Investigating Acrylic Acid Polymerization by Using a Droplet-Based Millifluidics Approach

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Summary: We present herein the basic concept of droplet-based millifluidics as an original tool to monitor polymerization kinetics. As a proof of concept, we use aqueous droplets of acrylic acid mixed with sodium persulfate at various pH as polymerization microreactor models. According to the pH and the temperature, completion could be obtained within a minute. Despite the fact that this reaction is quite fast and exothermic, we were able to acquire data in order to obtain valuable information about the polymerization kinetics. We were also able to estimate the overall activation energy for polymerization rate. Furthermore, offline analyses by Size Exclusion Chromatography show high molecular weights and high polydispersities. These results set the stage for further studies of polymerization reactions where detailed basic kinetic data must be acquired in conditions which cannot be investigated by using conventional batch glassware (i.e. high temperatures or concentrations). This new approach can also be used as an efficient High Throughput Screening tool.

Keywords: acrylic acid free radical polymerization; droplets as microreactors; inline monitoring; millifluidics; Raman spectroscopy

Introduction

Reactions in droplets in microfluidic channels is an attractive approach which is based upon micromanipulation of discrete droplets.[1,2] To the chemist, the main advantage by using these droplets is that they can be used as individual batch microreactors. Recently, this approach was used in order to synthesize polymeric particles like latex, vesicles, hybrids, Janus,[3] etc. Droplets are easily generated by using flow-focusing or T junction patterns. Immiscible and chemically inert oil is used as a carrier fluid between droplets. Thus, a string of identical droplets flows continuously within channels or tubes. There are many advantages to use these small droplet-based systems.[1,2] One can generate microreactors which have all the same size and shape, and will contain the same chemical composition. Moreover, internal mixing can be achieved by chaotic advections.[2,4] Then, due to their small sizes and high surface-area-to-volume ratios, heat exchanges are favored which improves safety at the laboratory. Thus, one can make polymerization reactions with experimental conditions which could not be used in conventional batch reactors: i.e. high concentrations or temperatures. Other key points to this miniaturized droplet-based approach consist in 1) droplets can manage high internal viscosity issues without plugging the channel. And 2) there is no residence time distribution. Indeed, on the contrary of single-phase flows, dispersion due to convection and diffusion is eliminated because the reactants are compartmentalized within droplets moving all at the same speed. This is particularly important since viscosity in polymerization reactions can dramatically

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increase to thousand of centipoises or even higher. The consequence is there is an equivalence between the position of the droplet within the channel and the time course of the reaction: i.e. according to the rate of the reaction, each droplet will have the same chemical composition when they reach the same position along the channel.

Microfabrication techniques allow producing transparent miniaturized devices. These ones hence can be coupled to nonintrusive techniques in order to observe the behavior of the droplets flowing within channels or to analyze their chemical compositions. By using the time-space equivalence and this *in line* monitoring capacity, one can determine concentrations at any time of the reaction.[5] This process eliminates sampling and handling like dilutions or filtrations, etc. which are required by HPLC or GC for instance.[6] Thus, this *in line* monitoring is a faster method than the chromatographic ones to obtain residual concentrations of the monomer in function of time. And kinetics of very fast polymerization reactions which are done in few minutes can be determined safely.

The main drawback in fabricating microfluidic devices is that it necessitates expensive clean-room and technologies and require a high know-how and expertise.[7] Moreover, the risk of failure in realizing the microchip could be important, and if plugged the device must be thrown away. This is a time and money consuming process which can be easily avoided. Recently, we have set up and used a miniaturized tool at a scale higher than that one commonly used in microfluidics: it consists in assembling Teflon tubing of about the millimeter with commercial connectors.[8–10] This millifluidic approach is cheaper, faster to set up and more flexible than microfluidic devices since one can use again the tubing in other configurations (i.e. length path, diameter size, etc.). We used it to produced continuously isometric particles made from Noa polymer or porous silica with a high control of their sizes (from 100 μm to few millimeters) and shape (spherical to ovoid).[11,12] By using simple coaxial tubing, stable emulsions were obtained without the need of surfactants,[13] and this tool was also used to monitor the kinetics of the redox synthesis of iodine by UV-visible spectroscopy.[14]

We present herein the general concept of droplet-based millifluidics as a high throughput platform. We choose to illustrate this concept by monitoring the fast and exothermic polymerization reactions of acrylic acid (AA) at various pH. In this case, droplets are stable water-in-fluorinated oil emulsions without the need of surfactants.

