ASSAY DEVELOPMENT · DIAGNOSTIC TRANSLATION

Closing the Assay Development Gap to Multimodal & Multiplexed Diagnostics

The Interferometric Reflectance Imaging Sensor (IRIS) as a single, configurable platform for developing robust diagnostic assays.

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Accurate diagnostic tests depend on translating laboratory assays into clinically deployable formats — a step that often fails when surfaces, biological matrices, detection strategies, or workflows change. This review shows how IRIS supports that transition by evaluating assay performance throughout development, using interleukin-6 (IL-6) as a representative biomarker.

The core idea

IRIS is not a replacement for ELISA, SPR, BLI, or electrochemical sensors — it is a bridge. Label-free imaging, digital counting, nanoparticle enhancement, and multiplexing let it identify limitations early and guide rational design.

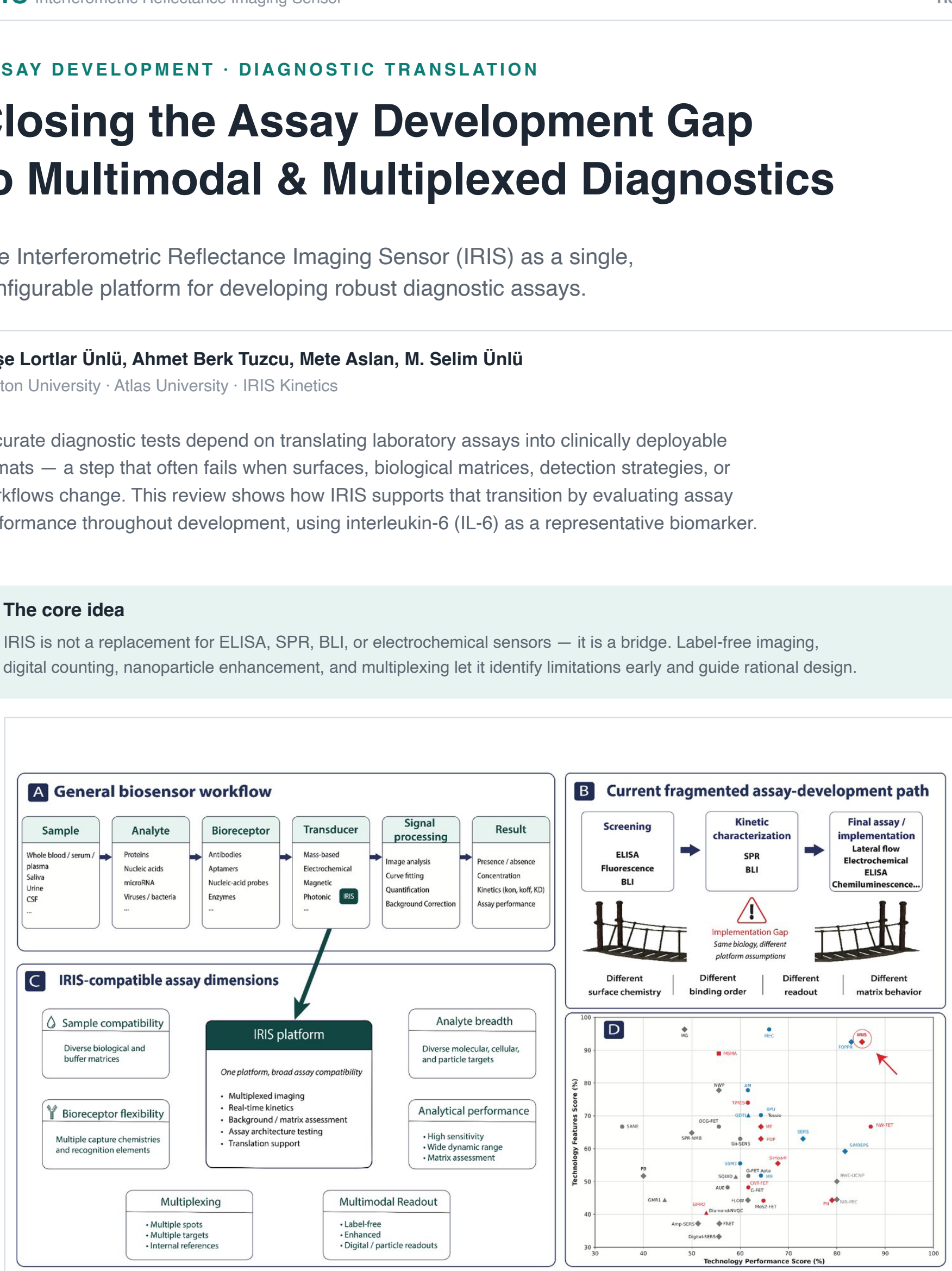


Figure 1. IRIS as a unified photonic platform. (A) General biosensor workflow. (B) Conventional development is fragmented across screening, kinetics, and implementation, creating a gap. (C) IRIS-compatible assay dimensions. (D) Feature–performance landscape.

THE ASSAY DEVELOPMENT–IMPLEMENTATION GAP

A fragmented technology landscape

Assay development relies on a heterogeneous toolkit, each platform optimized for one job but poorly integrated. Components chosen under one set of conditions rarely keep the same performance on a different surface, fluidic regime, or readout — so decisions must be repeatedly re-validated.

ELISA & fluorescence microarrays

Quantitative, accessible benchmarking; but labeled, wash-dependent endpoints miss real-time kinetics and final-format effects.

SPR & BLI

Label-free kinetics and affinity ranking; yet values are platform-dependent and may not predict membrane or electrode behavior.

Lateral flow assays

Simple, rapid, deployable point-of-care format; but capillary transport, drying, and matrix effects demand heavy re-optimization.

Electrochemical biosensors

Compact, inexpensive, quantitative; yet electrode interface, antibody size, and matrix fouling constrain protein assays.

Why translation fails

Surface chemistry, binding order, mass transport, matrix background, and readout mechanism differ at every handoff. Analytical sensitivity alone is not enough without robust, reproducible, integrated development workflows.

IRIS PLATFORM ARCHITECTURE

IRIS images patterned capture arrays on a SiO_2-on-Si chip: bound biomass raises the effective optical thickness, changing reflected intensity — a quantitative, label-free readout supporting ensemble and digital single-particle modes.

