INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

FISHss - Fluorescence In Situ Hybridization with Spectral Stoichiometry

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Research Tools and Reagents
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OVERVIEW

Fluorescence In Situ Hybridization with Spectral Stoichiometry (FISHss) is a platform technology that exponentially expands the number of genes measured in spatial omics assays using standard imaging equipment:

- Encodes gene-specific DNA barcodes by stochastically combining fluorescent dyes at single molecule locations, multiplying the detection capabilities compared to existing FISH methods.
- Enables high-throughput multiplexing—scaling from identifying 6 to 56+ genes in one round, and thousands in multi-round experiments—unlocking unprecedented spatial resolution, while using standard confocal microscopes.

BACKGROUND

Spatial transcriptomics allows researchers to see where specific genes are active within a tissue, combining high-throughput sequencing with imaging. This insight is critical for understanding diseases, cell interactions, and tissue architecture. Market growth reflects its transformative potential, with the global multiplex biomarker imaging market projected to reach more than $1.6 billion by 2034, driven by advances in personalized medicine, diagnostics, and spatial biology. However, current FISH technologies face key limitations: they only distinguish a handful of genes at once due to constraints in dye chemistry and encoding strategies, demanding solutions that deliver higher multiplexing capacity without expensive new hardware. FISHss directly addresses this bottleneck, responding to rising market and research demands for

scalable, efficient, and affordable spatial gene analysis.

INNOVATION

FISHss works by assigning DNA barcodes to genes, using combinations of fluorescent dyes with unique emission spectra placed in specific ratios at single molecule sites. Instead of relying on one dye per gene, it mixes two or more dyes; for example, with four different dyes, the platform creates six unique combinations, each matching a gene. By extending this strategy—more dyes, or more "positions"—the system identifies tens to thousands of genes per experiment. Multi-round hybridization further multiplies capacity (e.g., 56 dyes combinations in two rounds yield 3,136 distinct gene readouts). Crucially, this approach maintains sensitivity and robustness and can be visualized using existing confocal microscopy, making it widely accessible, and sidestepping the need for entirely new equipment. Compared to prior methods, which are limited by simple color-coding, FISHss's spectral stoichiometry allows exponential scaling—directly solving the multiplexing problem, lowering cost barriers, and accelerating biological discovery.