Microfluidic Devices

ESI Special Topics: September 2007
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A Research Front Map INTERVIEW with Dr. Rustem Ismagilov

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In the interview below, Special Topics talks with Dr. Rustem Ismagilov about his paper, "A microfluidic system for controlling reaction networks in time" (Song H, Tice JD, Ismagilov RF,* Angew. Chem. Int. Ed. *42[7]: 768-72, 2003), which is part of our Research Front on Microfluidic Devices, with 100 citations to its credit. In Essential Science Indicators℠, Dr. Ismagilov's record includes 63 papers, mainly in the field of Chemistry, with 2,160 cites to date. Dr. Ismagilov is Associate Professor in the Department of Chemistry and the Institute for Biophysical Dynamics at the University of Chicago.

ST: Would you please describe the significance of your paper and why it is highly cited?

We recognized that standard single-phase microfluidic experiments were limited by two problems—slow mixing and the dispersion of solutes along the channel (which occurs even in the absence of flow). This manuscript describes our microfluidic system to overcome these limitations by localizing reagents within aqueous droplets, or "plugs," separated by water-immiscible carrier fluid, and utilizing chaotic advection to achieve rapid mixing within plugs.

Emulsions have been a focus of a broad range of work, including microfluidics, but this system described how droplet-based microfluidic systems may be used for performing chemical reactions and assays. For example, there is a simple method of forming plugs of multiple reagents at controlled concentrations—an essential component for performing reactions in plugs.

Dr. Rustem

We also devised methods for splitting and merging these plugs to create complex microfluidic networks that can

"We are now able to use microfluidics to study complex biochemical networks including blood

Ismagilov's most-cited paper with 218 cites to date:

Kenis PJA, Ismagilov RF, Whitesides, GM, "Microfabrication inside capillaries using multiphase laminar flow patterning," *Science* 285(5424): 83-85, 1 July 1999. 218 cites.

Dr. Rustem Ismagilov's paper(s) represented in the Research Front map with 100 cites to date:

Song H, Tice JD, Ismagilov RF, "A microfluidic system for controlling reaction networks in time," *Angew. Chem. Int. Ed.* 42(7): 768-72, 2003.

Source: *Essential Science Indicators*.

be used for high-throughput parallel analysis of samples. This system also enables the conversion of spatial evolution of chemical systems into temporal evolution (the conversion of distance into time).

coagulation (hemostasis) and protein crystallization."

This fundamental technology offers unprecedented control over chemical reaction networks on the nanoliter scale from milliseconds to years and paved the way for the use of microfluidics for many important chemical assays, including high-throughput screening and optimization of reaction conditions, organic reactions, kinetic assays, and protein crystallization, and even the synthesis of reaction networks on-chip.

ST: How did you become involved in this research, and were there any particular successes or obstacles that stand out?

My lab focuses on understanding complex biochemical systems at the organismal, network, and molecular levels. We developed droplet-based microfluidics to overcome the limitations of traditional microfluidics and extend the applicability of microfluidics to study these systems. We are now able to use microfluidics to study complex biochemical networks including blood coagulation (hemostasis) and protein crystallization.

ST: Where do you see your research and the broader field leading in the future?

Miniaturization and microfluidics are making a big impact across many fields, from engineering to biology. Technology is advancing at a rapid pace and tools are being developed to give us unprecedented abilities to control chemistry and biology on many time and length scales. We are working to take advantage of these advances and push the field in new directions.

We are particularly interested in the potential for microfluidics to bridge the gap between current and powerful analytical methods and the complex biological systems that are difficult to study because of size or time constraints. In addition, these systems are proving to be practically useful.

ST: What are the practical applications of your work, if any?

Microfluidic and other lab-on-a-chip technologies have innumerable practical applications in engineering, physics, biology, and chemistry. We and others have developed microfluidic technology to enable high-throughput crystallization of soluble and membrane proteins on the nanoliter scale for pennies per trial. In addition, there is a broad effort to develop high-throughput methods of performing reactions and assays in droplet-based systems.

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Chicago, IL, USA

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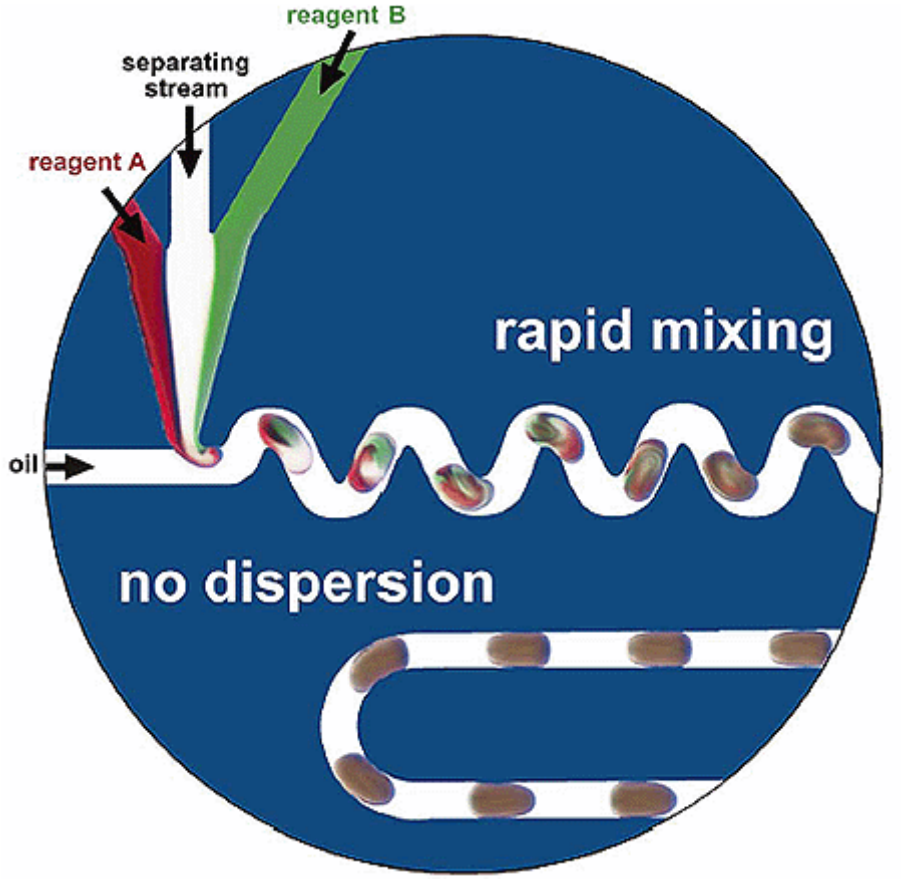
A Closer Look...

