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High-throughput screening of supported catalysts in massively parallel single-bead microreactors: Workflow aspects related to reactor bonding and catalyst preparation

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Abstract

We demonstrate the possibility to anodically bond a 625-parallel single-bead microreactor filled with supported catalysts resulting in a hermetically closed reactor assembly. The bonding process enables excellent microfluidic properties by eliminating fluidic cross-talk between adjacent microreaction chambers. The bonding significantly facilitates handling of the reactor assembly, including mounting, dismounting, archiving, regeneration and re-use of the reactor, and protection of the catalytic materials. Regarding the comparison of a single-bead, non-contact incipient wetness preparation method with the corresponding conventional laboratory scale catalyst synthesis procedures, we show that the miniaturized single-bead synthesis is almost as accurate and reproducible as the conventional approach. The standard deviation of the observed conversion degree of the individually prepared single-bead catalysts in CO oxidation as model reaction is quantified to be in the range of 5–7%, while it is in the range of 3–6% for conventionally prepared catalysts. Both bonding and single-bead catalyst preparation enable a complete massively parallel single-bead workflow that may be a very accurate, elegant and last but not least highly competitive approach for high-throughput catalyst screening programs.

Keywords: Single-bead reactor; High-throughput experimentation; Catalyst screening; Single-bead synthesis; Anodic bonding; Microreactor

1. Introduction

Parallel catalyst screening approaches for heterogeneously catalyzed gas phase reactions have gained increasing popularity within the past years, as the development of novel and better catalysts for chemical processes is still mainly an empirical process utilizing existing technical know-how and experiences.

The main target in stage-I screening, the discovery stage of high-throughput experimentation programs in catalysis, is the identification of hits from large catalyst libraries. The number of catalysts tested in parallel should be a few hundred on a small reactor footprint. Therefore, specific library preparation methods resulting in very low amounts of the single materials are required. The information depth of the analytical methods employed is often reduced in favour of a high analytical speed. Generally, some challenging requirements that have to be met by primary screening reactors are: (i) the reactor design has to accommodate catalysts made by a simple, fast and scalable catalyst preparation method; (ii) many catalysts should be tested simultaneously under steady-state conditions and continuous flow; (iii) the analysis method should have a high spatial resolution and allow a good estimate of conversion degree and selectivity, while still being very fast and reproducible. Finally, all those specific tasks have to be solved in an integrated fashion allowing efficient automated workflows with low costs per tested material.

The first description of a stage-I screening approach dates back to 1996, where Moates et al. [1] used a simple setup of a substrate-based library and an IR-camera to detect catalytic activity. Holzwarth et al. [2] extended this principle to emission corrected infrared (IR) thermography with high temperature resolution to resolve reaction heats spatially over libraries of catalysts of transition metals in amorphous microporous mixed oxides on a flat substrate that was cross-flowed by the reactants. Flat substrates with catalysts produced as thin films were also used by Cong et al. [3]. By means of two concentric capillaries for supplying and withdrawing reactants the catalyts were tested sequentially in a transient mode by a special mass

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spectrometer. Later, this methodology was simplified and extended by Orschel et al. [4], using small amounts of catalyst particles in each well on the substrate.

Obviously, continuously operated microfluidic reactors present a number of interesting properties being worthwhile to use in stage-I catalyst screening. Those reactors provide excellent heat and mass transfer properties and can be operated under isothermal conditions. The response times to changes of the reaction conditions are very low and a number of additional static or even active elements can be integrated into the device besides the reactor itself. Owing to their potential mass fabrication, miniaturized reactors may prove cost-efficient. Accordingly, several approaches for the application of microfluidic reactors were presented in the past. Those approaches can be categorized by the chosen catalyst synthesis strategy, as this strategy has, from our point of view, the most important impact on reactor design. From the early days of microreaction engineering, catalytic coatings have been discussed intensively for application in microreactors. This is reflected by the use of catalytic coatings on microstructured substrates, as extensively described in Refs. [5,6] and later adopted by Müller and Drese [7] and Men et al. [8]. Typically, special catalyst preparation methods, such as anodic oxidation of aluminum or washcoating, are required. The preparation is usually done ex situ of the reactor which may require considerable manual work for handling and filling the reactor with the catalysts.

