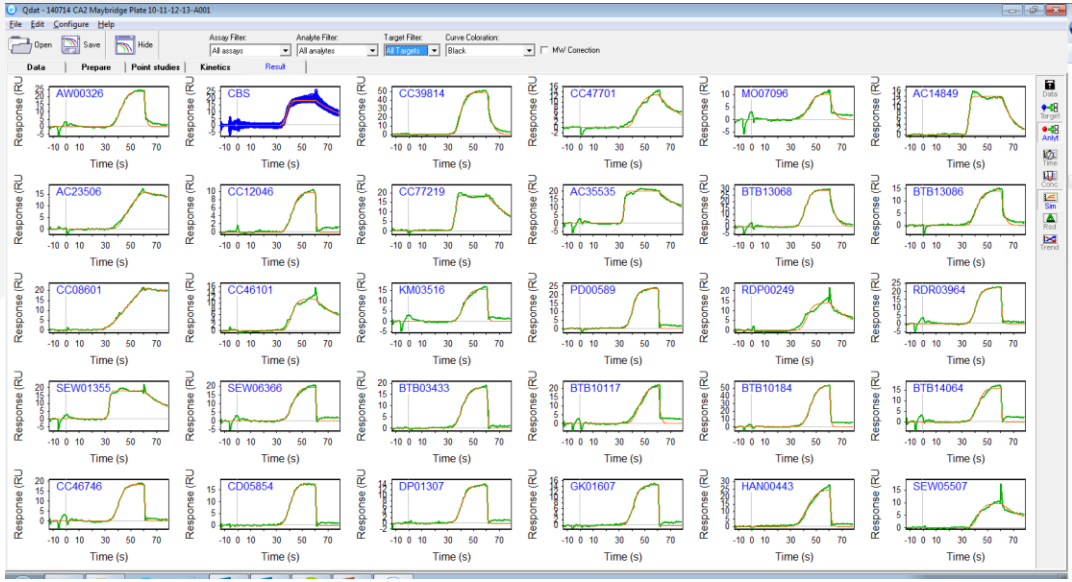
- 1000 fragments tested in an S51 and SensiQ
- Data scaled according to fractional binding occupancy
- Less apparent noise in the SensiQ experiment