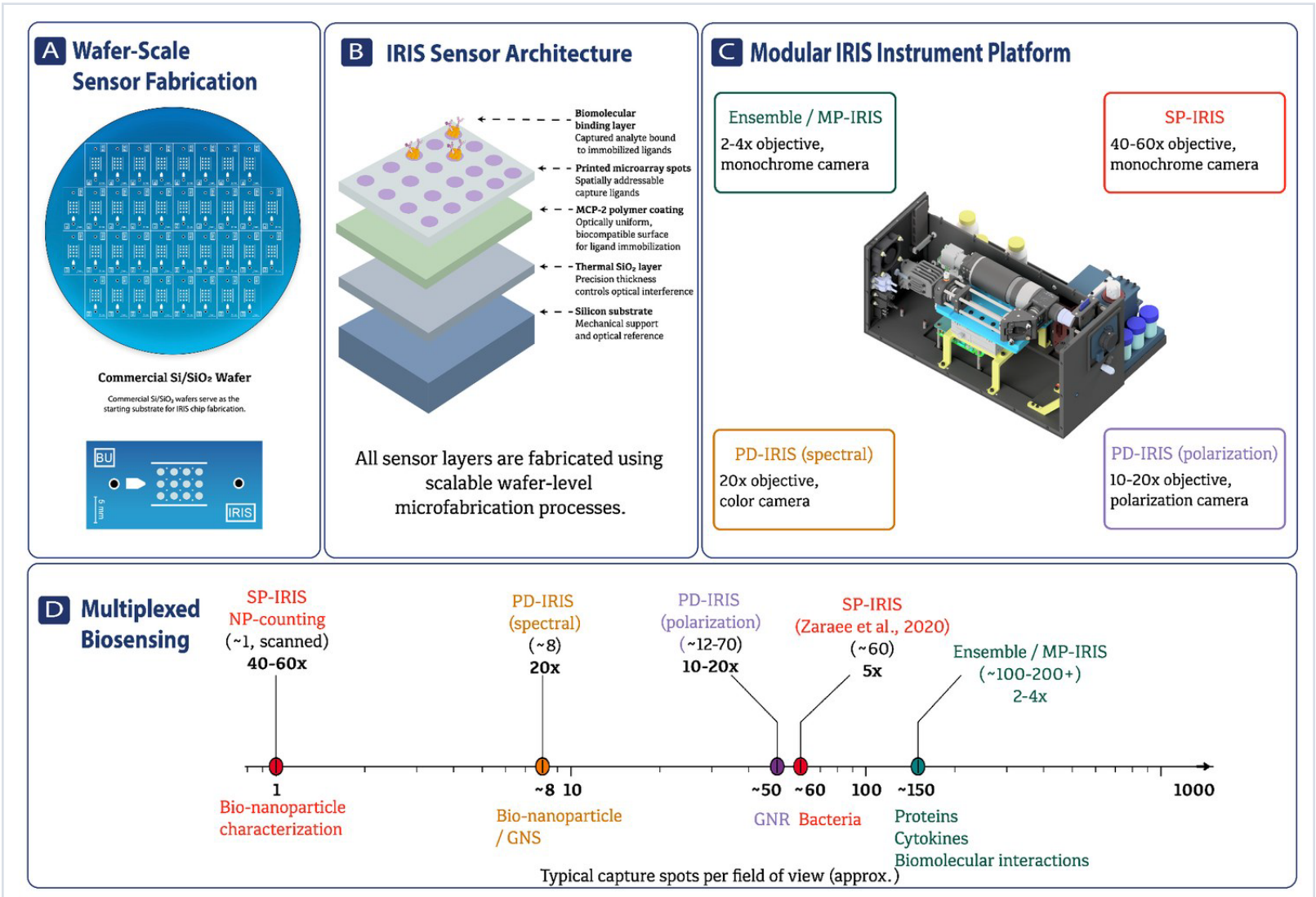


Figure 2. IRIS platform architecture. (A) Scalable wafer-scale fabrication. (B) Layered SiO_2/Si sensor and interference principle. (C) Modular, interchangeable optics enabling multiple modalities. (D) Multiplexed microarray layout.

ONE CHIP, MANY READOUTS

Match the readout to the assay bottleneck

The same interferometric architecture is reconfigured for different problems: label-free sensing for binding and kinetics, nanoparticle enhancement for weak signals, digital counting for discrete targets, and polarization or multiparametric imaging for background and matrix correction.

