In situ Spatiotemporal Characterization and Analysis of Chemical Reactions using an ATR-Integrated Microfluidic Reactor

Supplementary Information

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1. Microreactor fabrication

Top wafer (Mempax 525 µm)

Step	Process description		Remarks
1	**Substrate**	525 µm glass borofloat wafer	
2	**Standard cleaning**	• Beaker 1: HNO_3 (99%) 5min • Beaker 2: HNO_3 (99%) 5min	
3		Quick dump rinse (DI resistivity is > 10.5ΩM)	
4		Drying (2500 rpm, 60 sec)	
5	**Cr/Au deposition**	Use the following conditions: • Cr [01:00,01:00] • Au [00:30,02:00]	
6			
7	**Coating Olin Oir 907-17**	Dehydration bake (120˚C, 10 mins)	Optional: UV Ozone treatment for better adhesion of Au/Cr to resist
8		HDMS Priming (4000 rpm, 30s)	
9		Olin oir 907-17 (4000 rpm, 30s)	
10		Prebake (95°C, 60 s)	
11	**Alignment & Exposure** **MASK Channel layer**	Dose: 105 µC Exposure Time: 4 sec Constant dose, Intensity Mix Top side, hard contact	
12	**Development** **Olin OiR resist**	Post exposure bake (95°C, 60 s)	
13		Developer OPD4262 Beaker 1 (30s) Beaker 2 (30s)	
14		Quick dump rinse	
15		Single wafer dryer (2500 rpm, 60 sec)	
16		Post-bake (120°C, 10 min)	
17	**Au/Cr etching**	Au etchant	Quick rinse with DI water
18		Cr etch	
19		Quick dump rinse	
20		Drying (2500 rpm, 60 sec)	
21	**25% HF Glass etch**	**Prevention:** Use dicing foil on backside to prevent the wafer from etching. Heat at 70˚C for 2-3 mins for better	Prepare 25% HF: 2. Add 1 part DI water to Teflon container 3. Add 1 part 50% HF

		adhesion of foil to wafer.	4. Let it stabilize for >3 hours
22		Etch rate = 1 µm/min	
23		Quick dump rinse	
24		Drying (2500 rpm, 60 sec)	
25	**Strip resist**	Beaker 0: HNO_3 (99%) 5min	
26		Quick dump rinse	
27		Drying (2500 rpm, 60 sec)	
28	**Au/Cr etch**	Au etchant	
29		Private Cr etch	
30		Quick dump rinse	
31		Drying (2500 rpm, 60 sec)	
32	**RCA 2 clean**	$HCl:H_2O_2:H_2O$ (1:1:5)	
33	**Wet bench 9/10**	Quick dump rinse	
34		Single wafer dryer (2500 rpm, 60 sec)	
35	**Powder blast**	Apply foil/resist on wafer Foil used: Harka I-HE	
36	**Coating**	Laminate Roller speed 2 at 70˚C	
37	**Alignment and Expose** **EVG 620 Mask aligner** **Manual bottom side** **MASK Inlet/Outlet**	Exposure Time: 4 sec	
38		Place dicing foil on backside of the wafer to protect during powder blast Heat foil at 70 ˚C for 2-3 mins,	
39	**Development**	Warm water tool.	
40	**Powder blasting**	29 µm particles 2 cycles 10 mm/s	
41	**Development**	5% sodium bicarbonate solution. Leave wafers in for >30 mins Peel off dicing foil and powderblast foil. Rinse with water	
42		Sonication >30 mins	

Bottom wafer (Si [100] 525 µm)

Step	Process description		Remarks
1	**Substrate**	525 µm Si wafer	
2	**LPCVD of low stress SiRN**	Standard cleaning: • Beaker 1: HNO_3 (99%) 5min • Beaker 2: HNO_3 (99%) 5min	
3		Quick dump rinse	
4		Cleaning in 69% nitric acid 5 mins	
5		Quick dump rinse	
6		Etching in 1% HF 60 s	
7		Quick dump rinse	
8		Batch drying (up to 25 wafers)	
9		Load wafers in G3 furnace Target thickness = 100 nm	
10	**Coating Olin Oir 907-17**	Dehydration bake (120˚C, 10 mins)	
11		HDMS Priming (4000 rpm, 30s)	

12		Primus spinner Olin oir 907-17 (4000 rpm, 30s)	
13		Prebake (95°C, 60 s)	
14	**Alignment & Exposure** EVG6200 Mask aligner **MASK Si facets**	Dose: 105 µC Exposure Time: 4 sec Constant dose, Intensity Mix Top side, hard contact	
15		Post exposure bake (95°C, 60 s)	
16	**Development** **Olin OiR resist**	Developer OPD4262 Beaker 1 (30s) Beaker 2 (30s)	
17		Quick dump rinse	
18		Single wafer dryer (2500 rpm, 60 sec)	
15		Post-bake (120°C, 10 min)	
16	**Direction RIE od SiRN by CHF_3/O_2 Plasma**	Etch rate = 42 nm/min Etch time = 3 mins.	
17		Chamber clean	
18	**Stripping of resists**	Recipe 04: 40 mins	
19	**Standard KOH etch**	Etching in 1% HF (60s)	
20		Quick dump rinse	
21		KOH etch Si<100> = 1 µm Si <111> 12.5 nm/min Temp = 75° C	Time = 7 hours.
22		Quick dump rinse	
23		Drying (2500 rpm, 60 sec)	
24	**RCA 2 clean** **Wet bench 9/10**	$HCl:H_2O_2:H_2O$ (1:1:5)	
25		Quick dump rinse	
26		Drying (2500 rpm, 60 sec)	
27	**Etching in 50% HF**	Private beaker Standard 50% HF Time = 30 mins	
28		Quick dump rinse	
29		Drying (2500 rpm, 60 sec)	

