Biocompatible microfibers developed as the basis for tissue engineering

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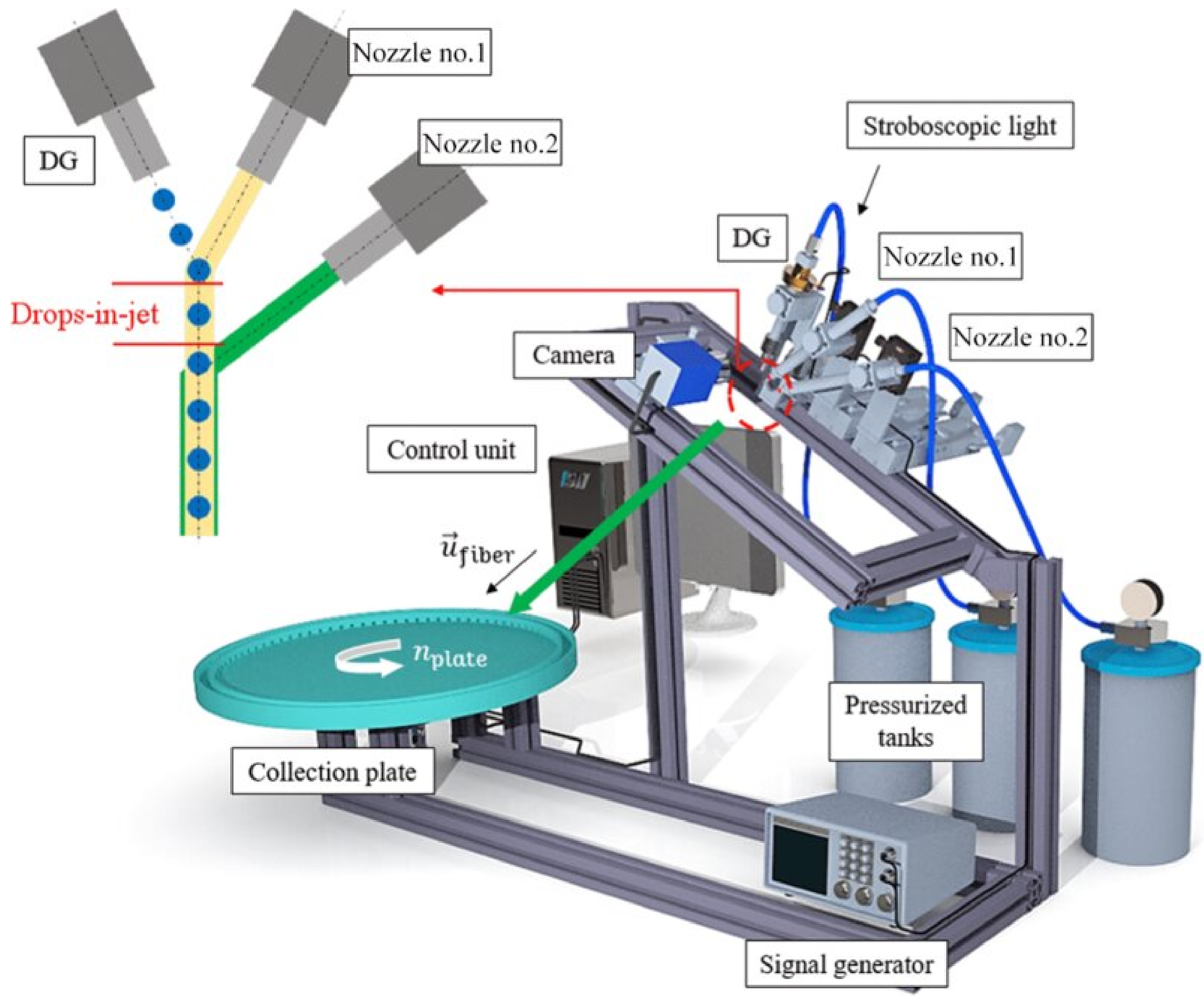


Schematic illustration of the experimental setup (prototype) designed for the production of advanced fibers. (Left) Zoom into the two subsequent collisions respectively involving droplets (blue) and jet_1 (yellow), and the drops-in-jet structure with jet_2 (green). (Right) Overview of the various components enabling the controlled collisions and collection. Credit: *Physical Review Applied* (2023). DOI: 10.1103/PhysRevApplied.19.054006

In biomedical technology, tissue engineering for the ex-vivo production of skin or organs is becoming increasingly important. This requires biocompatible microfibers with enclosed microcapsules of controlled size and shape, as the cells used for tissue engineering must be embedded in material that is as similar as possible to the natural arrangement in vivo.

Until now, the production of such fibers at low output has been quite costly and time-consuming. Researchers at Graz University of Technology (TU Graz) have now developed a new method for producing microfibers with the desired properties that can be used in pharmaceuticals and biomedicine, and which provides significantly higher yields than previous methods while requiring much less production effort.

In a paper published in *Physical Review Applied*, Carole Planchette and her team from the Institute of Fluid Mechanics and Heat Transfer at TU Graz explain how their development can produce several meters of this microfiber in seconds. The current methods manage at most a few centimeters in the same period of time.

This acceleration has been made possible by moving away from the production of microfibers in a liquid environment using microfluidic chips to a production that is possible in sterile room air. As a result, the necessary process steps as well as the costs were greatly reduced and potential sources of errors and blockages minimized.