Materials and Methods

Reagents

Filtered water at 18.2 MΩ.cm (at 25 °C) was obtained from the Synergy unit (Millipore) in which a 0.22 μm pore diam. is mounted. AA (Merck, >99%), potassium nitrate (KNO_3, VWR Normapur, 99%) and sodium peroxodisulfate as the initiator (I, VWR Normapur, 99%), were use as received. Aqueous solutions of monomer or initiator were deoxygenated by nitrogen flush prior to use (about 30 minutes). Fluorinated oil FC-40 from 3M was used as the carrier fluid without further purification.

Set up of the Millifluidic Device

We have built a millifluidic prototype with cheap commercial tubes and fittings from Upchurch. A first stage of the device consists in assembling these parts in a rough but reliable capillary-based co-flow device as shown in Figure 1. The second stage is the main part of a FEP tube (1/8″ OD with 1/16″ ID) rolled up on a metallic cylinder. This is defined as the tubular reactor. High precision syringe pumps (neMESYS from Cetoni) were used to feed the tubular reactor. Inside the metallic support, a cooling fluid flows against the current of reagents that flowed within the tubular reactor. Temperature of the cooling fluid is controlled by a Lauda thermostat

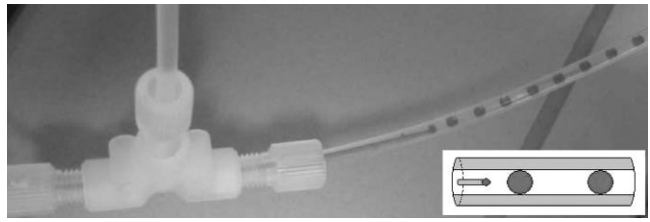

Figure 1.
Picture of our capillary-based coflow device.

(PROLINE RP845). Polymerization occurs only within the part of the tubular reactor which is heated (about 4.50 m long). At the end of the tubular reactor two different containers can be connected: one as a waste and another one in order to sample some droplets. Aqueous solution was recovered from the carrier fluid by decantation.

Sequence of Operations During Polymerization Monitoring

Aqueous stock solutions of monomer and initiator and the carrier oil were separately prepared and degassed by nitrogen bubbling. Concentrations and other experimental details are given in Table 1. All deoxygenated fluids were added into degassed syringes and mounted on the syringe pump. A home-made dynamic stirrer was used in order to mix the aqueous solutions prior the droplet generation. Before the experiment, the tubular reactor filled with the carrier oil was first equilibrated at room temperature. Then, droplets of diluted AA into the initiator solution flowed along the tubular reactor. As soon as the equilibrium is reached the Raman spectrum of the pure diluted AA solution was recorded as a reference for the whole experiment. Thus, the time t_0 of the experiment corresponds to this acquisition. Then, the tubular reactor was heated. And as soon as the temperature set is reached, we started the flow of aqueous droplets again in order to form a new set of diluted AA/initiator microreactors with well controlled concentrations. During the experiment, constant flow rates were applied in order to set the residence time equal to the total time of the polymerization (e.g. droplets can be heated for 15 minutes maximum). Since the position of a droplet within the tubular reactor corresponds to the time course of reaction (i.e. conversion), each droplet reaching a position are identical in terms of concentrations. Recording Raman spectra at different positions along the tubular reactor leads to plot concentrations (hence conversion) in function of time. The first droplets were thrown in the waste container. Samples were withdrawn by collecting few droplets at the edge of the tubular reactor. And the

Table 1.
Parameters of the polymerization reactions.[a)]

#	$[AA]_o$	$[AA]_o$[b)]	$[I]_o$[b)]	$[AA]_o/[I]_o$	T	pH
	$g.mL^{-1}$	$mol.L^{-1}$	$mol.L^{-1}$		°C	
1	0.2	2.8	0.028	100	72	1.8
2	0.3	4.2	0.028	150	72	1.8
3	0.4	5.6	0.028	200	72	1.8
4	0.4	5.6	0.028	200	60	1.8
5[c)]	0.4	5.6	0.028	200	95	1.8
6[d)]	0.2	2.8	0.028	100	60	5.5
7[e)]	0.2	2.8	0.028	100	72	5.5
8[f)]	0.2	2.8	0.028	100	60	1.8