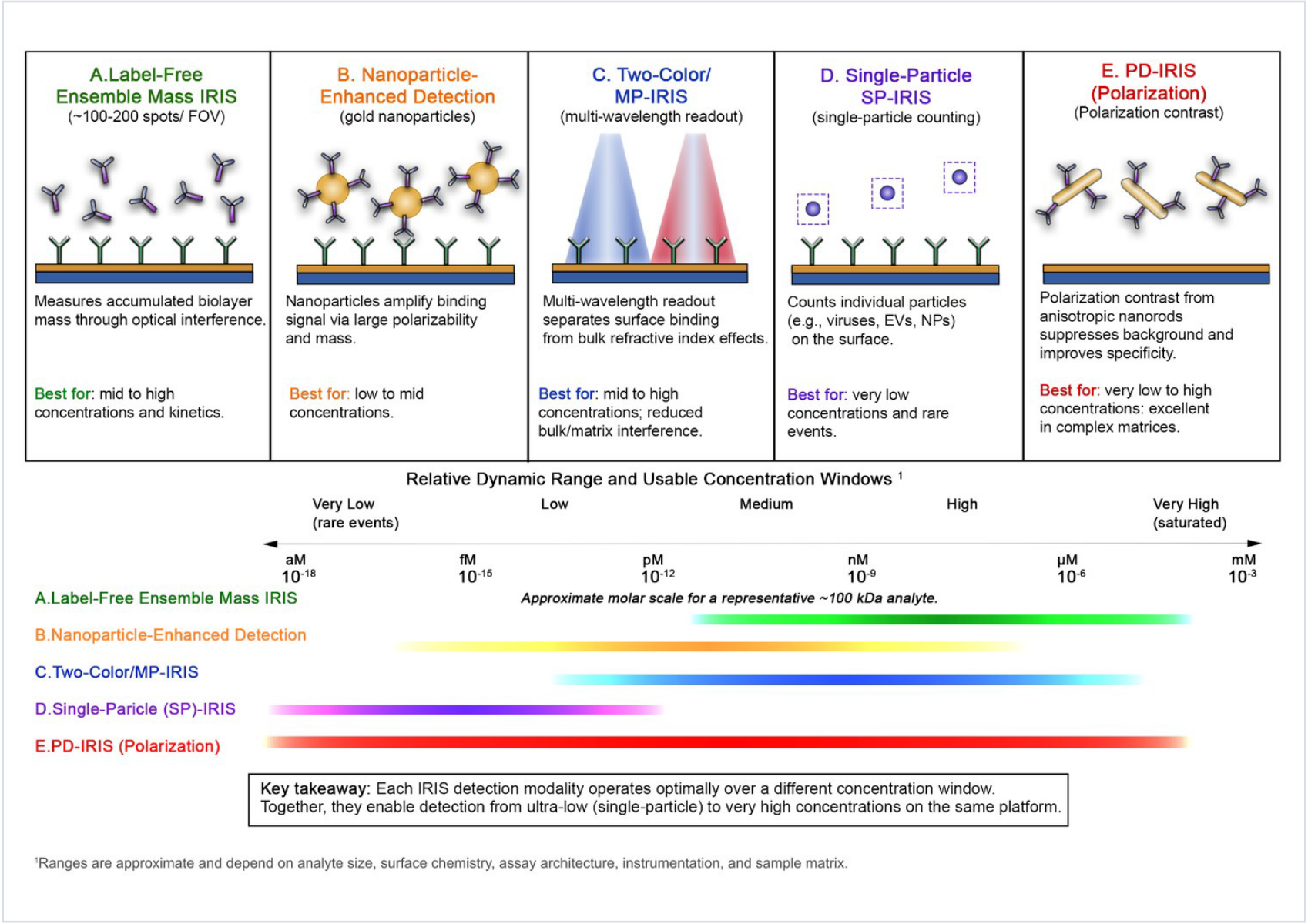


Figure 3. Configurable IRIS detection modalities and their approximate usable concentration windows, from single-particle (attomolar / rare events) to saturated ensemble regimes — complementary ranges on one platform.

A UNIFIED ASSAY-DEVELOPMENT BRIDGE

- **Binder screening**
  Compare capture reagents, surface chemistries, and controls as a spatially resolved experiment — not just endpoint signal.
- **Kinetics & assay order**
  Image the same spots over time to resolve capture, detection, labeling, washing, and dissociation as distinct phases.
- **Matrix & specificity**
  Target, replicate, reference, and negative-control spots in one field of view separate true binding from artifact.
- **Signal & readout choice**
  Start label-free; add gold nanoparticles or go digital only when sensitivity demands — each trade-off checked spatially.

A bridge, not a replacement

IRIS reveals surface, matrix, kinetic, and readout risks early, then guides which established format (ELISA, SPR/BLI, lateral flow, electrochemical) is most appropriate for final validation, manufacturing, and deployment.

CASE STUDY — INTERLEUKIN-6

A clinically hard biomarker, developed on one chip

IL-6 spans a wide clinical range and is challenged by serum background, making it an ideal test of assay development. A multiplexed Si/SiO_2 chip carried anti–IL-6 capture, Protein A/G as positive control, and anti–TNF-α as negative control. Antigen detection antibody 40 nm gold nanosphere (GNS) amplification were each resolved in real time rather than collapsed into one endpoint.

