Electronic Supplementary Material (ESI) for Reaction Chemistry & Engineering.

Supporting Information

A miniature CSTR cascade for continuous processing of reactions containing solids

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1. Procedure for mixing properties assessment of the CSTR cascade

The residence time distribution (RTD) measurement was carried out using the pulse injection method. The carrier phase was water and the tracer was methylene blue, which is UV-Vis sensitive. A 6-way valve (IDEX Health & Science LLC., MXP7900-000) was used to inject the tracer into the reactor. The UV-Vis light source (Ocean Optics, Inc., DH-2000-BAL) and spectrometer (Ocean Optics, Inc., HR2000+) were used to measure the concentration profiles at the inlet and outlet of the reactor. LabVIEW was used to control the system to realize automatic tracer injection and UV-Vis signal recording.

The amount of tracer used was determined by the number CSTR chambers that were tested. A certain level of tracer concentration is required to get strong enough UV-Vis signal response. In this RTD measurement, the amount of the tracer was proportional to the number of CSTRs in series.

Measurement was stopped while there was negligible amount of tracer in the outlet stream. The concentration profiles of the inlet stream and outlet steam were normalized by the total amount of the tracer in each stream, which was obtained by integration over the whole measurement time.

2. Procedure for heat transfer efficiency validation of the CSTR cascade

Isoprene and maleic acid anhydride were prepared in the DMF solvent. The concentration of isoprene solution is 1 mol/L and the concentration of maleic acid anhydride solution is 1.5 mol/L. The solutions were all used immediately after preparing in order to avoid degradation of the reagents due to the air or light.

The scheme of the setup for evaluating the heat transfer efficiency is shown in the Figure S1. Two HPLC pumps (AZURA P 4.1S) were used to deliver two solutions into the reactor. The flow rates for both streams were equal to 200 μL/min. 1-, 3-, 5-, 7- unit CSTR cascades were tested using the same flow rate. The reactor was placed on a magnetic stirrer (VWR, VMS-C7 Advanced magnetic hotplate stirrer), which is integrated with the heating system. The magnetic stirrer operated at the 600 revolutions per min (rpm). In order to prevent the heat loss due to the free convection of air, mineral wool was used to insulate the reactor. The temperature was set at 50 ^{o}C.

The CSTR cascade was preheated to the setting temperature before pumping two reagents into the reactor. As the reaction continuously proceeded in the reactor, the samples were collected after five reactor volumes, which was considered to be at steady state. Three samples were taken at fifth, sixth, and seventh reactor volumes. As soon as the samples were collected, the mixture was diluted using ethyl acetate (1:20) and cooled down to 0 ^{o}C in the ice bath in order to quench the reaction. The gas chromatography (Agilent 6890 Gas Chromatograph) was used to obtain the conversion of the samples.

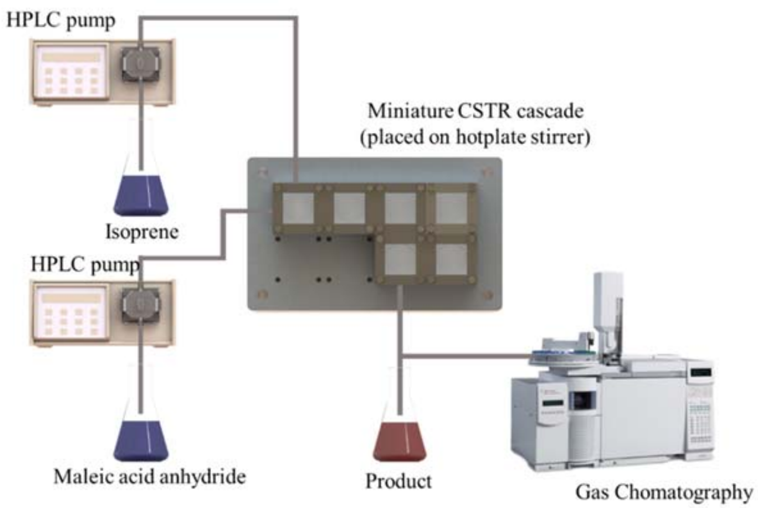

Figure S1. The scheme of the heat transfer efficiency validation using Diels-Alder reaction.