[a)] $Q_{oil}/(Q_{AA}+Q_I)=2$; $Q_{oil}=1190.3\ \mu L.min^{-1}$; $Q_{AA}=446.4\ \mu L.min^{-1}$; $Q_I=148.8\ \mu L.min^{-1}$; total residence time was 5 minutes for experiment #1 to 4; KNO_3 was added to the monomer stock solution at 6% wt./v.[b)] Molar concentrations within the droplets; calculated according concentrations of stock solutions and flow rates.[c)] $Q_{oil}=2380.6\ \mu L.min^{-1}$; $Q_{AA}=892.7\ \mu L.min^{-1}$; $Q_I=297.6\ \mu L.min^{-1}$; total residence time was 2.5 minutes.[d)] $Q_{oil}=198.4\ \mu L.min^{-1}$; $Q_{AA}=74.4\mu L.min^{-1}$; $Q_I=24.8\ \mu L.min^{-1}$; total residence time was 30 minutes, pH 5.5 was obtained by addition of NaOH in the monomer stock solution.[e)] $Q_{oil}=396.8\ \mu L.min^{-1}$; $Q_{AA}=148.8\ \mu L.min^{-1}$; $Q_I=49.6\ \mu L.min^{-1}$; total residence time was 12.5 minutes, pH 5.5 was obtained by addition of NaOH in the monomer stock solution.[f)] $Q_{oil}=595.2\ \mu L.min^{-1}$; $Q_{AA}=223.2\ \mu L.min^{-1}$; $Q_I=74.4\ \mu L.min^{-1}$; total residence time was 10 minutes.

reaction mixture was recovered by extracting the aqueous solution from the fluorinated oil. At the end of the experiment, the system was cleaned with the carrier fluid.

Confocal Raman Spectroscopy

The millifluidic device was placed under the confocal microscope of the Raman spectrophotometer (10× objective). Raman scattering spectra were measured through the window of the millifluidic device. They were obtained by a double monochromator Raman spectrometer HR800 (Horiba Jobin-Yvon) with Near Infrared laser diode (785 nm; 300 mW) as excitation source. Note that the spatial resolution of the focused laser beam was about 30 μm in width and 50 μm in depth. The acquisition time for one spectrum was about 90 seconds (average 2).

Size Exclusion Chromatography (SEC)

The poly(acrylic acid) (PAA) solutions collected at the end of the millifluidic tube (i.e. at the end of the reaction) were analyzed offline by SEC, using both traditional column calibration with PEG/PEO standards (EasyVial from Varian/Polymer Laboratories), and light scattering measurements. Samples were diluted into eluent at a concentration $< 0.1\%$ wt./v. The Agilent 1100 series SEC system included a vacuum degasser, an isocratic pump, an auto-injector, and three Shodex OH-Pack SB806-HQ columns used at room temperature. After filtration on 0.2 μm pore diam., water stabilized with 0.1 M $NaNO_3 + 100$ ppm NaN_3 was used as eluent at a flow rate of 0.80 mL/min. The detector train included a refractometer from Agilent as a mass concentration detector.

Results and Discussion

The monitoring of the AA polymerization is based on the carbon-carbon double bond signal at 1640 cm^{-1} (cf. Figure 2). From the spectra recorded at different positions along the flow pathway, one can see that both the area and the height of this peak decrease. Thanks to the time-space equivalence, it hence means the monomer is converted in polymer in function of time. Although spectra were obtained while aqueous droplets separated by carrier fluid plugs flowed, their quality is good enough to use them quantitatively: they present a high signal/noise ratio and there is no fluorescence in the analyzed range. However, this

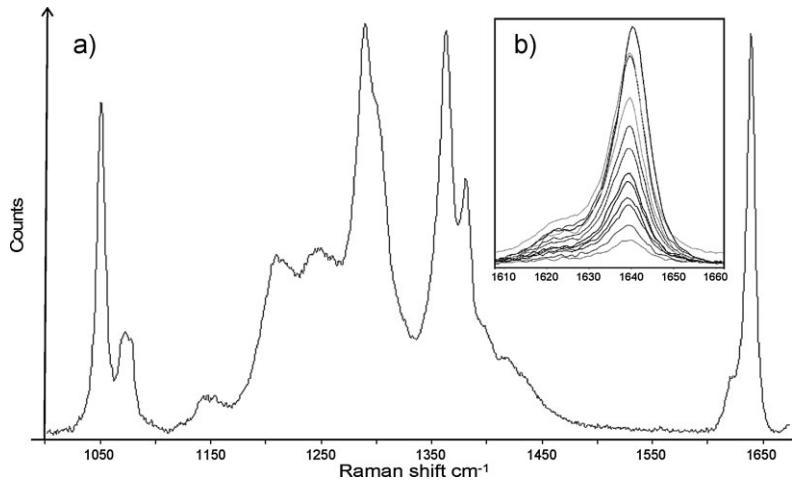

Figure 2.

acquisition time was long enough that about 850 droplets were analyzed. Thus, we used the signal of KNO_3 at 1050 cm^{-1} as a reference in order to normalize the Raman spectra. Note the relative intensity of the peak of the reference diluted in the aqueous droplets do not significantly varies from one spectrum to another, as expected.