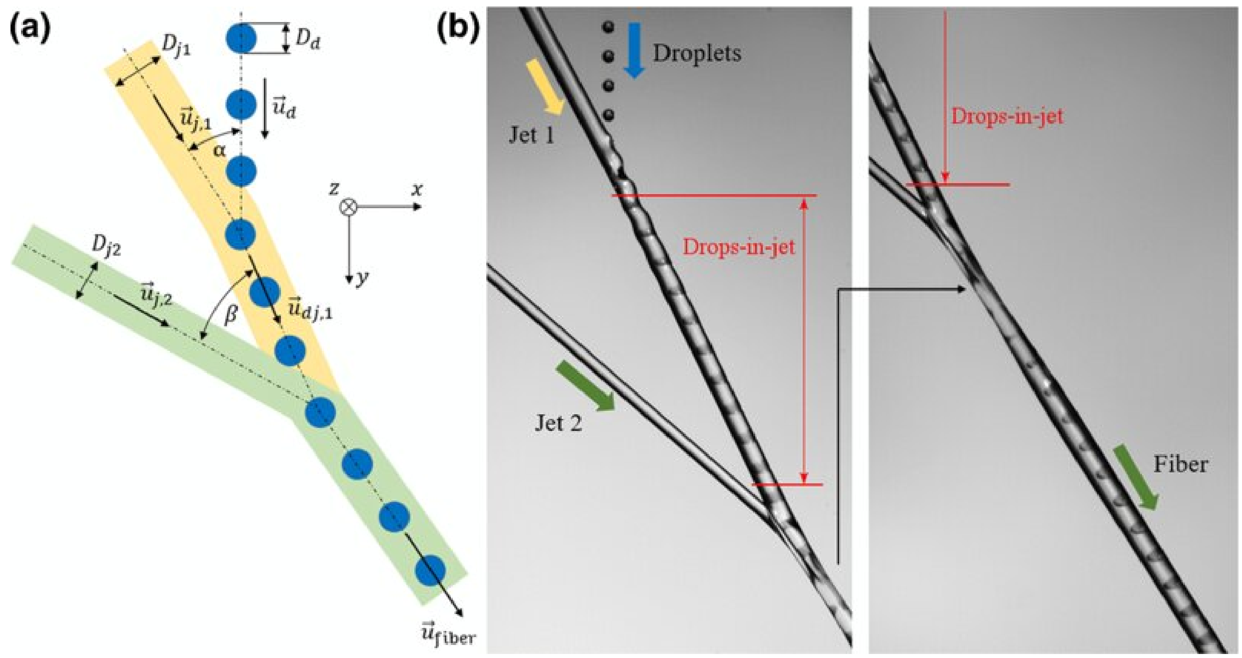
Droplets meet liquid jet

In the new method, a regular stream of droplets containing cells or active substances is combined with a liquid jet of aqueous alginic acid solution. The alginic acid obtained from brown algae forms upon contact with calcium cations an elastic hydrogel called alginate—similarly to the process commonly used in molecular cuisine to form caviar pearls.

This hydrogel is fully biocompatible and also prevents the embedded droplets from coalescing together. Therefore, to cure the alginic acid solution stream, a second stream with calcium cations is jetted continuously on top. The resulting fiber, which can be grown at up to 5 meters per second, can then simply be collected on a turntable. All these steps take place in the air and not in liquid microfluidic production as before.

In a few years, it should be possible to produce a fiber assembly mimicking the skin from human cells using this new method. The integration of cells into the microfiber is the next step for Planchette and her team. The expected result could be, for example, a great help for burn victims, as new and personalized skin for transplantation could be produced from a patient's own intact skin cells in a very short time.

In this perspective, researchers at TU Graz are working together with the Medical University of Graz on research into the production of artificial skin. Looking much further into the future, certainly more than ten years, one day it may also be possible to produce artificial organs using this microfiber.



(a) Kinetic and geometric parameters relevant for the production of fibers with regular inclusions. (b) Pictures of the collisions observed in the collision plane. The collisions between the droplets and jet_1 enable the formation of the liquid drops-in-jet structure, which subsequently solidifies thanks to the supply of cations ensured by the collision with jet_2. Credit: *Physical Review Applied* (2023). DOI: 10.1103/PhysRevApplied.19.054006

Replacement for animal testing

In addition to tissue engineering, the new and faster production method opens up other areas of application for the biocompatible microfiber, such as cell screening. In the near future, it will be possible to test new molecules for medical agents much more extensively on cells to determine whether or at what point they are toxic.

Due to the available fiber length, different temperatures or concentrations could be tested in a single run. For such tests on a large scale, animal experiments have been used up to now, and this could be largely avoided.

"For me, it is particularly interesting when I can use fundamental aspects of fluid mechanics to find new and innovative solutions to previously unsolved problems," explains Planchette.

"This allows us to discover pathways to new applications and our manufacturing method of biocompatible microfibers with regular inclusions at high output and low cost demonstrates this. The possibilities for cell screening, tissue construction and eventually organ production that this opens up can be of great benefit to many disciplines. For me, this is also a clear sign of how important the role of basic and multidisciplinary research is, thereby creating the fundament for ground-breaking applications."

More information: Francesco Marangon et al, In-Air Microfluidic Strategy for the Production of Sodium Alginate Fibers with Regular Inclusions at Very High Throughput, *Physical Review Applied* (2023). DOI: 10.1103/PhysRevApplied.19.054006

Provided by Graz University of Technology

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