Alignment & bonding

Step	Process description		Remarks
1	**Piranha clean**	Time: 15 mins	
2		Quick dump rinse	
3		Drying (2500 rpm, 60 sec)	
4	**Stack alignment** **EVG20 & Anodic bond chuck**	Man. Anodic bonding Crosshair, 30 µm separation	
5		Load bottom wafer in the anodic bond chuck	Glass wafer
6		Load top wafer in the anodic bond chuck	Si wafer
7		Insert flags and align	
8		Clamp wafer	

9	**Bonding** Anodic bonder	Load wafer and pull-out flags carefully	
10	**Dicing** Dice Saw Micro Ace 3	Laminate dicing foil (transparent, 100 µm) on both sides	
11		Put ring around wafer and cut to size	
12		Load wafer	
13		TC-300 blade Program: 8 RPM: 30k Speed: 3mm/s Stack height (measure) -> 1140 Wafer size: 110 mm x-translation: 20.3 mm (pitch A) y-translation: 18.3 mm (pitch B)	
14		Align cut lines	
15		Press height sense to measure diameter of blade	
16		Make a single dummy cut	
17		Align marker lines on dummy cut	
18		Move blade to top of wafer. Press cut auto	
19		Turn the wafer 90°. Check alignment and cut again.	
20		Dry wafer	
21		5 min UV light to easily peel off dicing foil	