Molar conversion $\rho(t)$ is then calculated according the following equation:

$$\rho(t) = 1 - \frac{\frac{h_{AA}(t)}{h_{KNO_3}(t)}}{\frac{h_{AA}(t_0)}{h_{KNO_3}(t_0)}} \quad (1)$$

where $h_x(t)$ is the height measured at a time t at the top of the peak corresponding to the chemical x. These height ratios allowing to eliminate all calibration constants, and the molar concentration of AA is thus: $[AA]_t = [AA]_0$ x $[1\text{-}\rho(t)]$. By using the law mass conservation one can calculate molar PAA concentrations in function of time. As first approximations, we assume an ideal mixing and we have neglected any variation of the volume of the microreactors which occurs during the polymerization reaction due to the difference between the mass densities of the monomer and polymer. As shown on Figure 3, we can plot molar monomer conversion in function of time. Using either height or area leads to the same conversion plot.

Table 2.
SEC results and estimations of α from the first-order fits.[a)]

#	M_w	M_n	I_p	α	Error
	g.mol^{-1}	g.mol^{-1}		s^{-1}	s^{-1}
1	1 600 000	213 000	7.5	0.0127	4×10^{-4}
2	3 197 000	329 000	9.7	0.0154	7×10^{-4}
3	5 260 000	363 000	14.5	0.021	1×10^{-3}
4	NA	NA	NA	0.0076	4.0×10^{-4}
5	860 000	160 000	5.4	0.11	1.6×10^{-2}

[a)]NA: Not Applicable.

Few amounts of stock solutions are needed to perform one experiment with this droplet-based millifluidic approach. Thus, it is very easy to investigate quickly several experimental conditions including pH or temperatures without preparing other sets of monomer or initiator solutions. Both effects of the temperature or the pH on the molar conversion are shown in Figure 3. The reaction rates are given in Table 2. As expected, the rate increases with increasing temperature or decreasing the pH respectively. When we added the base the AA was in its ionized form and the propagation rate coefficient was hence lower than that one at low pH.

Data can be fitted by using a first-order with respect to initial monomer concentration, i.e. $\rho(t) = (1\text{-}e^{-\alpha t})$ where α is the apparent propagation rate coefficient.

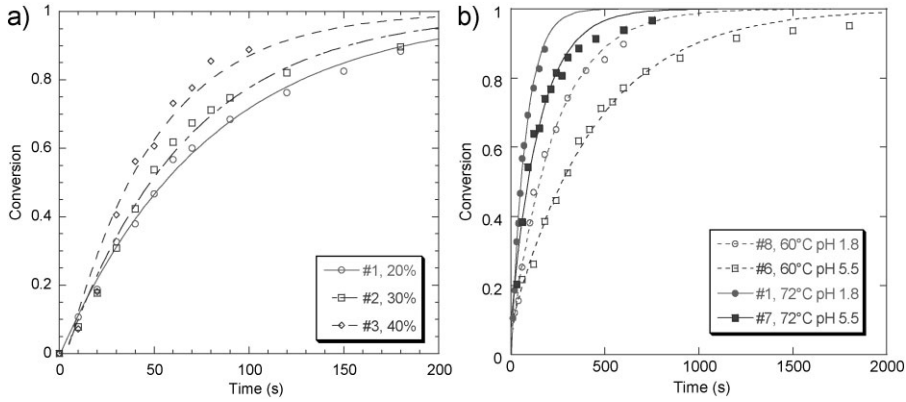

Figure 3.
a) Molar conversions of AA in function of time for various monomer concentrations. b) Molar conversions of AA in function of time for different pH and temperatures.

