iRiS Kinetics multiplexed affinity

iRiS *Kinetics* introduces:

Interferometric Reflectance Imaging Sensor (IRIS)

newest innovation in *label-free* biomolecular interaction analysis

IRIS platform offers:

- Highly multiplexed (100s of probes)
- Quantitative
- Repeatable
- Highly sensitive (<250Da molecular weight)

kinetic binding measurements.

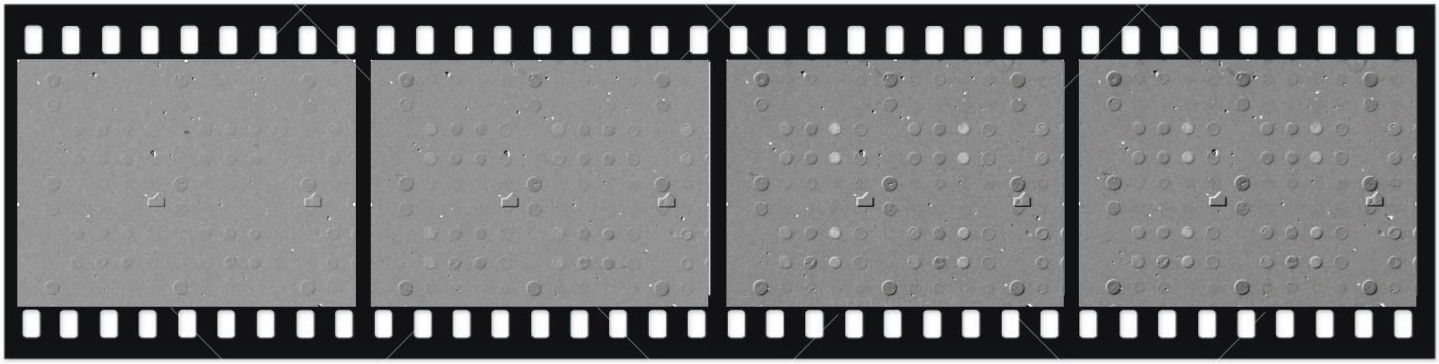
We cover the entire range of biological analytes including **proteins, nucleic acids, peptides, and small molecules**

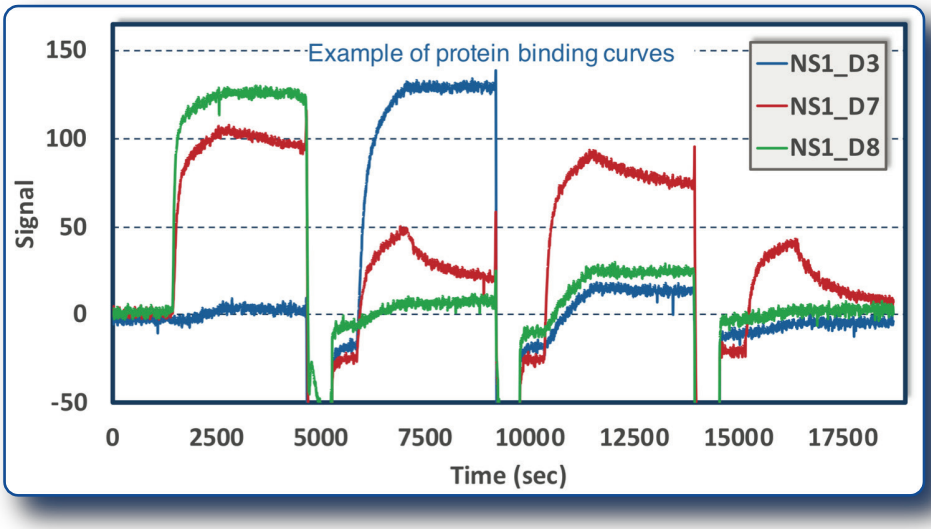
On a **compact, robust, low-cost, fully-automated, and easy-to-use** research instrument with versatile and **inexpensive consumables**.