Quickly identify and characterize hits with diSPR®

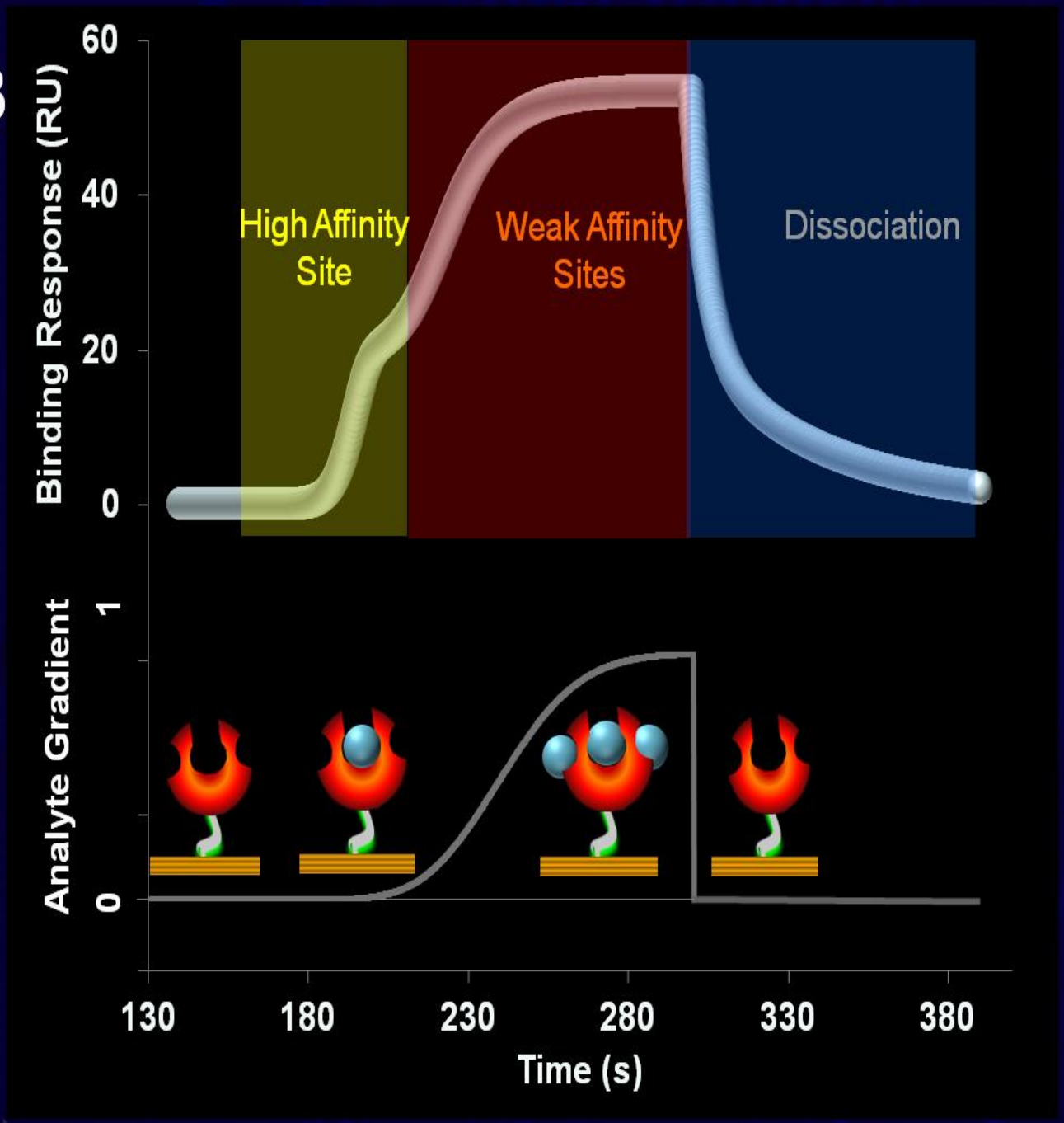




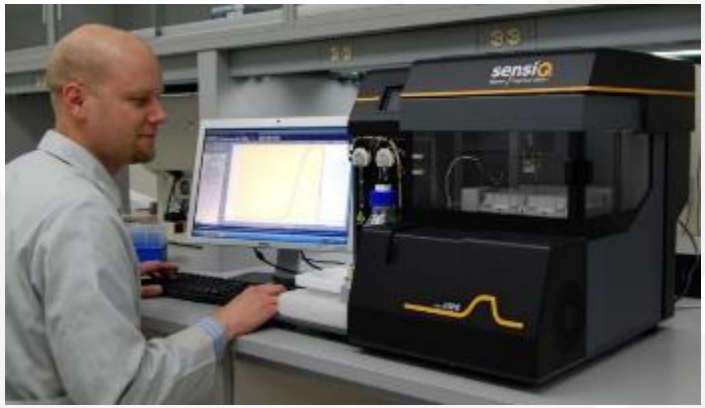
Primary diSPR® screens enable rapid data triage and include kinetic/affinity characterization. Hits from the Maybridge Ro3 library are identified and characterized in the first experiment.

COMPLEX BINDING

t_{0-3}


Binding Response (RU)
60
40
20
0
High Affinity Site
Weak Affinity Sites
Dissociation
Analyte Gradient
1
0
130
180
230
280
330
380
Time (s)

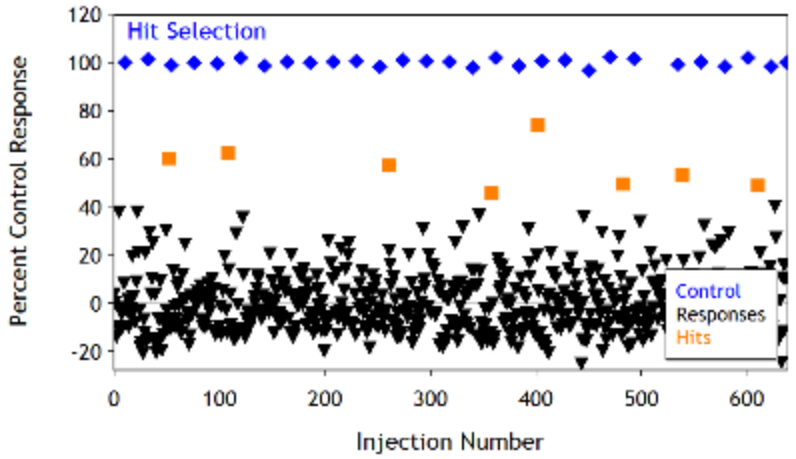
Fragment Screening on Steroids
The Power of OneStep Injections