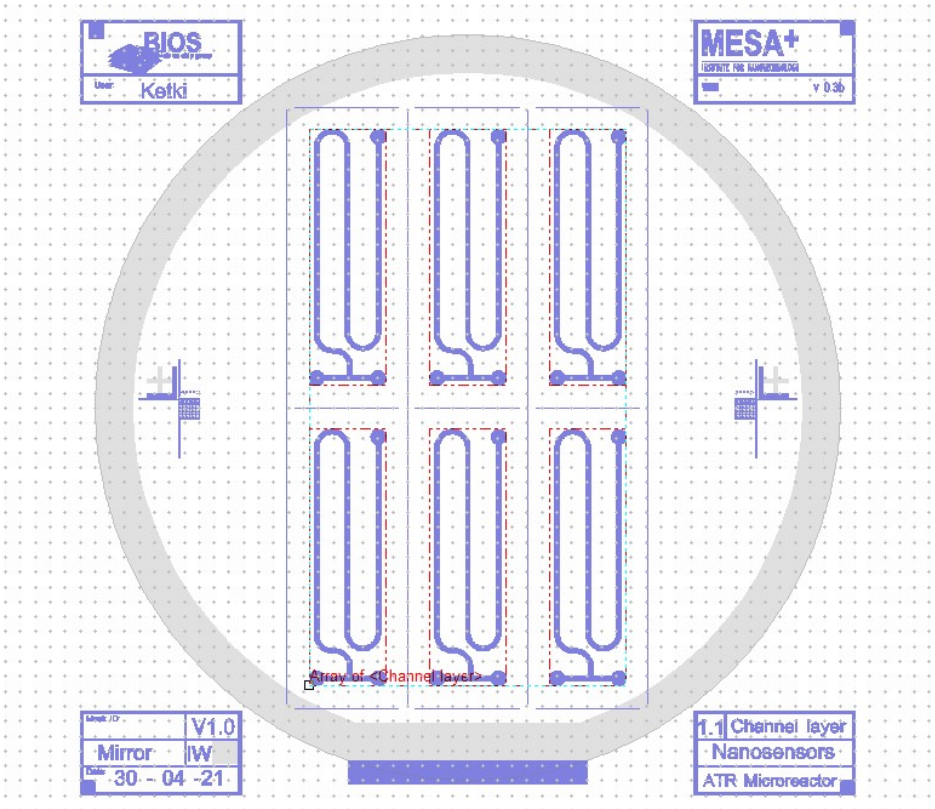

Figure S1 (a): Mask 1: Channel layer

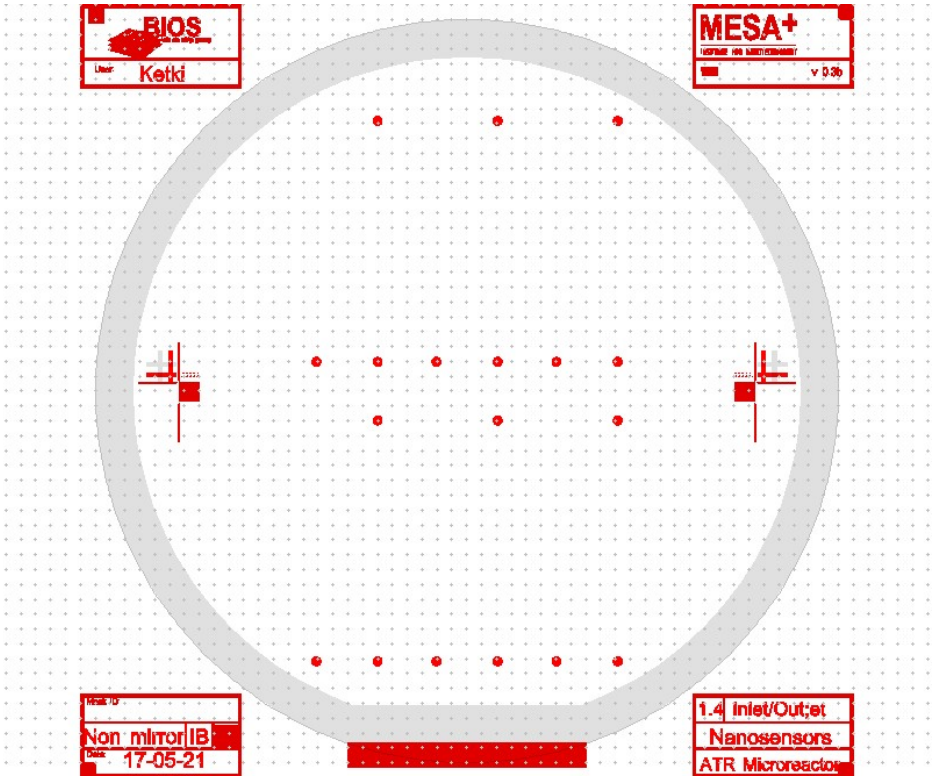

Figure S1(b): Mask 2: Inlet/Outlet

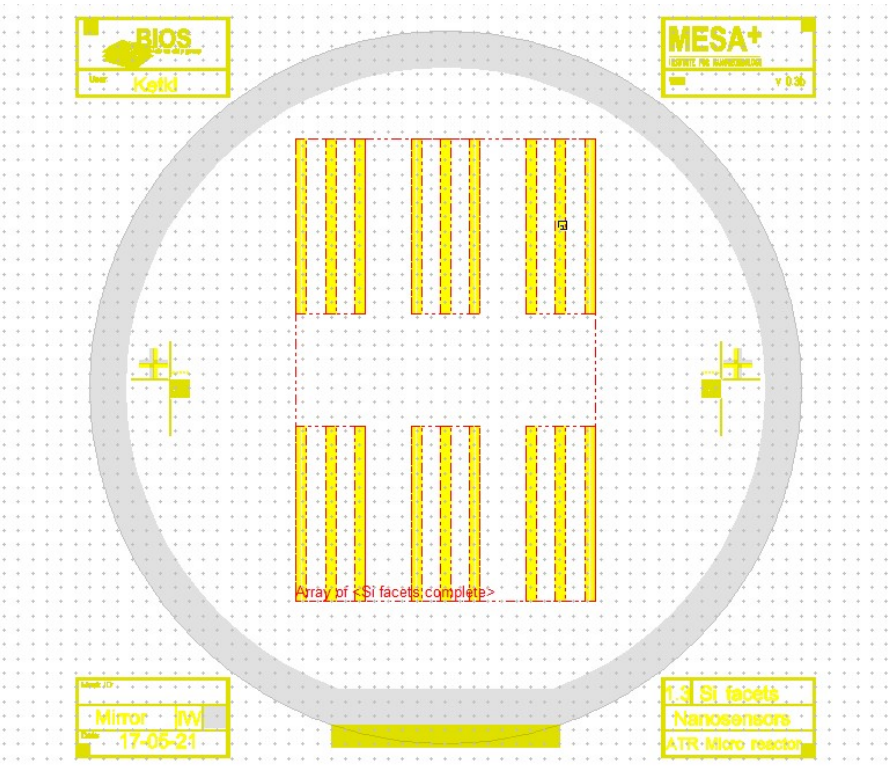

Figure S1(c): Mask 3: Si Facets

2. Experimental methods

2.1 S_N2 Reaction – benchtop measurements

In situ reaction monitoring was made possible by using a reaction reservoir secured to a 60° Si face angle crystal (FAC) mounted on a Bruker Vertex 70v FT-IR spectrometer with a 55° AOI and settings of 32 co-added interferograms, 8 cm^{-1} resolution and 40 MHz scanning velocity. First, a measurement of the solvent, neat dimethyl sulfoxide (DMSO) was collected and used as the background. Next, 200 µL of 0.1 M SA (Sigma-Aldrich) was added to the reaction reservoir along with 200 µL of 0.1 M BB (Sigma-Aldrich). To monitor the reaction, a repeated absorbance measurement began the moment reagents were combined in the reservoir. Absorbance measurements were continuously collected until the reaction was complete, ~5 minutes.

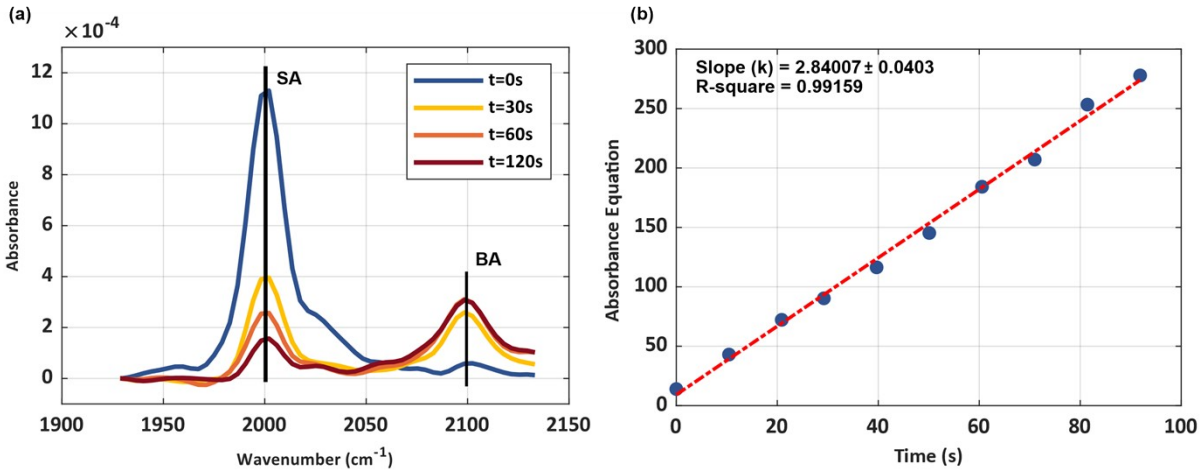

Figure S2: Benchtop reaction monitoring results. (a) In situ absorbance measurements of SA and BA. (b) Linearized concentration of SA with respect to time. Slope of fitted line is the rate constant.