To avoid the catalyst handling problems, single channels of a reactor having parallel microchannels have been coated with different catalysts [9] (see Fig. 1). This example nicely illustrates the problems that may be associated with an in situ preparation of catalytic coatings by solution-based chemistry. As can be seen from the REM images, the coating may be inhomogeneous within the channel, as the solution may stick to the edges of the channel which is caused by the surface tension. Good adhesion and unwanted cracking of the coating is often a problem. As can be seen from Fig. 1b, the coating may also be found in areas where it should be avoided, such as in the fluid distribution manifold (caused by capillary forces) or on the wafer surfaces that may be needed for bonding the device (caused by imperfect fluid dispensing). Undoubtly, it is possible to produce better coatings than the ones shown in Fig. 1. However, the principal target should be to prepare catalysts, and not to develop special coating techniques.

Another interesting example of the application of a microfluidic reactor in high-throughput experimentation in catalysis was described by Bergh et al. [10], who used an arrangement of reaction chambers with thin- or thick-film catalysts on a flat substrate in connection with a ‘‘binary tree’’ capillary manifold for parallel catalyst testing. Again, catalytic coatings are used which typically again require special preparation methods differing from those conventionally used. However, workflow integration is relatively straightforward, as reflected in another paper by Bergh [11]. This is not surprising, as an application in industry requires integratability and easy handling.

The ability to work directly with catalysts in the form used in the industrial process is obviously the driving force for an approach described by Jensen and co-workers [12]. Here, small catalyst particles are used in the form of a micro-fixed bed in a microfluidic reactor. The transfer of catalytic results gained with such a reactor type to larger scale reactors may be significantly easier than for the coatings approaches, however, the parallelization degree may definitely be limited by the required catalyst preparation, milling, sieving and handling steps.

As shown from those examples, the choice of the preparation method and strategy has tremendous implications on the overall catalyst screening workflow and total cost. Furthermore, handling of the reactor in an automated screening workflow becomes increasingly important with higher throughput. Therefore, we have developed the single-bead approach based on using individual beads in a massively parallel arrangement of microreaction chambers on a chip with excellent scalability to very high numbers of parallel reaction chambers that have not been realized before in continuous flow applications [13,9,14].

The scope of this paper is to discuss important workflow issues coupled to reactor handling and catalyst preparation for

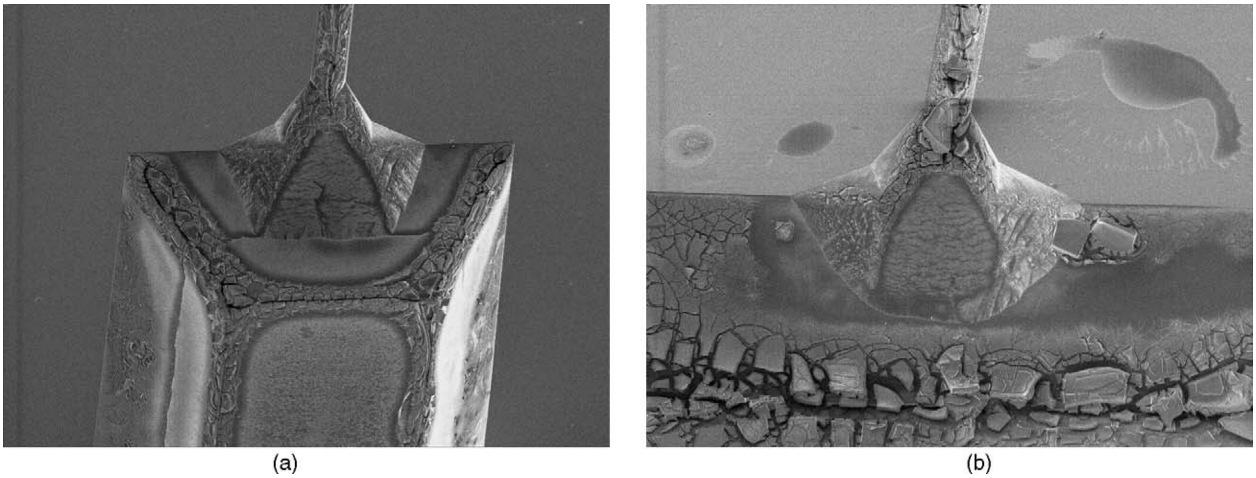


Fig. 1. REM images of catalyst coatings prepared by the sol–gel technique inside microchannels on a 16-parallel silicon microchannel reactor [9].

stage-I catalyst screening and to propose strategies to solve these problems.