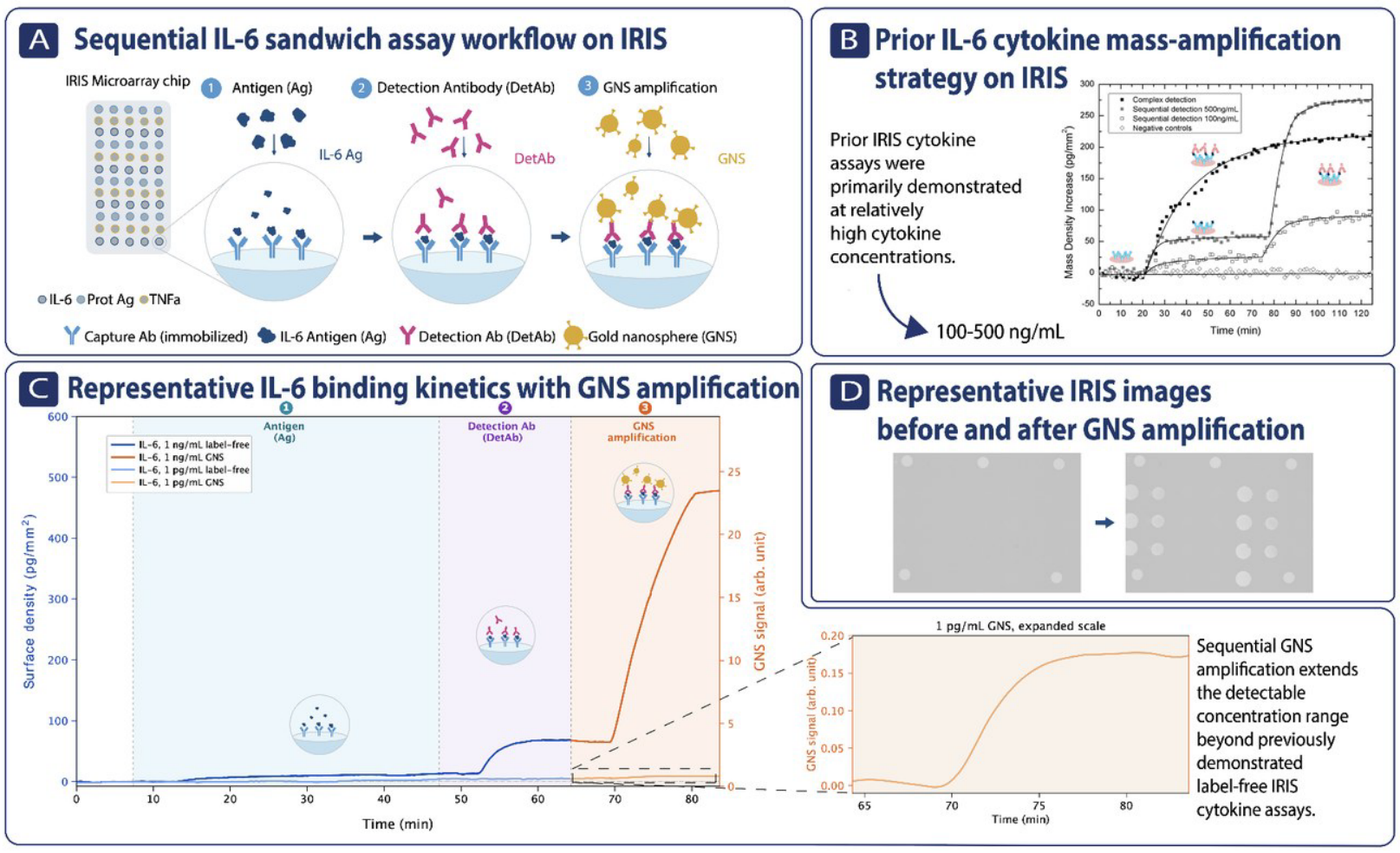


Figure 4. Representative IL-6 assay on IRIS. (A) Sequential sandwich workflow with GNS amplification. (B) Prior cytokine mass-amplification context. (C) Label-free kinetics at 1 ng/mL and 1 pg/mL. (D) FOV and spot images across stages.

1 ng/mL IL-6

+64.7 pg/mm²

cumulative label-free response

1 pg/mL IL-6

+6.2 pg/mm²

label-free, before GNS

+ GNS step

detectable

extends range to low IL-6

CONCLUSION

Modern diagnostics demand development strategies that go beyond optimizing individual methods. IRIS integrates binder screening, kinetic characterization, multiplexed measurement, digital detection, and assay optimization in one framework — reducing the gap between development and implementation while complementing ELISA, SPR, and BLI. Assays optimized on research IRIS can transition to a diagnostic counterpart for high-sensitivity, quantitative, rapid, multiplexed testing with minimal sample preparation.

IRIS

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