2.2 S_N2 reaction kinetics

Characteristic absorbance peaks of BB could not be visualized and therefore, the reactions kinetic parameters were determined by following the evolution of the second reactant, SA. Although this is a second order reaction, in the specific case where the initial concentrations of both reactants are equal the integrated rate law is

$$\frac{1}{[SA]} - \frac{1}{[SA]_0} = kt \tag{1}$$

Where [SA] and $[SA]_0$ is the concentration of SA at any time throughout the reaction and initial concentration of SA. If we assume Beer's law (path length has been omitted), where ε is the molar absorptivity coefficient of species I and [i] is the concentration

$$Abs_i = \varepsilon_i[i] \tag{2}$$

applies then a rearranged form for equation 1 can be written

$$\frac{\left(Abs_{SA_0} - Abs_{SA}\right)\varepsilon_{SA}}{Abs_{SA_0}Abs_{SA}} = kt \quad (3)$$

Equation 3 requires the molar absorptivity coefficient, ε, of SA to determine the rate constant, k. To determine the molar absorptivity, a calibration cure was constructed using the same spectrometer and experimental set up used to measure the reaction progression. Finally, the molar absorptivity coefficient was applied to equation 3 and the rate constant was calculated.

2.3 Starting reagents calibration curves

Benchtop measurement

25 mL 0.5 M solution of SA was made up with DMSO in a volumetric flask. Aliquots from this 0.5 M solution were then added to six additional 5 mL volumetric flasks resulting in a seven-point calibration curve with concentrations of 0.01 M, 0.05 M, 0.1 M, 0.2 M, 0.3 M, 0.4 M, and 0.5 M. Absorbance measurements were collected for each concentration with a background of DMSO using a reaction reservoir secured to a 60° Si face angle crystal (FAC) mounted on a Bruker Vertex 70v FT-IR spectrometer with a 55° AOI and settings of 32 co-added interferograms, 8 cm^{-1} resolution and 40 MHz scanning velocity. The band at 2000 cm^{-1} characteristic of SA was then integrated to calculate its area. Finally, the absorbance area was plotted with respect to the concentration to yield figure S3(a) from which the molar absorption coefficient, ε_{SA}, was determined to be 1.07 M^{-1}. A five-point calibration curve was made for BB by weighing the reagent in a volumetric flask and making it up with DMSO to give concentrations of 0.1 M, 0.2 M, 0.3 M, 0.4 M and 0.5 M. Each was measured on the benchtop spectrometer and absorbance spectra calculated, followed by integration of BB characteristic band at 1230 cm^{-1}. The band area was then plotted against concentration and the molar absorption coefficient was determined to be 0.119 M^{-1}.

Synchrotron Measurement

The Reagents solutions used for the calibration curved measured using the microreactor were prepared in the same way as described in the previous paragraph. Each solution was loaded into syringes and flown through the device at a rate of 2 µL/min. Measurements were collected at p1 (see Figure 1) with the synchrotron radiation focused at the channels centre along the x-axis. The reagents characteristic band was then integrated and plotted with respect to the concentration to yield figure S3(b). From these the molar absorption coefficients were determined to be 1.497 M^{-1} and 0.0515 M^{-1} for SA and BB, respectively.

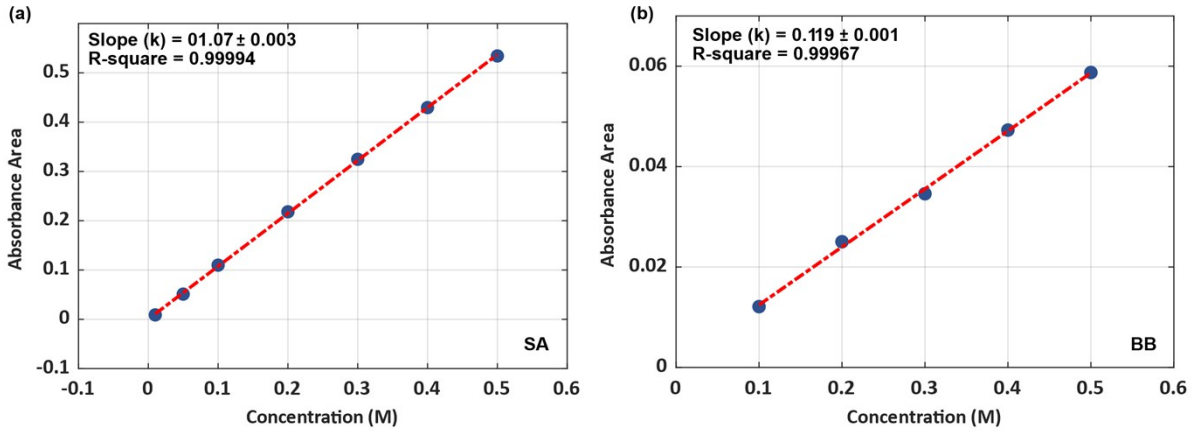

Figure S3: Calibration curves of starting reagents (a) SA and (b) BB measured on a benchtop spectrometer