The *Pioneer FE* delivers binding affinity constants

- **10X faster than the Biacore T200**
- **4X faster than the B4000.**

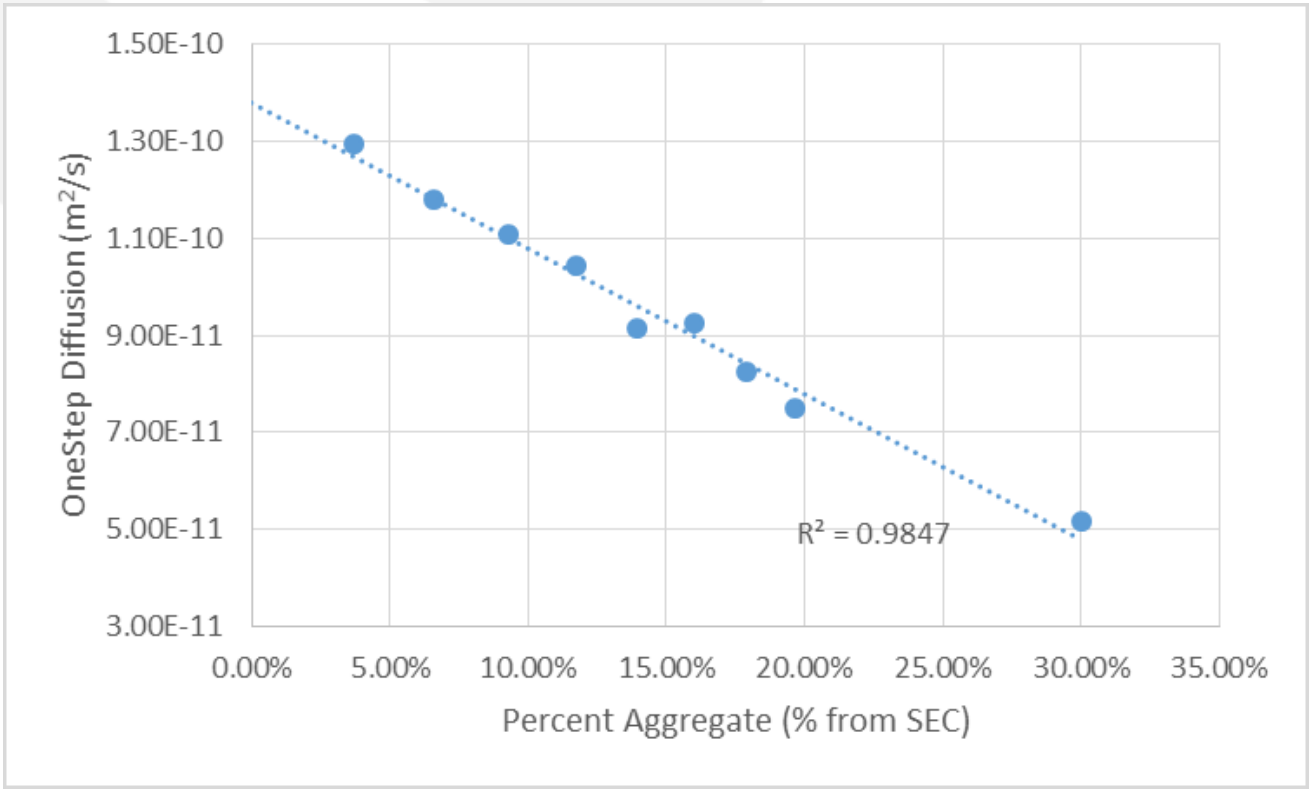




OneStep® creates a new standard in fragment screening workflow by eliminating secondary screening and providing integrated hit selection software.

New characterization capabilities for SPR

Recenty, SensiQ introduced the capability to measure protein aggregation using the diffusion-coefficient based OneStep injection technique. This is particularly useful in the pipeline of developing a biotherapeutic drug. https://www.sensiqtech.com/news/62/25/Protein-Aggregation-Tech-Note/



Conclusions

SPR-based biosensors are well suited for and have a significant role in biotherapeutic and small molecule-based drug discovery.

Commercial solutions of biosensors are available for studying biomolecular interactions at essentially every economic and application entry point.

Numerous biosensor technologies are available in the BIA market but new solutions are being added every year. Costs are lowering as a result.

For biosensors in general, portable or POC solutions seem to be a challenge. Perhaps nanotechnologies/MEMS are the enabling technologies for portable/POC solutions.

Applications of biosensors are still growing, even in established markets (eg BIA), as evidenced by the new application of Label-free SPR to measure protein aggregation

Questions/Comments

- **Send questions & comments to**

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