Interferometric Reflectance Imaging Sensor, IRIS – builds on strong lineage of basic and applied research at Boston University and offers high-sensitivity and quantitative detection through an approach defying the conventional wisdom. Instead of enhancing the signal through optical resonances, we exploit the power of signal averaging in shot noise limited operation to achieve virtually unlimited sensitivity in a simple interferometric platform. IRIS technique also overcomes the Achille's Heel of label free detection: the bulk effect – the background signal due to concentration and temperature variations in the analyte solution.

Real-time visualization of the microarray on the sensor surface provide intuitive monitoring of binding experiments.

Video link ☞





Multiplexed binding curves are extracted from the images acquired in real-time.

Antibodies with unique binding characteristics for dengue NS1 are shown here (*). Rapid determination of the serotype specificity for each antibody will aid in the creation of serotype specific immunoassays.

E. Özkumur, et al., "Label-free and dynamic detection of biomolecular interactions for high-throughput microarray applications" *PNAS*, Vol. 105, pp. 7988-7992, 2008

M. S. Ünlü, et al., "Structured Substrates for Enhanced Optical Surface Profiling," US Patent No: US9599611B2, issued on March 21, 2017, Adjusted expiration June 3, 2030

G. G. Daaboul, et al., 'LED-based Interferometric Reflectance Imaging Sensor for quantitative dynamic monitoring of biomolecular interactions,' *Biosensors and Bioelectronics*, Vol. 26, pp. 2221-2227, 2011

(*) Binding data from: James W. Needham, "Multiplexed Antibody Kinetics using the Interferometric Reflectance Imaging Sensor," PhD Dissertation, Boston University, 2019

iRiS Kinetics

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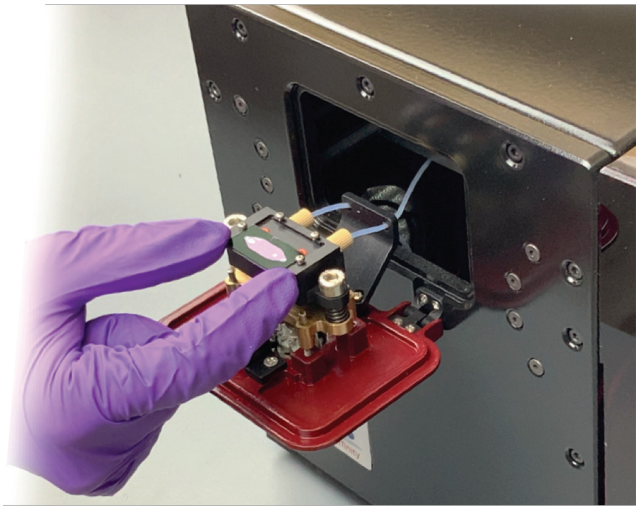
Low-cost Sensor Chips and Disposable Cartridges

innovations in Si-based microfluidics for interferometric biosensing

IRIS platform offers:

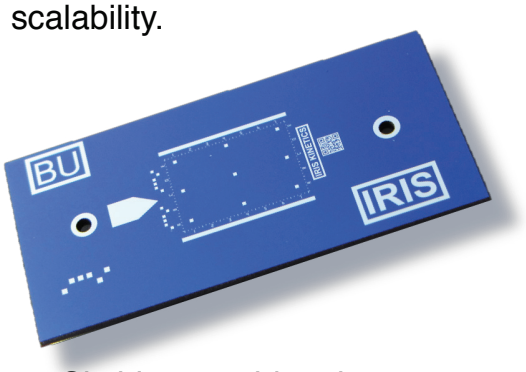
sensor chips and microfluidic cartridges (patent pending)