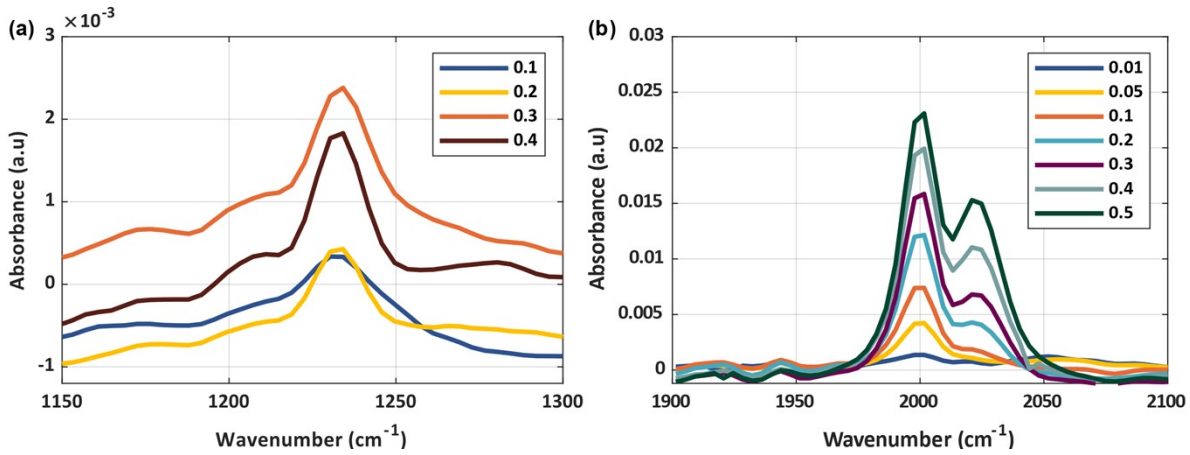

Figure S4: Raw data for calibration curves of starting reagents (a) SA and (b) BB measured in the microreactor with synchrotron radiation.

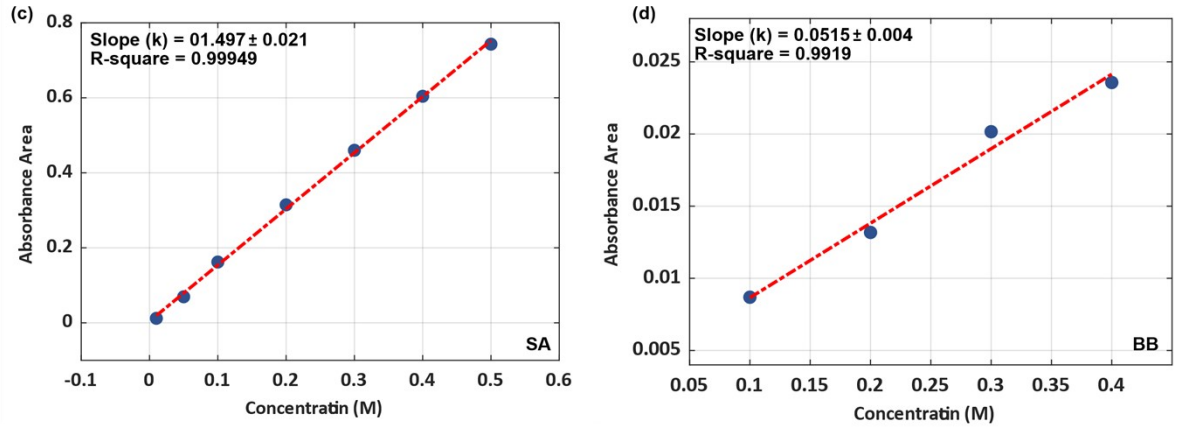

Figure S4: Calibration curves of starting reagents (c) SA and (d) BB measured in the microreactor with synchrotron radiation.

3. COMSOL Simulations

The following COMSOL files were used for the simulations.

File Name	Modules	Results
Diffusion_all_channels.mph	Creeping flow, transport of diluted species	Simulated diffusion coefficients for BB and SA
Channel_noHB_Canada_final_BB_SA_BA_3.mph	Creeping flow, transport of diluted species and chemical reaction engineering	Simulated reaction kinetics for $BB + SA \rightarrow BA$