3. Procedure for continuous handling of reactions containing solids

Setup for continuous handling of solids. The scheme of the setup is shown in the Figure S2. The reagents for the reactions were separated into two streams and they were pumped into the CSTR cascade by HPLC pump. There was an in-line pressure sensor connected at the inlet of the reactor in order to measure the pressure profile in the system. The CSTR cascade was placed on the magnetic stirrer for providing driven force to spin the magnetic stir bars in the CSTR chambers. The rotation speed of stir bar in each chamber was set to be the same, which was 600 RPM. 600 RPM was the upper limit of rotation speed that can keep the magnetic stir bars spinning on a single magnetic stirrer for a long period. Beyond this rotation speed limit, the magnetic stirrer (Corning® 11 x 11 Inch Top PC-611 Stirrer) could not provide enough magnetic coupling force to spin the stir bars (VWR® Spinplus® Magnetic Stir Bars, 58947-820), which would lead to shaking of stir bars instead of rotation. Operation under the maximum RPM of the system improved mixing, and at the same time, provided high local flow speed to keep particles suspended against gravity, particle-wall interaction, and particle-particle interaction.

Since the two reaction examples that were used in this section could proceed under the atmosphere temperature, heating was not required in this setup. The magnetic stirrer was placed vertically in order to operate the CSTR cascade in the vertical mode, which helped to minimize clogging at the outlet tube of the reactor. Products were collected at the outlet of the reactor using a flask.

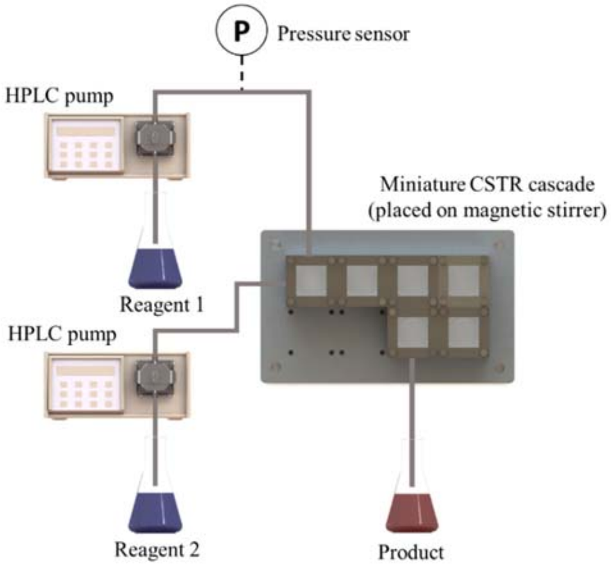

Figure S2. The scheme of using the miniature CSTR cascade to handle solids in flow.

The optical characterization of the solid particles formed in the CSTR cascade were carried out by using the optical microscope (ZEISS Axiovert 200). 100 μL of well-mixed slurry was loaded onto the glass slide, and another glass slide was used to cover the sample in order to prevent evaporation of the solvent. In this case, the crystals would remain unchanged under the microscope.

The particle size distribution was measured by the Malvern particle sizer (Malvern Mastersizer 2000). Original solvent was used to make sure that the particle size and morphology did not change when injecting the samples into the particle sizer. With the solid concentration coming out of the reactor, 0.5 mL sample was enough to fulfill the low limit of detectable particle concentration that was needed for the machine to measure the size distribution. Only the product from the first reaction example, imine formation reaction, was measured. The crystals generated in the second reaction were needle-shape, and the results given by the Malvern particle sizer would not represent the meaningful sizes of the crystals because the Malvern particle sizer assumes that the shape of particles is close to sphere.

Continuous processing of the imine formation reaction. Glyoxal and cyclohexylamine were dissolved into the ethanol. The concentration of the glyoxal solution was 0.4 mol/L and the concentration of the cyclohexylamine solution was 0.8 mol/L. Full conversion can be achieved in 15 min. The conversion was measured using gas chromatography.

Continuous processing of the sulfonylation of alcohol reaction. All reagents were separated into two streams. One stream contained 2-octanol, triethylamine and DMAP, and they were prepared in the DCM solvent. The concentrations of 2-octanol, triethylamine and DMAP were 0.6 mol/L, 0.72 mol/L, 0.08 mol/L. Methanesulfonyl chloride was prepared in the other stream, and the concentration was 0.5 mol/L. The conversion was measured using gas chromatography.

4. RTD measurement concentration profiles

The inlet and outlet concentration profiles were measured by in-line UV-Vis. The outlet concentration profiles given by the convolution of inlet concentration and regressed EMG model show excellent agreement with the experimentally measured outlet concentration profiles (Figure S3).