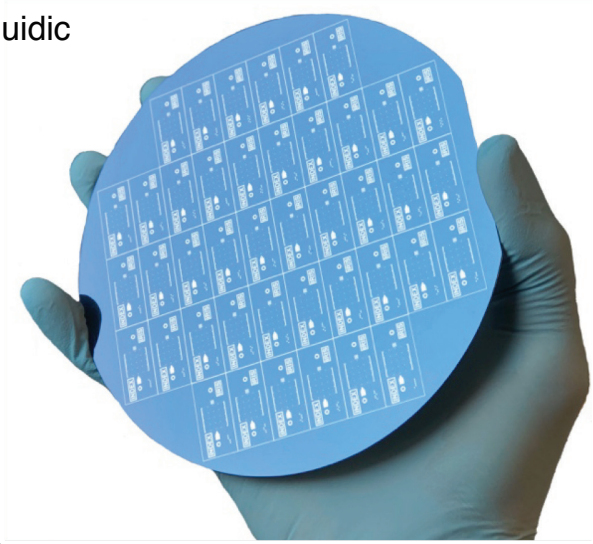
- Low-cost – truly disposable, no more reusing old sensor chips!
- Oxide coating compatible with glass surface chemistries
- Channel height from 50μm to 500μm
- Chamber volume from 2μl to 50μl
- Intuitive on-chip markings and rulers
- Large sensor area (5mm X 7mm)
- Superb quality control
- Easy to assemble and load



Video link

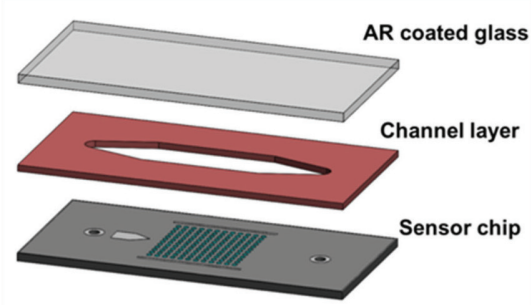
We offer low-cost and disposable sensor chips and microfluidic cartridges (patent pending) compatible with IRIS platform. Manufacturing using standard Si processing techniques provides superb quality control ensuring repeatability and scalability.

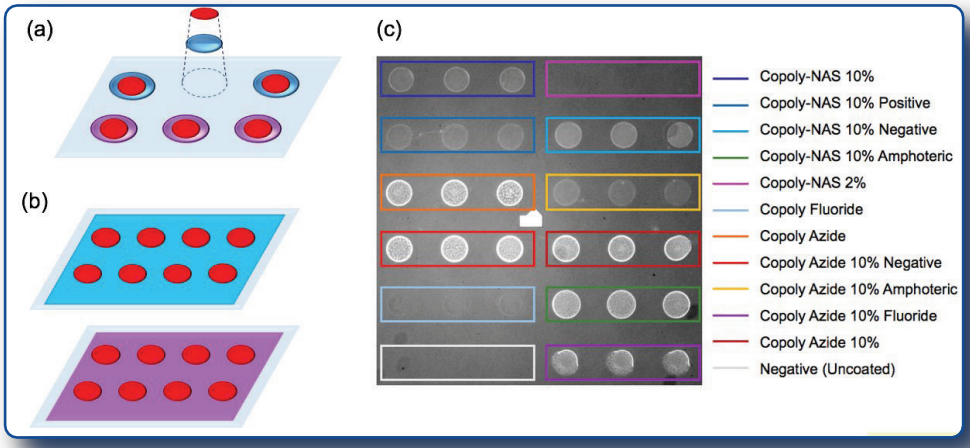




Si chips provide a large sensor area (5x7mm) and guide markings for robotic spotters for printing a microarray of ligands (*). Reference regions and rulers enable automated image analysis and quantification (†).

Easy and intuitive assembly of disposable cartridges at room temperature protects the biological activity of immobilized ligands (‡).





Oxide surface provides compatibility with glass surface chemistries.

Multiple surface chemistry coatings can be used on the same IRIS chip all at once (§).