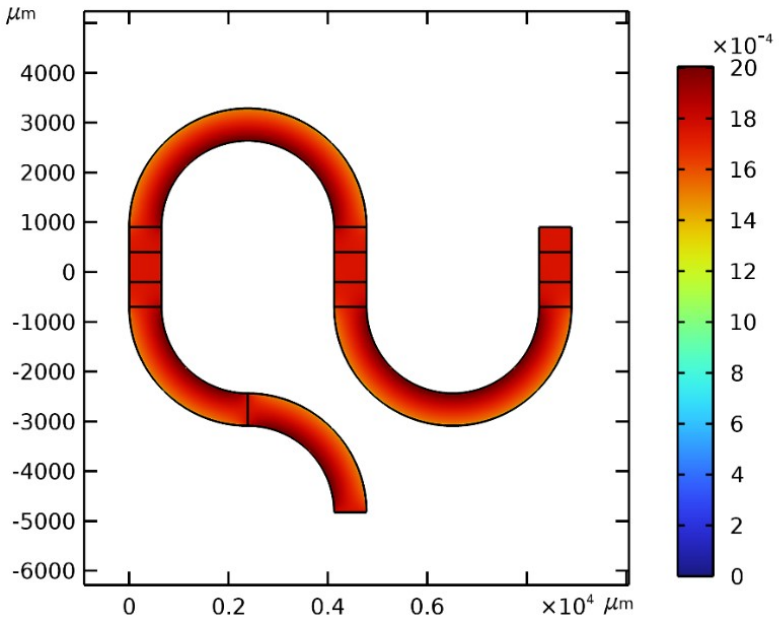

Figure S5: (a) Surface velocity plot (m/s) for microreactor simulated in COMSOL

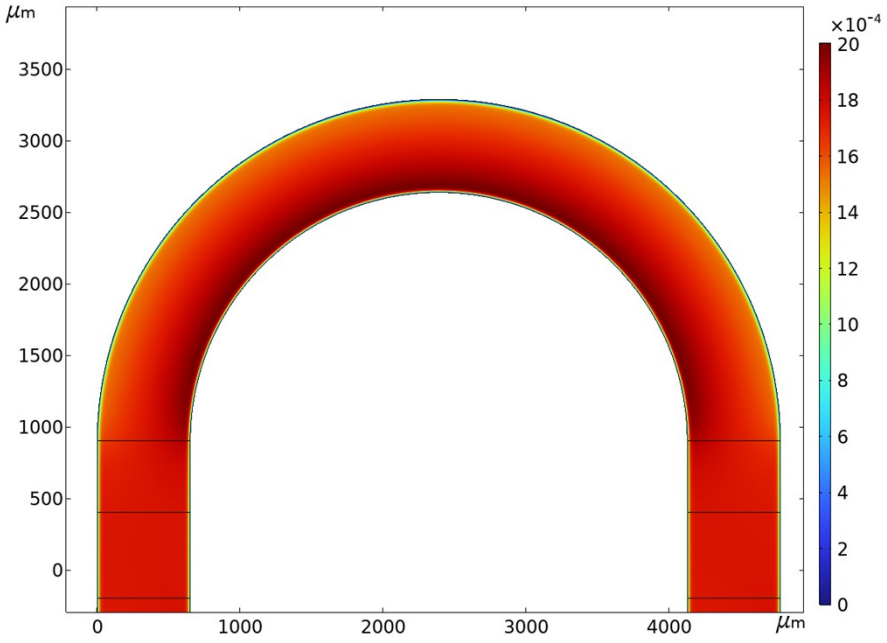

Figure S5: (b) Zoomed inset of Velocity (m/s) at "U" turn; microreactor simulated in COMSOL

The change in the surface velocity is noticeable especially at the sharp turns, where a higher surface velocity is observed for the inner bends compared to the outer bends. This arises due to the relative difference in the hydraulic resistance experienced by flow in the inner and outer bends. As fluid has a smaller channel length to travel for the inner bend, it experiences a reduced hydraulic resistance.

$$R_h = 12\frac{\eta L}{wh^3} \tag{4}$$

Here, R_h is the hydraulic resistance, η is the viscosity of the fluid, L is channel length, w is channel width and h is channel height. As, hydraulic resistance is inversely proportional to the surface velocity, the inner bend that experiences a lower hydraulic resistance therefore has a higher surface velocity.

4. Determination of diffusion coefficient

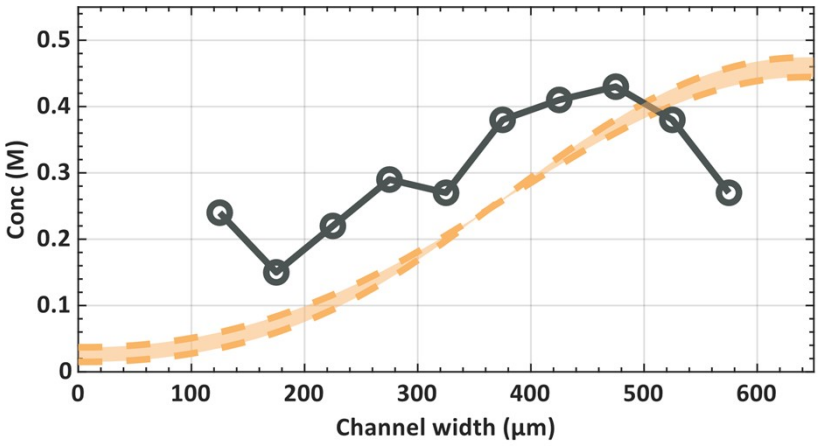

Figure S6(a): Diffusion coefficient simulated and experimental data sets for BB at p2. $D_{BB} = 0.367 \pm 0.115 \cdot 10^{-9}\ m^2/s$

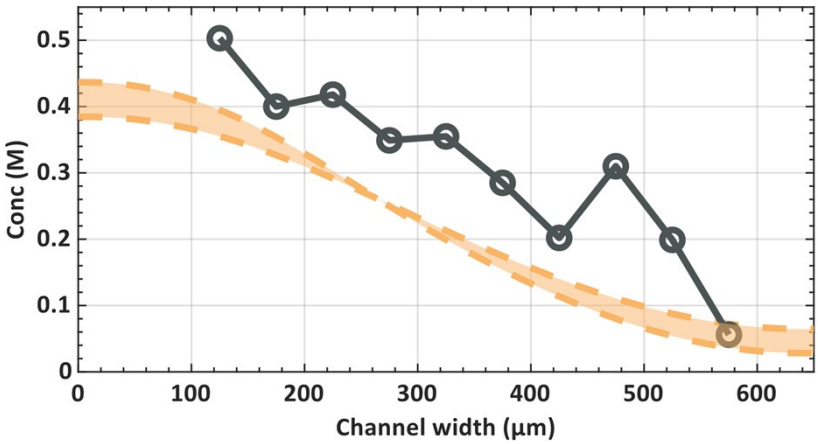

Figure S6(b): Diffusion coefficient simulated and experimental data sets for BB at p3. $D_{BB} = 0.367 \pm 0.115 \cdot 10^{-9}\ m^2/s$

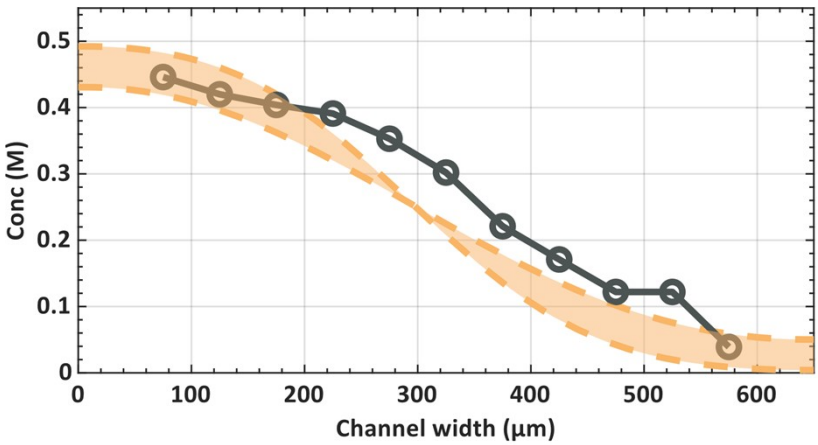

Figure S6(c): Diffusion coefficient simulated and experimental data sets for SA at p1. $D_{SA} = 1.17 \pm 0.723 \cdot 10^{-9}\ m^2/s$