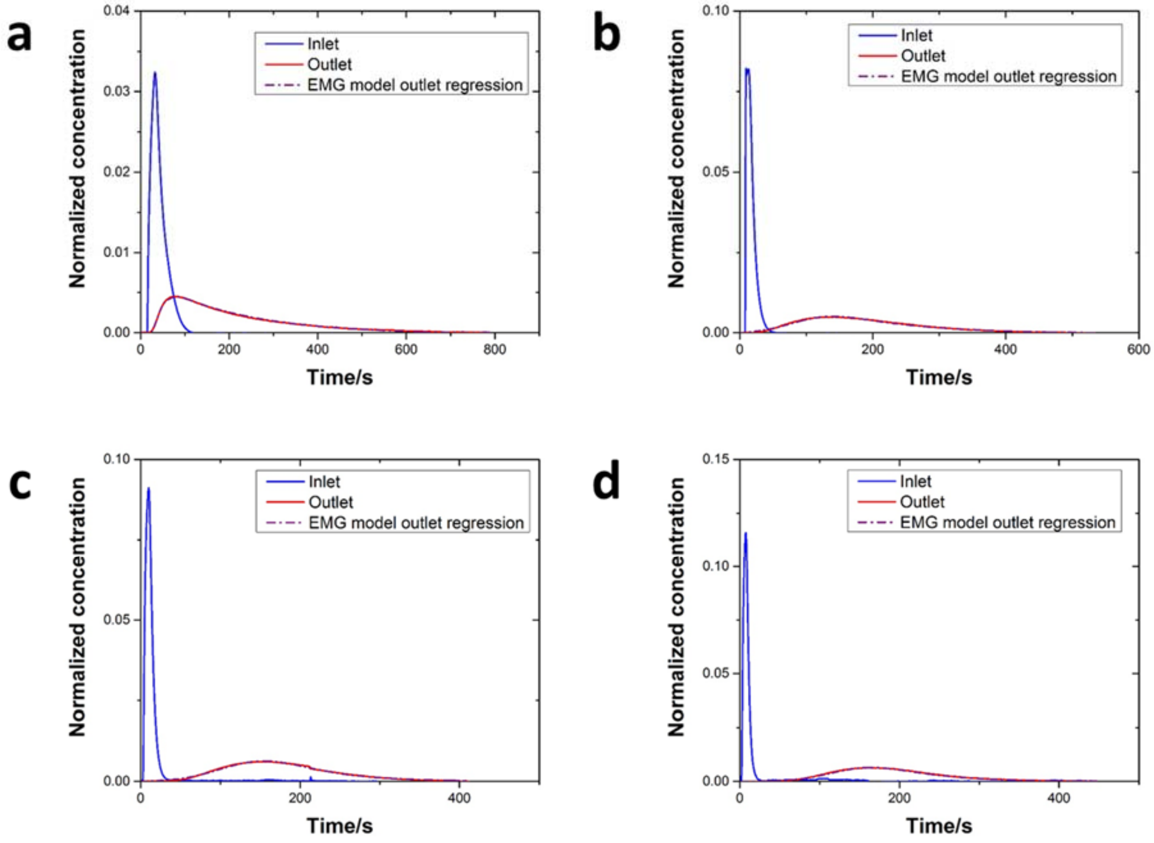

Figure S3. The inlet and outlet concentration profiles, and the outlet concentration profiles given by the EMG model regression. The CSTR cascade with different numbers of reactors are tested: (a) n=1; (b) n=3; (c) n=5; (d) n=7.

5. Individual rotation speed control system

A relatively more complex system was designed to individually control the rotation speed of stir bar in each chamber. The design is shown in Figure S4. For each chamber, a motor with magnets on the motor shaft provides the magnetic coupling force to spin the stir bar. The speed of rotation can be controlled individually by controlling the voltage applied to the motor.

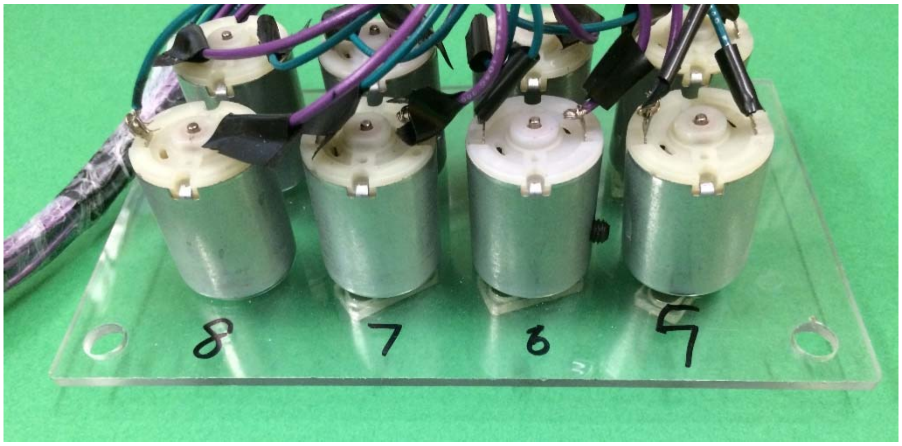

Figure S4. Photo of individual rotation speed control system.