effect on senescence. Moreover, telomere erosion was not apparent, suggesting that some cells senesce by telomere- and p16-independent mechanisms. One possible mechanism is DNA damage caused by the reactive oxygen species that mediate RAS-dependent mitogenic signals (*6*).

Finally, Braig *et al*. (*5*) used a mouse model in which oncogenic Ras (Eμ-*N-Ras*) is constitutively expressed in hematopoietic cells. The study shows that a deficiency in Suv39h1, a histone methyltransferase, markedly accelerates the development of lethal tumors. Suv39h1 is thought to promote the heterochromatic silencing of growth-promoting genes in senescent cells. This silencing causes the senescence response of lymphocytes to oncogenic Ras. Lymphomas that develop in Eμ-*N-Ras* mice undergo senescence in response to chemotherapy, but this did not occur in Suv39h1-deficient tumors. Rather, Suv39h1-deficient tumor cells underwent apoptosis. Thus, cell senescence suppressed lymphomagenesis in these mice.

Together, these papers support the idea that cellular senescence, like apoptosis, plays an important role in suppressing tumorigenesis in mice and humans in vivo. Needless to say, many questions remain. What are the mechanisms that determine whether cells undergo senescence or apoptosis when challenged by potentially oncogenic insults? Are there pathways other than the p53 and p16-pRB pathways that cause the senescence response? And, is senescence as effective as apoptosis at preventing cancer? The latter question is especially important because senescent cells secrete factors that can stimulate the proliferation and malignant progression of neighboring cells (*7*, *8*). And thus, a potential irony lurks: Prolonged presence of senescent cells may eventually facilitate the development of malignant cancers from benign lesions.

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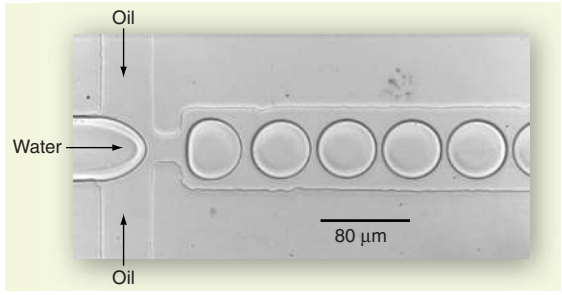
APPLIED PHYSICS

# Droplet Control for Microfluidics

**Mathieu Joanicot and Armand Ajdari**

Nanoliter droplets of uniform size spontaneously form in microchannels when two immiscible fluid streams merge (*1*) (see the figure). This nonlinear process involves basic physics (*2*), with the local geometry and surface chemistry of the microchannel strongly affecting the competition between viscous forces tending to draw the fluids along the channel and capillary forces tending to form droplets so as to minimize the total interface between the two fluids. This results in droplets of sizes comparable to the channel diameter (*3*), and these sizes can be tuned by adjusting the flow rates of the various streams (*4*, *5*). The determination of which liquid is inside the droplet and the extension of the regime where droplets are emitted periodically are controlled by the wetting competition (which fluid preferentially interacts with the channel surfaces) and by added surfactants (*6*). This new route for easy and steady production of calibrated emulsions opens a stimulating field for applications of microfluidic devices [for a recent review, see (*7*)].

Typical microfluidic channel sizes (height and width) are in the range of 10 to 100 μm, and flow rates are between 10 and 1000 nl/s. This leads to nanoliter-size droplets, produced at frequencies of 10 Hz to 10 kHz, moving at speeds from micrometers per second to centimeters per second. As a result, these tiny droplets are almost ideal chemical reactors because they create homogeneous controlled conditions (*8*). In the first place, the very high surface-to-volume ratio (owing to the small size of the droplets) grants very fast thermal transfer. In addition, each droplet moves as an independent nanoliter batch reactor, with no hydrodynamic dispersion. For a steady flow, each location along the channel directly corresponds to a unique residence time after droplet formation. And internal recirculation within the droplet permits fast and efficient mixing, especially if wiggly channels are used (*8*). Such ideal reactors allow one to follow reactions in time. An interesting tool for such studies is confocal Raman microspectroscopy, which can be used to determine the chemical composition anywhere along the channel, providing a mapping that is a direct measurement of the whole kinetics at once. For short distances and high flow rates, reaction times as short as a few milliseconds can be measured (*8*). By varying the initial composition of the droplets, one can assess its effect on yield and kinetics, providing a useful operational research tool for laboratories. Control of residence time also enables synthesis of quite monodisperse small particles within the droplets.




**Tunable droplets.** Water droplets form at a rate of 1000 per second in an asymmetric microchannel containing hexadecane. The channel is 30 μm high.

There is another area in which these devices can be valuable tools for materials engineering, namely the transformation of each droplet into a single colloidal object. For example, one can dissolve the desired molecules or polymers into an organic phase and flow the latter into an aqueous stream to generate droplets. To dry the resulting emulsion, the organic solvent is either exchanged with the aqueous phase or slowly evaporated through it. A last step of ultraviolet-induced cross-linking or polymerization can then be used to solidify the colloids. The polydispersity of the particles can be as low as a few percent, far better than what is achievable with classical means of generating emulsions. Colloids of various shapes (disks, cylinders, and so forth) can be obtained by solidifying confined droplets (*9*). Monodisperse droplets of liquid crystals can also be obtained (*10*).

