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Cell-Free Hydrogel Bead Platform for High-Throughput Protein Characterization and Screening

Stanford researchers have developed a novel, cell-free platform for rapid and high-throughput protein function analysis. This technology harnesses hydrogel bead-based emulsification to parallelize and screen DNA-encoded protein libraries in a scalable, efficient manner.

Proteins are crucial in biomedicine and industry for their functional versatility and engineering potential, with applications in diagnostic assays, therapeutic development, and sustainable biocatalysis. However, existing methods for high-throughput protein characterization rely on time-consuming cell-based assays or complex microfluidics that require specialized expertise and costly equipment, limiting protein engineering, functional characterization, and AI-driven protein design efforts.

The inventors' approach utilizes porous hydrogel beads to encapsulate DNA molecules and form discrete, single bead-templated emulsion droplets, enabling parallelized DNA amplification and *in vitro* transcription and translation (IVTT). Each bead captures a unique DNA template and spatially associates the corresponding protein variant to the same bead, ensuring each protein is paired with and barcoded by its DNA template. With covalent genotype-to-phenotype linkage, this workflow supports large-scale functional assays—including binding, fluorescence, stability, and enzymatic activity screens. The platform is compatible with standard laboratory equipment and numerous proteins and assay conditions, offering an accessible, scalable alternative to traditional techniques and advancing protein design, enzyme engineering, and product development.

Figure

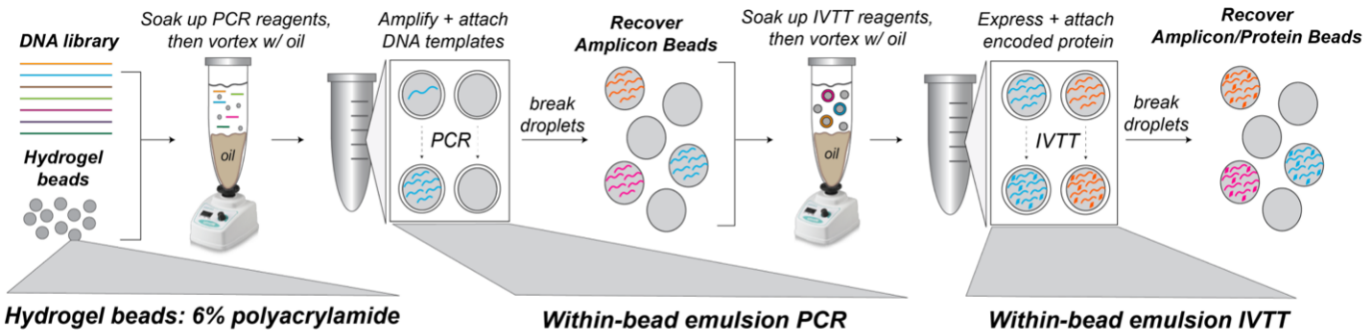

Figure Description: Inventors' workflow for generating hydrogel beads that display a DNA-encoded protein library, enabling downstream protein functional characterization.

Stage of Development
Proof of concept — *in vitro* data

Applications

- High-throughput characterization of large protein libraries in a single assay
- Drug development, discovery of peptide and antibody therapeutics, functional analysis of variant alleles for precision medicine, and industrial biocatalysis innovation
- Rapid generation of rich datasets linking protein sequence to function to train AI models for protein engineering and design

Advantages

- Cell-free workflow enables simplified, scalable protein characterization
- Reliable genotype-to-phenotype linkage ensures efficient and reproducible high-throughput screening
- Compatible with common lab equipment, reducing infrastructure costs and eliminating the need for specialized equipment and training

Publications

- Daria R Passow, Anvita Gupta, Samuel Thompson, Anshul Kundaje, Polly M Fordyce (2026). "Amplicon/Protein Bead Display enables quantitative in vitro biochemistry at scale." *bioRxiv* 2026.05.28.728566.

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