IRIS allows the user to quickly understand which surface chemistry would better suit any specific ligand/analyte combination. Furthermore, IRIS eliminates the limitation regarding the number of molecules with different chemistries that can be immobilized on the same support.

(*) M. S. Ünlü, D. D. Sevenler, J. T. Trueb, and S. Scherr, “Disposable Fluidic Cartridge for Interferometric Reflectance Imaging Sensor,” PCT/US18/64927, priority date 12 December 2017

M. S. Ünlü, “Interferometric Reflectance Imaging Sensor using Si-based Microfluidics,” *OSA Advanced Photonics,* 2018

(†) R. S. Vedula et al., ‘Self-Referencing Substrates for Optical Interferometric Biosensors,’ *Journal of Modern Optics*, Vol. 57 (16), 2010

(‡) J. Needham, N. Lortlar Ünlü, and M. S. Ünlü, “Interferometric Reflectance Imaging Sensor for Molecular Kinetics with a Low-Cost, Disposable Fluidic Cartridge,” *Biomimetic Sensors, Springer Methods in Molecular Biology*, 2019

(§) E Chiodi et al., “Simultaneous Evaluation of Multiple Microarray Surface Chemistries Through Real-Time Interferometric Imaging,” *ChemRxiv*, submitted to *Biosensors and Bioelectronics*, 2019

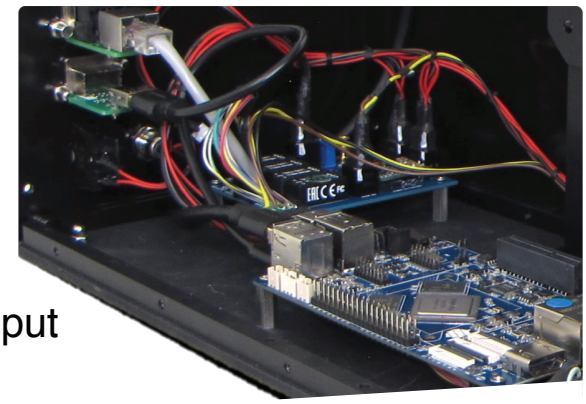
Robust and Automated Instrument

compact, flexible design with scalable throughput

IRIS platform offers:

compact instrument with 12” X 18” footprint including all fluidics.

- Electronic controller integrated with on board computer
- Platform independent user interface, run experiments on your iPad!
- Wireless control
- Fully automated experiments
- 8-channel fluidics
- Small dead volume
- Removable fluidic tray
- Fluidics with flexible configuration
- Future expansion possibility for high throughput



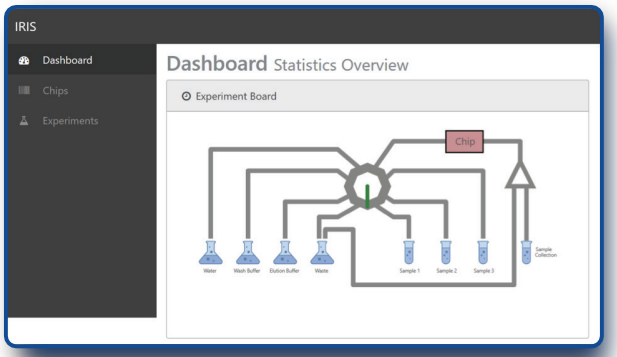
IRIS is configured to have four Eppendorf tubes for samples and four 250ml bottles for wash, buffer and waste. The minimum sample volume is 100 *µl* and can be further reduced.

Video link ☞

Automatic fluid handling allows for collecting and saving a sample. Flowrate can be adjusted across a large range using a syringe pump.

Custom electronic controller is integrated with an on-board computer for image acquisition and processing. User interface is platform independent and can be accessed via a web browser on local WiFi network.

Compatible with handheld devices.
Run experiments using your iPad.
Check the status without leaving your desk.