As suggested earlier, the use of hydrophobic channels results in formation of water droplet in a stream of hydrophobic liquid (oil), whereas hydrophilic channels favor creation of water-in-oil droplets. Now imagine a two-step process whereby a hydrophobic channel, in which a water-in-oil emulsion is generated, connects to a hydrophilic channel in which water flows. This can result in a multiple emulsion of

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water-in-oil-in-water (*11*) by encapsulation of the initial simple emulsion. In principle, the size, the number, and even the composition of the drops can be controlled at each step of the process, leading to a unique way of producing monodisperse, perfectly controlled, multiple emulsions. However, mastering the surface properties of the channel is a prerequisite for this process to run smoothly and controllably. A way around this is to produce the multiple emulsion in one step, using three concentric flows so as to avoid contact of the inner streams with the channel wall. Such a geometry is difficult to fabricate within the usual two-dimensional microfluidic structures obtained by lithography, but it was recently achieved with a clever multiple-micropipette device. Monodisperse core-shell particles and capsules (*12*) were obtained, as well as polymerosomes of controlled sizes synthesized from block copolymers (*13*).

Microfluidics can thus be a powerful and versatile tool for materials or colloidal engineering. It is the only technique that can produce 100% encapsulation of an active substance by means of a one-step process. Engineering new controlled materials then becomes a game limited only by the number of combinations of the basic products, and by one's imagination.

A controversial question naturally follows: Besides being a smart research tool, can microfluidic droplet devices be used as production tools (chemical plants on a chip)? With a flow rate of 1000 μl/hour per channel, one needs 1000 channels in parallel to produce a liter of material per hour. High levels of integration can be reached on a chip, but likely a linking up of many devices will be necessary, potentially leading to complications for connections and control. Developing the corresponding technology may be economically sensible only for materials with very high added value (such as those in biology, pharmaceuticals, or cosmetics), but not for conventional chemistry or basic material production.

A large number of research reports and patents attest to the ongoing attempts to develop new research tools for biological or pharmaceutical applications by means of droplet microfluidics. The goal is to handle the many droplets that can be generated with only a minute amount of material, and to divide and recombine them in a multiplicity of nanoreactors so as to perform high-throughput screening and combinatorial studies (*14*). Some would like to see this approach as the next-generation technology that will replace the widely used combinatorial robotic platforms.

What is required is on-chip control and reproducibility of many droplet processes: fabrication, sorting, storage, fusion, breakup, and trafficking (*3*, *8*, *15*), among others. For example, droplet generation is currently controlled by tuning the input flow rates. Unfortunately, this affects simultaneously the frequency, size, composition, and speed of the droplets, whereas one would want to control each of these parameters independently. A natural microfabrication strategy is to integrate actuators to achieve local control of droplet motion. Pneumatic actuators have proven highly integrable in a different microfluidic context (*16*), and electrostatic actuation with integrated electrodes is also being investigated. The gain in control may unfortunately result in somewhat sophisticated and specialized chips with limited flexibility and versatility. It may be necessary to standardize a few basic on-chip functions, with a drift toward passive strategies that often combine simplicity and robustness.

Improvements in design should be guided by attention to basic physics and chemistry. Interfaces are essential at such small scales, and surfactants should be avoided as much as possible. Hence, a synergy between microfabrication requirements and surface chemistry is needed to yield robust channel wetting properties. This will create the needed reproducibility of droplet generation for a range of flowing liquids and flow rates. The complex dynamics of thousands of droplets flowing in channels with long-range hydrodynamic correlations will require modeling, possibly with the help of concepts borrowed from dynamical system theories. The result will be the design of smart network topologies and (ideally passive) functionalities (*15*), opening the way to control, reproducibility, and versatility in on-chip droplet management, ultimately at the droplet level.


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PLANETARY SCIENCE

# The Enigma of the Martian Soil

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Since the two Viking landers touched down on Mars in 1976, the ubiquitous surface soil and dust have defied attempts to model their properties and understand how they formed. The fine soil that gives Mars its red color holds clues to the presence of liquid water, the rock weathering processes, and the potential biological history of the planet. Through dust storms, it plays a key role in the climatic cycles of Mars. It may hamper exploration by interfering with robotic and human performance, but may also offer a valuable resource by supplying water and fuel and supporting plant growth and food production. What is known and what is still puzzling about the martian soil? And do we have similar soils on Earth? Recent results from the Mars exploration rovers Spirit and Opportunity and from terrestrial studies add to our understanding and open new questions.

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Data from the Viking landers and orbiters and the Pathfinder rover (*1*–*6*) show that the surface of Mars is covered by a blanket of fine-textured soil compositionally similar to the atmospheric dust (see the figure). The soil contains silicon, iron, aluminum, magnesium, calcium, titanium, sulfur, and chlorine at unique elemental proportions (that is, relatively rich in sulfur and chlorine compared to most terrestrial soils). It lacks organic matter and shows strong oxidizing activity—a combination that suggests the possibility of rapid chemical decomposition of organic matter leading to the decimation of living organisms. It is rich in

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