Below are images sent in by Dr. Rustem Ismagilov which correspond with the featured paper, or current research.



Aqueous droplets of 250 pL formed in a microfluidic channel in a continuous flow of a water-immiscible fluid act as microreactors that mix the reagents rapidly and transport them with no dispersion. These Droplets may also be used to control chemical reaction networks on millisecond time scale.

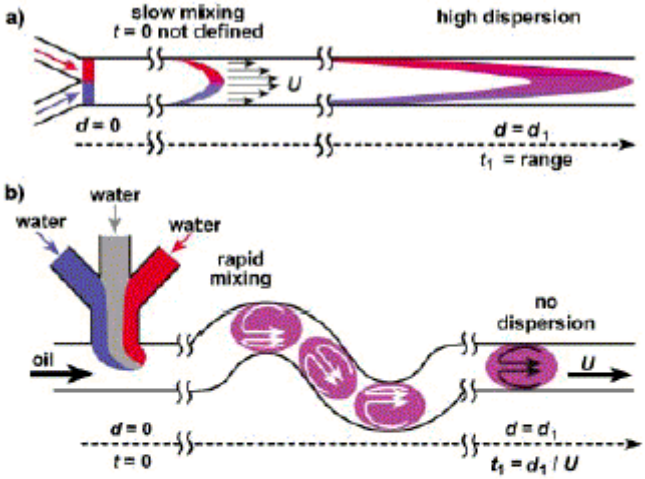


Figure 1. Schematic comparison of a reaction A + B conducted in a standard pressure-driven microfluidic system device (a) and in the microfluidic device described here (b). a) Reaction time $t \neq d/U$. b) Reaction time $t = d/U$. Two aqueous reagents (red, A and blue, B) can form laminar streams separated by a gray "divider" aqueous stream in a microchannel. When the three streams enter the channel with a flowing immiscible fluid, they form droplets (plugs). The reagents come into contact as the contents of the droplets are rapidly mixed. Internal recirculation within plugs flowing through channels of different geometries is shown schematically by arrows.

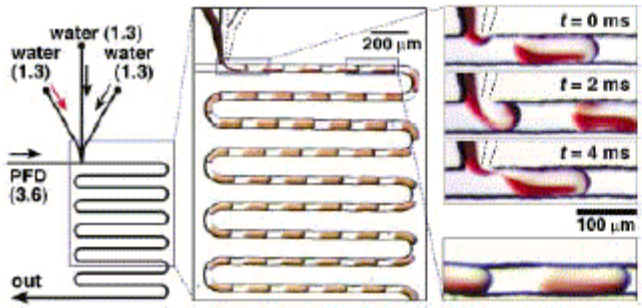


Figure 2. Spontaneous formation of uniform plugs out of multiple aqueous streams. Left: Schematic diagram of the microchannel network. Volumetric flow rates for all streams (in $\mu L min^{-1}$) are given in parenthesis. Middle: Microphotograph (10 μs exposure) of plug formation and transport. Right: Magnified microphotographs (10 μs exposure) of the plug-forming region at different time points. All microchannels had $50 \times 50\ \mu m^2$ cross sections. Total flow rate in the main channel: 7.5 $\mu L min^{-1}$ (50 mm s^{-1} average flow velocity); $Re \sim 2.5$ (water), ~0.93 (PFD). PFD here stands for a 10:1 mixture of perfluorodecaline and $C_6F_{11}C_2H_4OH$. Red stream: solution of $[Fe(SCN)_x]^{(3-x)+}$ prepared by mixing 0.067 M $Fe(NO_3)_3$ with 0.2 M KSCN; colorless streams: 0.2 M KNO_3.

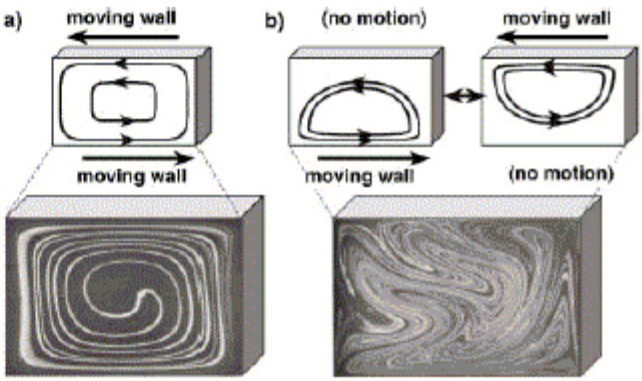


Figure 3. Mixing by steady (a) and time-periodic (b) flows in flow cavities. a, b) Top: Schematic illustration of the flow cavity. The vertical walls are stationary and the horizontal walls move as shown. Bottom: Images (reprinted with permission of Cambridge University Press from ref. [21]) that illustrate the flow patterns. For details, see text.

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