Docket #: S24-293

Optoelectronic orchestrated microdroplet reactors for solid-phase reactions

Stanford researchers have developed a microfluidic system that uses optoelectronics for microdroplet manipulation to build synthetic oligonucleotides. Current solutions for building oligonucleotides suffer from high error rates, low yields as the chains get longer, and high solvent use and waste production.

The Stanford device (Figure 1) is inexpensively fabricated using standard PDMS soft lithography mass manufacturing technology. Multiple integrated microfluidic channels introduce single droplets of consistent size onto the optoelectronic substrate. The optoelectronics precisely encapsulates and decapsulates individual solid supports (i.e., polystyrene microbeads) with corresponding picoliter volume reagent microdroplets. Complete encapsulation ensures uniform reagent exposure, which reduces errors and improves the final yield rate significantly. In addition, picoliter droplet reactors replace microtiter plates, which reduces reagent consumption and waste generation by up to a million-fold. The Hesselink Group successfully demonstrated the on-chip enzymatic oligonucleotide coupling reaction and are adapting the platform for a wider range of reactions. This light-orchestrated microdroplet reactor platform provides quicker, more affordable, more efficient, and sustainable oligonucleotide synthesis.

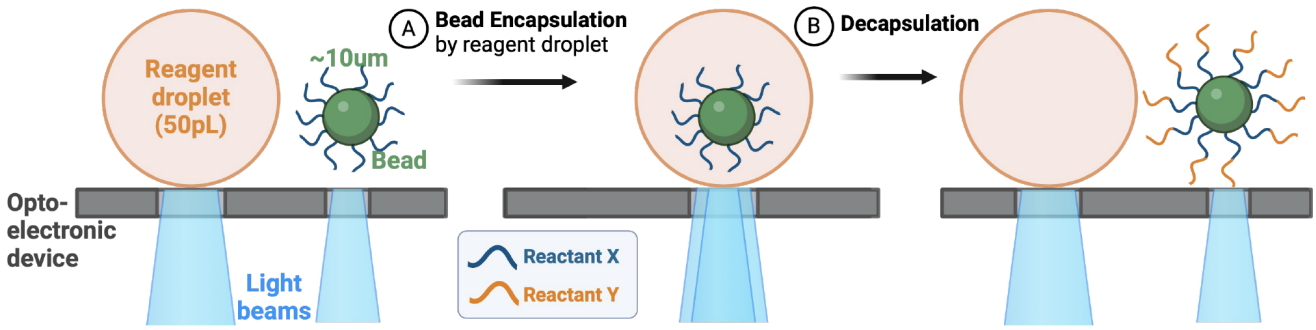


FIgure 1 Schematic light-orchestrated microdroplet reactors for solid-phase reactions

Stage of Development – Prototype
The Hesselink Research Group successfully demonstrated ssDNA ligation through copper-catalyzed azide-alkyne cycloaddition (CuAAC) using the platform. The group continues optimization and research expanding possible applications.

Applications

- **Compact benchtop DNA printer** for researchers
- Quick, affordable, **custom oligonucleotide, peptide, and organic synthesis** for biotech and pharmaceuticals
- **Automated solid-phase assays** for disease diagnosis and drug discovery screening
- **Automated solid-phase extraction (SPE) and solid-phase combinatorial chemistry reactors** for pharmaceutical analysis and development, environmental testing, and forensic science

Advantages

- **Lower error rate and higher yield** long strand oligonucleotide and peptide synthesis through uniform reagent exposure, and higher spatial resolution droplet delivery compared to current microarray based solid-phase synthesis platforms
- **Affordable, more sustainable, million-fold waste reduction** through reduced reagent consumption

- **Expected higher throughput** as picoliter sized droplet reaction rates are expected to be faster than existing larger reagent volume platforms

Publications

- Wu, M. (2024, 16-22 August). *Light-orchestrated microdroplet solid-phase reactor towards efficient and sustainable oligonucleotide synthesis* [Conference Presentation Abstract]. ACS Fall 2024, Denver, CO, United States.
- Padhy, P., Zaman, M. A., Jensen, M. A., Cheng, Y. T., Huang, Y., Wu, M., Galambos, L., Davis, R.W., & Hesselink, L. (2024). Dielectrophoretic bead-droplet reactor for solid-phase synthesis. *Nature Communications, 15*(1), 6159.

Patents

- Published Application: WO2026039758

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