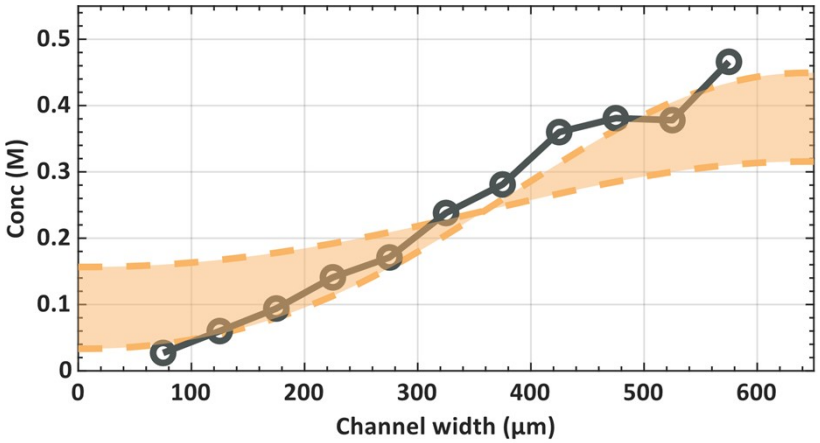

Figure S6(d): Diffusion coefficient simulated and experimental data sets for SA at p2. $D_{SA} = 1.17 \pm 0.723 \cdot 10^{-9}\ m^2/s$

6. IR Spectra

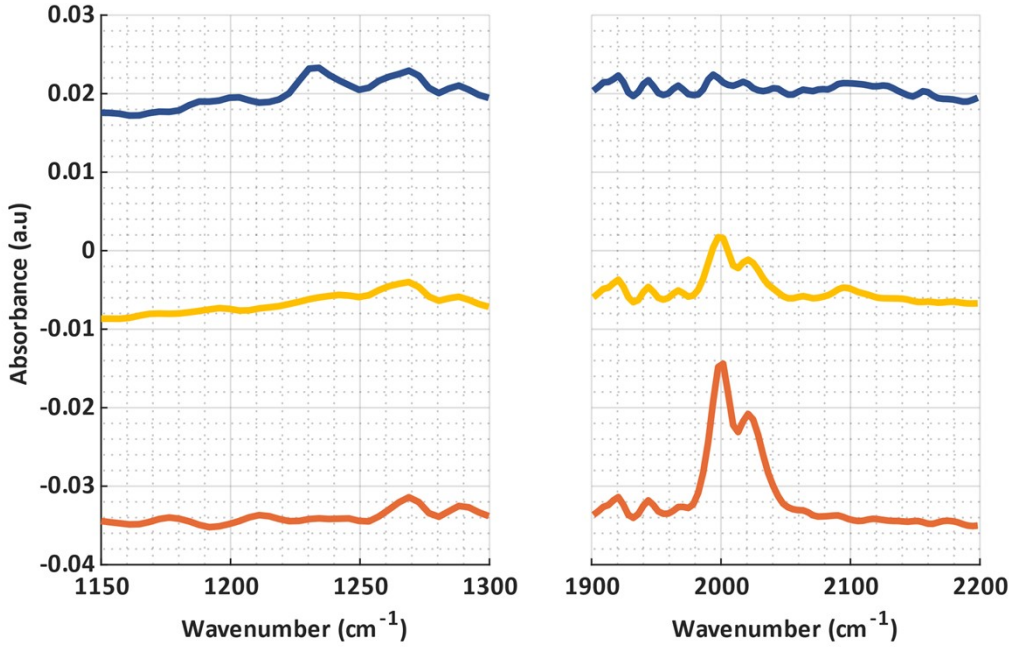

*Figure S7(a): IR spectra for the chemical reaction **position p1** at x = 75 µm (blue) , 225 µm (yellow) and 425 µm (orange). Characteristic peaks for BB, SA and BA can be detected at 1230 cm^{-1}, 2000 cm^{-1} and 2100 cm^{-1} respectively.* Absorbance is x3 for spectra between 1150 cm^{-1} and 1300 cm^{-1}.