Previous published works have found that partial orders of AA radical polymerization rates in aqueous solution vary from ~1.0[15,16] to 1.7.[17,18] It was assumed these higher orders were due to side reactions like secondary monomer-enhanced decomposition step of the initiator. Although determining partial rate orders is beyond the scope of this article one can see deviations from this first order in Figure 3, meaning this polymerization rate exhibits higher than first order rate. Determination of these the partial rate orders were published elsewhere.[19]

Due to the small size of the droplets and their high surface-area-to-volume ratio, we were capable to polymerize safely high AA concentrations at high temperature (i.e. 5.6 mol.L^{-1} at 90 °C and pH 1.8). In these latter experimental conditions, the polymerization reaction is very fast. And the heat removal could not be controlled at the laboratory by using conventional glassware. Moreover we were able to monitor such a fast reaction. This would not be possible by using neither manual sampling nor robots. This monitoring capacity is a unique feature of our droplet-based millifluidic approach. An Arrhenius plot was obtained from the initial rate of polymerization $R_{p,0}$ and is shown in Figure 4. The overall activation energy for the rate of polymerization seems to be temperature dependant since we do not observe a linear dependence. Discussion about this temperature-dependence is studied in more detail elsewhere.[19]

The polymerization reaction is almost complete at the end of the monitoring, meaning the collected droplets are constituted by PAA in solution essentially. Since polymer concentration could be high, droplets look like gels and could be difficult to dissolve into the SEC eluent. However, after sonication or mixing during a long time (e.g. overnight), samples can be diluted and analyzed by SEC. Results reported in Table 2, show quite high molecular weights, and M_w from #4 must be overestimated since the highest standard used do not exceed 2 000 000 g/mol. Moreover, molecular weights of sample #5 are outside the SEC column range: $M_w > 10^7$ g/mol and $M_n > 2.10^6$ g/mol.

When polymerization were done at low pH, according the Henderson-Hasselbalch equation about >99.5% of the AA was nonionized. Therefore the chains in solution were preferably in their coiled form. We hence expect ideal polymerization kinetics. As expected, molecular weights vary according the temperature of the free radical polymerization reaction: they increase as temperature decrease (#5) and they decrease as temperature increase (#6). Moreover, molecular weights also increase by increasing the initial monomer concentration (#1, 2 and 3 in Table 2) and

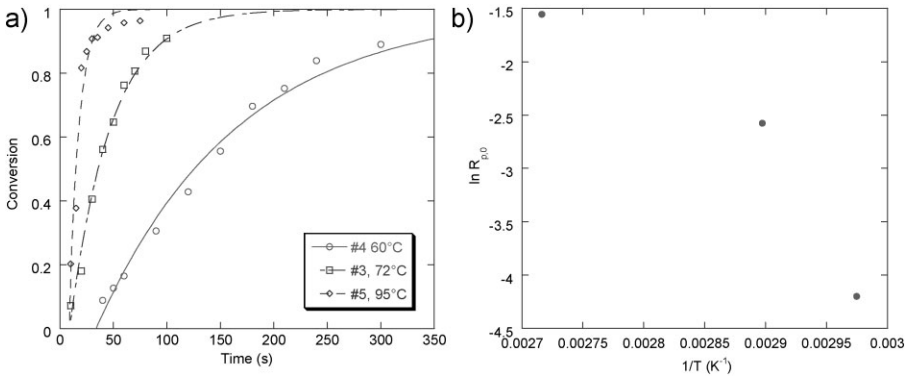

Figure 4.
a) Molar conversions of AA in function of time for several temperatures. b) Temperature dependence of α.

by decreasing the amount of initiator (#1 and 4 in Table 2), as expected.

SEC analysis also shows quite high polydispersities ($I_p > 5.4$). Polydispersities increased by a factor ~2 by increasing the initial monomer concentrations from 20 to 40 wt. %, while it remained constant for experiment #1 and 4, which were done at the same monomer concentration. These high polydispersities should be due to the weak internal mixing within droplets during the polymerization. Moreover, a gel effect is possible at these elevated initial monomer concentrations.[16] Further works must be done to fully characterize this phenomenon.

Conclusion

These results validate our cheap, easy-to-use and versatile droplet-based millifluidic approach and show it can be used as a powerful High Throughput Screening (HTS) tool when coupling with nonintrusive analytical system. In particular, it proves its usefulness in monitoring fast and exothermic polymerization reaction which could not be studied in conventional batch reactors, i.e., high monomer concentrations or temperatures. This was possible thanks to the time-space equivalence characteristics of the use of droplet as microreactors. Molecular weight measurements on final products showed high molecular weights and polydispersities. Further investigations are in progress at the laboratory to understand this observation.

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