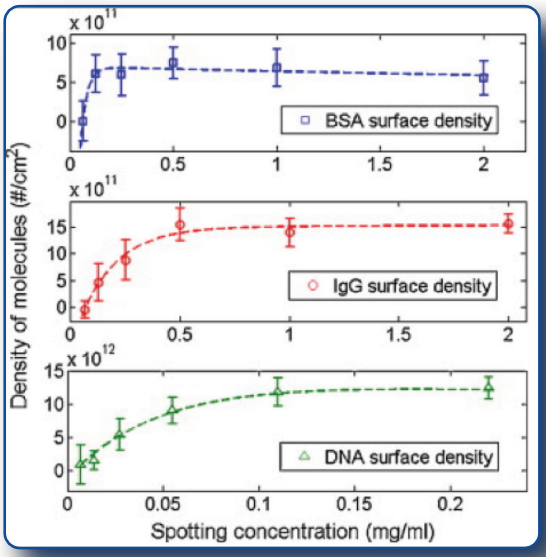


Intuitive graphic user interface to plan experiments.

Automatic spot finding compatible with *.gal* files.

User configurable binding experiments.

Real-time image analysis and curve generation.



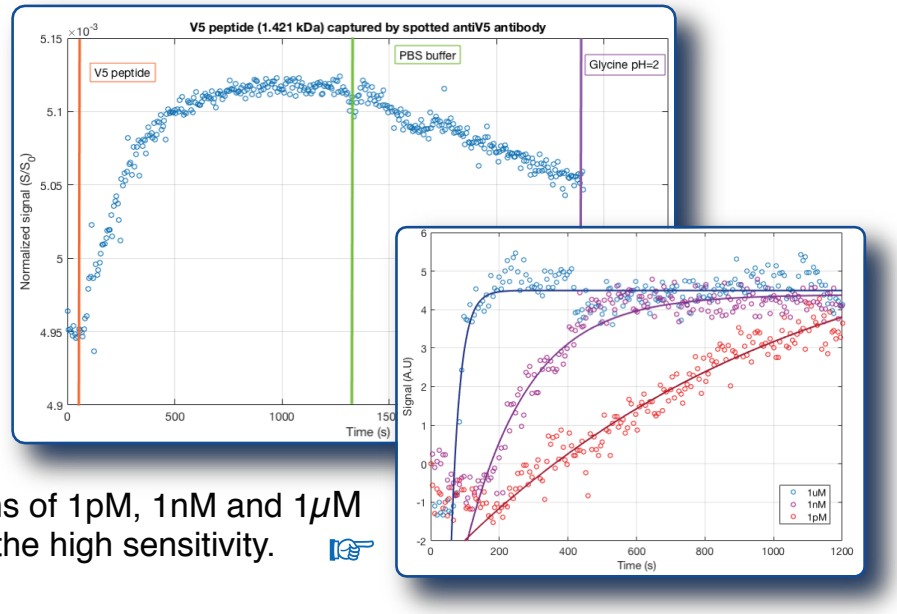
Quantified Measurements:

We have quantitatively calibrated the interferometric sensing to the surface-bound concentrations and masses of adsorbed layers of nucleic acids and proteins allowing us to calibrate the measured height to the absolute density of surface-bound molecules. IRIS has a linear dynamic range of nearly 4 orders of magnitude, which is comparable to standard SPR and considerably better than multiplexed alternative (SPRi) (*).

(*) E. Ozkumur, A. Yalcin, M. Cretich, C. Lopez, D. A. Bergstein, B. B. Goldberg, M. Chiari, M. S. Ünlü, “Quantification of DNA and protein adsorption by optical phase shift,” *Biosensors and Bioelectronics*, Vol. 25, pp. 167-172, 2009

Examples with small MW analytes:

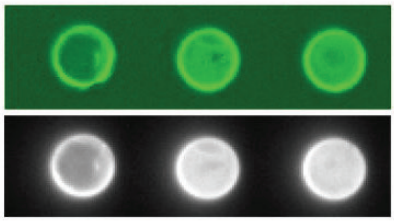
We have demonstrated high signal-to-noise ratio measurements of 1.4 kDa V5 peptide binding to immobilized antibodies. ☞



These results display average signal from 60 spots indicating >10-plex capability for peptide and small molecule analytes.

