Embedded droplet printing-technology controllably prints and processes droplets that are suspended in place

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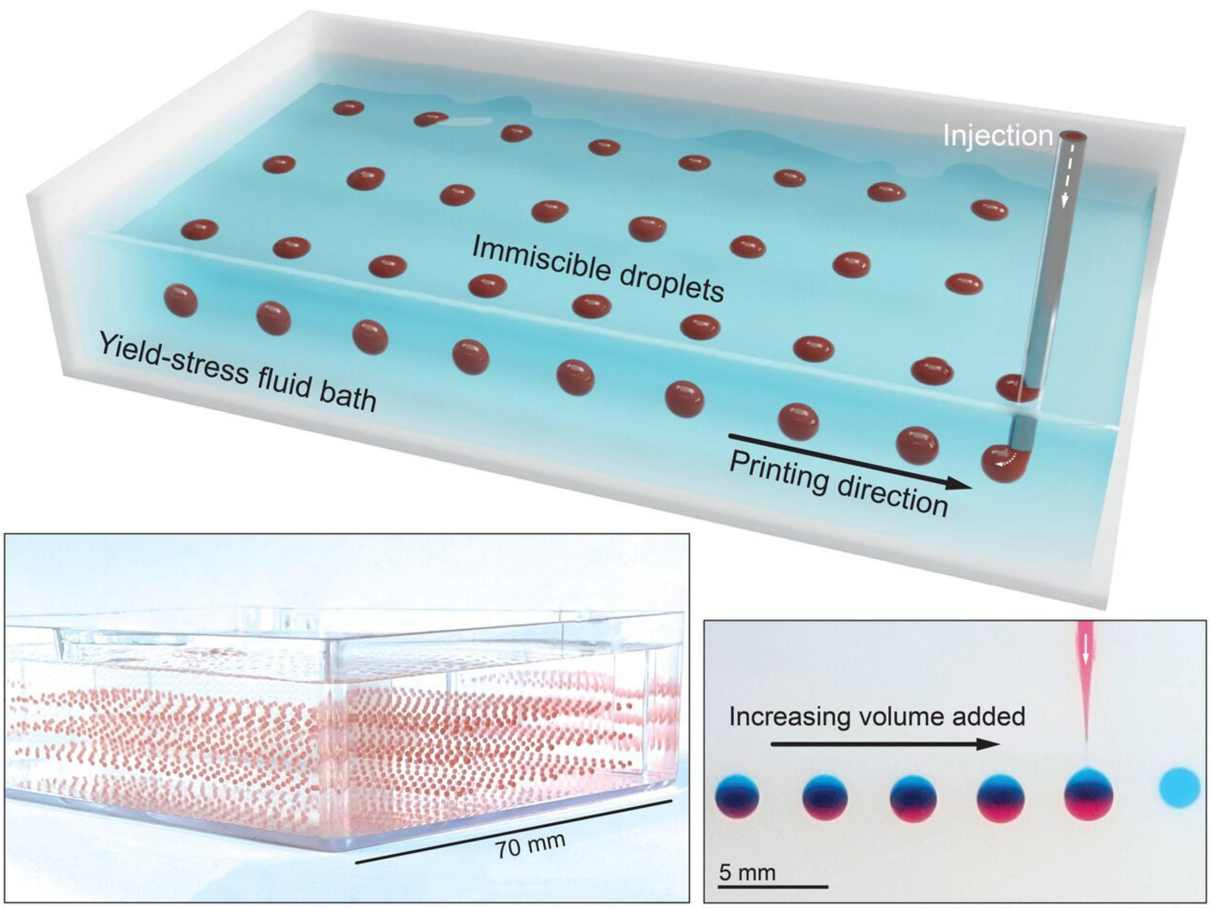

The new embedded droplet printing method suspends 3-D arrays of droplets in a uniquely isolated state that allows for precise processing and experimentation Credit: Singapore-MIT Alliance for Research and Technology (SMART)

Researchers from Singapore-MIT Alliance for Research and Technology (SMART), MIT's research enterprise in Singapore, and National University of Singapore (NUS) have developed a unique method for generating and processing fluid droplets under previously unattainable conditions. The discovery can be transformative in a range of scientific applications including the study of biological and chemical processes, and can pave the way for more exquisite and targeted pharmaceutical and consumer products.

The new process is explained in a paper titled "Embedded droplet printing in yield-stress fluids", published in the prestigious journal, *Proceedings of the National Academy of Sciences* of the United States of America (*PNAS*).

Dr. Arif Zainuddin Nelson, a researcher under SMART and Intra-CREATE's project Advanced Manufacturing of Pharmaceutical Drug Products using Modular Microfluidic Processes, led the development of the new method, which is the first of its kind to take advantage of yield-stress fluids to create the ideal conditions for experimentation, processing or observation of samples. Using the embedded droplet printing approach, the research team was able to produce suspended and perfectly spherical drug-laden particles. The new approach avoids malformations that are common in conventional methods, which produce particles that are ovoid in shape and result in poor flowability during manufacturing of medicines.

"We have developed a set of tools that allows us to observe and process many different applications under this unique method, including chemical and biological reactions," said NUS Professor Saif Khan, who is also part of the research team. "Pharmaceuticals is just one of the areas where this could produce transformative results, which is where our work is focused. We could change the way drugs are made, formulate them in a way that improves quality, revolutionize the way existing drugs are taken by patients, and envision entirely new drugs that cannot be made today."

The embedded droplet printing method, which can also be used to alter the size and dosage of existing drugs, would be particularly useful for designing high potency medicine that needs to be taken in very small doses, such as drugs taken by cancer patients. It can also lead to more tailored medicine as the new process would make it easier to develop small batches of specialized drugs for specific patients.

"With the exception of going into space to be in zero-gravity, this method is the only way to achieve an environment where various processes can be observed in such an isolated state," said Dr. Nelson. "However, achieving a zero-gravity state is prohibitively expensive, and we have created a substantially easier and cheaper process to achieve a unique environment where chemical and biological processes are undisturbed by the outside forces."

For pharmaceuticals, Intra-CREATE's new microfluidic process would circumvent the capital costs for the formation of high-quality drugs, leading to potentially cheaper medication, as well. The microfluidic process can also enable a range of other applications outside of the manufacturing of medicine, including:

- Antibiotic testing: bacteria colonies can be cultured within each individual droplet. Antibiotics and dosages can be tested on each droplet to quickly provide doctors and researchers with a view on potential antibiotics and cures. The unique environment allows manipulation of droplets in a way that could simulate infections
- Embedded chemical reaction chambers: Microfluidic systems are able to handle a high throughput of small and precise volumes of reagents. The new process enables an improved environment for chemical reactions by removing solid boundaries, and can be

used for nanoparticle production

Co-author of the research paper, MIT Professor Patrick Doyle, said, "The new microfluidic process can be a gamechanger in a range of scientific experimentation, and the generality and wide impact of this method couldn't have been achieved without SMART and NUS working together."

More information: Arif Z. Nelson et al. Embedded droplet printing in yield-stress fluids, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.1919363117

Provided by Singapore-MIT Alliance for Research and Technology

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