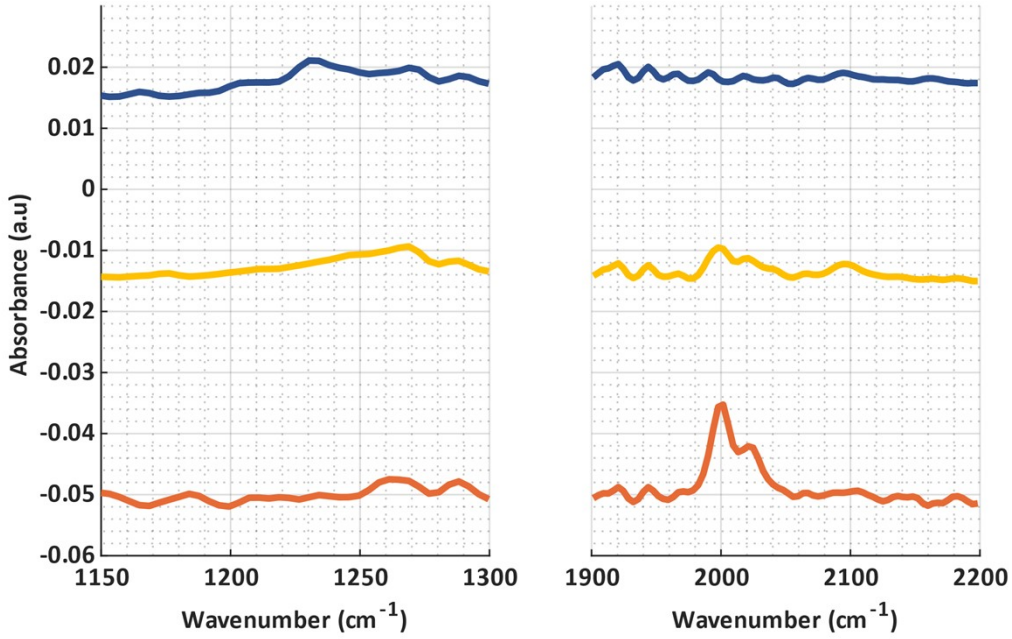

*Figure S7(b): IR spectra for the chemical reaction **position p2** at x = 75 µm (blue) , 225 µm (yellow) and 425 µm (orange). Characteristic peaks for BB, SA and BA can be detected at 1230 cm^{-1}, 2000 cm^{-1} and 2100 cm^{-1} respectively.* Absorbance is x3 for spectra between 1150 cm^{-1} and 1300 cm^{-1}.

7. Determination of rate constant

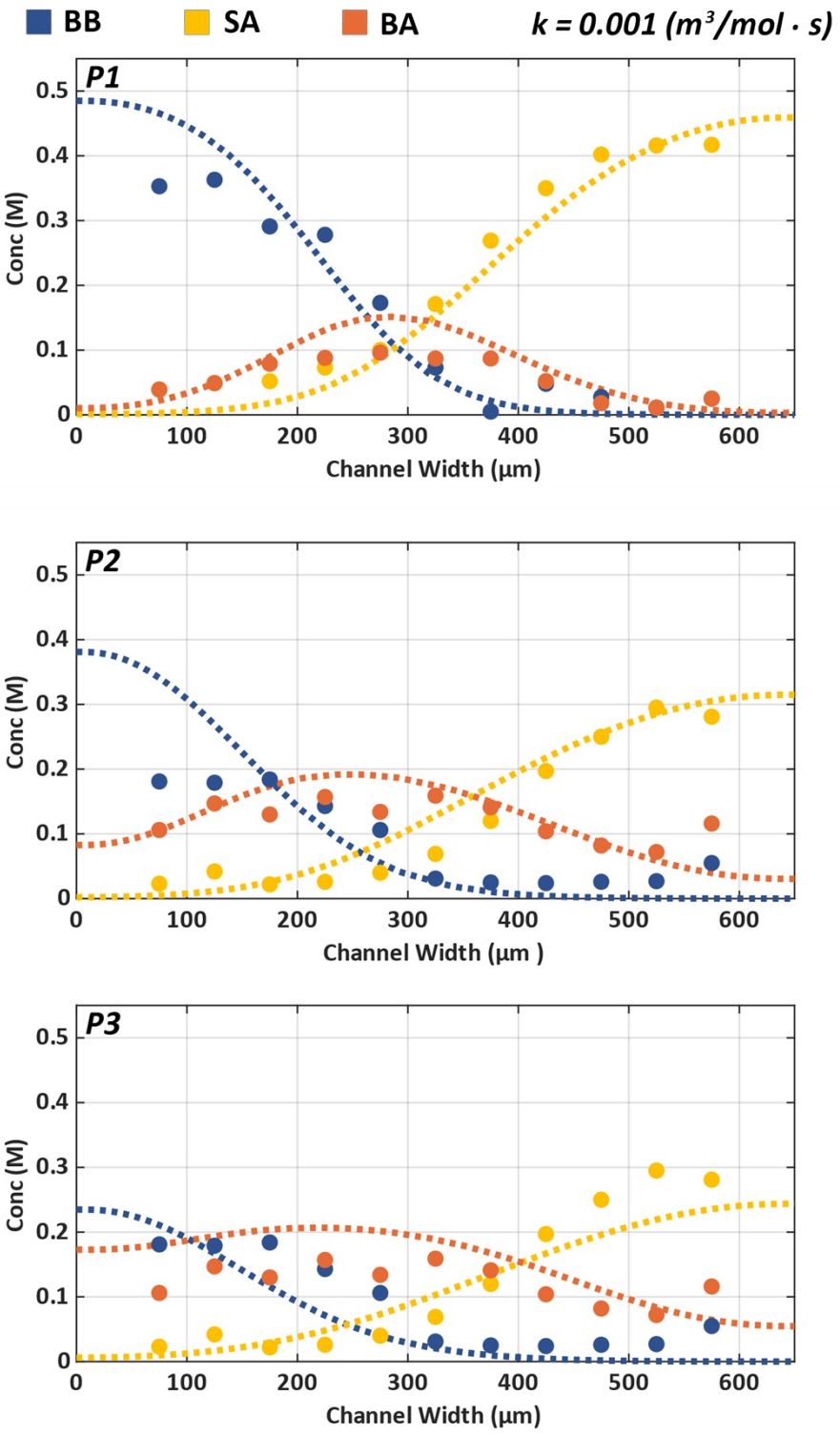

Figure S8: Experimentally measured (circles) and simulated (dashed lines) concentration profiles for BB (yellow), SA (pink) and BA (orange) for positions p1, p2 and p3 on the microreactor. Parameters used in simulations include: $D_{BB} = 0.367 \pm 0.115 \cdot 10^{-} m^2/s$, $D_{SA} = 1.17 \pm 0.723 \cdot 10^{-} m^2/s$ $D_{BA} = 0.367 \pm 0.115 \cdot 10^{-} m^2/s$ *and* $k = 0.001\ (m^3/(mol \cdot s))$