Biotin (244 Da) at analyte concentrations of 1pM, 1nM and 1μM binding to immobilized avidin validates the high sensitivity. ☞

IRIS Signal



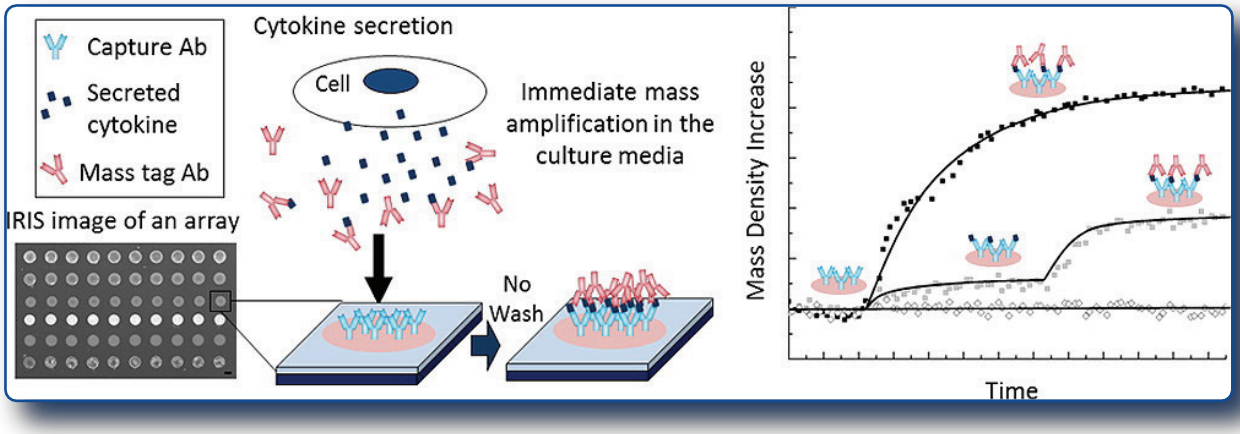
Chemiluminescence

Compatible with Fluorescence and Chemiluminescence:

A dual detection system for protein arrays that combines IRIS with chemiluminescence for hepatitis B surface antigen has been developed. The dual detection system allows to combine the analytical capability of optical interference detection with the established clinical utility of chemiluminescence detection (*). IRIS chips enhance fluorescence intensity by optical interference (†).

Dynamic Detection of Cytokine Secretion:

Monitoring cytokine release by cells allows the investigation of cellular response to specific external stimuli, such as pathogens or candidate drugs. We demonstrated a quantitative dynamic detection of interleukine-6 (IL-6), a pro-inflammatory cytokine and “mass tags” can be used concurrently with the target analyte to eliminate an additional wash and binding step. Successful label-free detection of IL-6 in cell culture medium (with 10% serum) has been reported (‡).



(*) C. Pereira et al., “Synergetic Chemiluminescence and Label-Free Dual Detection for Developing a Hepatitis Protein Array,” *Journal of Immunological Methods*, Vol. 371, No. 1-2, pp. 159-164, 2011

(†) M. Cretich et al., “Interferometric silicon biochips for label and label-free DNA and protein microarrays,” *Proteomics*, Vol. 12, pp. 2963-2977, 2013

(‡) S. Ahn et al., “A Mass-Tagging Approach for Enhanced Sensitivity of Dynamic Cytokine Detection Using a Label-Free Biosensor,” *Langmuir*, Vol. 29, No. 17, pp. 5369-5376, 2013

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