2. Single-bead reactor approach

2.1. Reactor design and fabrication

The basis of the single-bead concept is the use of single shaped bodies as the catalytic material of interest. These particles may in principle be of any shape, but usually spherical particles are used. In accordance with approaches known from combinatorial chemistry in organic chemistry and life science applications, such spherical particles are called ‘‘beads’’. Each bead represents one catalyst as a member of a library of solid catalysts. These beads can be prepared by different synthesis procedures and sequences like impregnation, coating, etc. In addition, bulk mixed metal oxide catalysts can also be formed into spherical particles. To avoid mass transfer problems while reacting the fluid on the bead, egg-shell type catalytic beads can be used.

For supported catalysts, a large number of industrially available support materials can be directly used with the single-bead reactor, as shown in Fig. 2. Those supports are available from different vendors and in different properties and qualities.

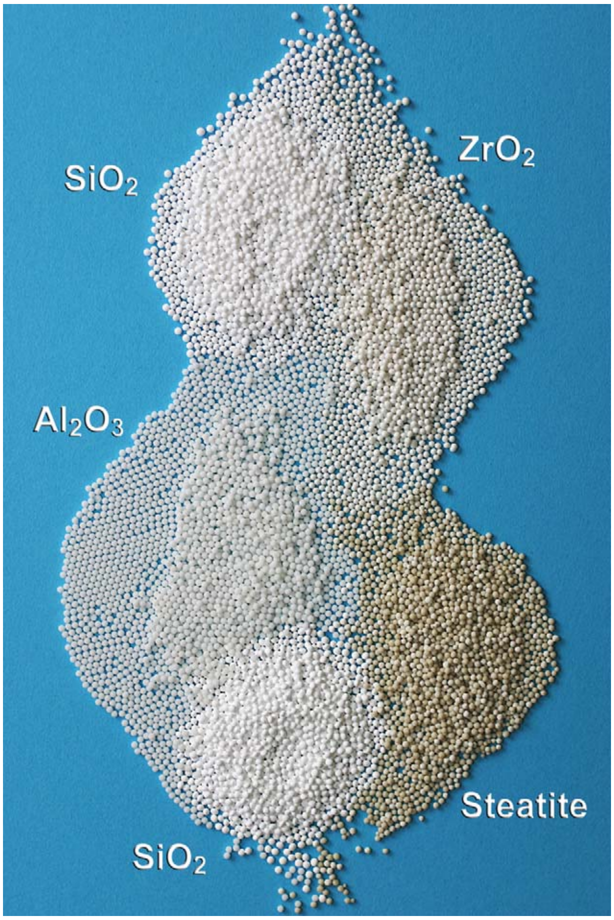


Fig. 2. Different commercial catalyst supports usable for catalyst screening with the single-bead approach.

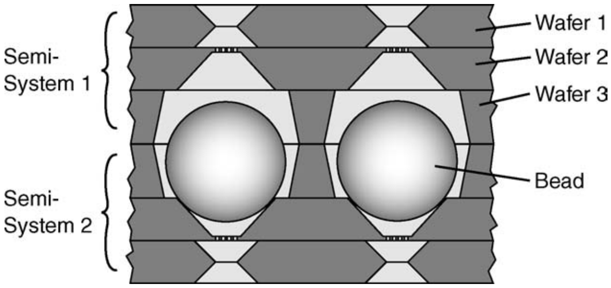


Fig. 3. Cross-section of two parallel reaction chambers of the single-bead reactor architecture consisting of two identical semi-systems that are pressed together in operation. The bead diameter is 1 mm.

Post-modification of the supports is easily feasible, and new supports may be produced with proprietary methods.

The basic principle of the single-bead reactor is the encapsulation of each catalytic bead in a single microreaction chamber on a chip containing a massively parallel, two-dimensional arrangement of such chambers [13]. The partial cross-section of a single-bead reactor is shown in Fig. 3. The reactor is made up of two identical semi-systems that each consists of an assembly of three individual structured wafers. Within that assembly, a number of different features are combined, among which fluid distribution and fixing the bead at a defined position within the chamber are the most prominent. Because of the high demands regarding the accuracy of the microstructures as well as its excellent thermal stability, silicon was chosen as the primary reactor material.

The different wafers are processed by a combination of standard silicon micro-machining techniques (wet chemical anisotropic etching and reactive ion etching) and micro powder blasting that is described in detail in Ref. [14]. The wafers are oxidized thermally after the structuring process in an O_2-atmosphere at 1050 °C to obtain a thin SiO_2-coating on the inner reactor surface. The wafers of each semi-system are then assembled by silicon fusion bonding. The resulting semi-system contains very fine pore structures for fluid distribution while the whole inner surface of the reactor is coated with a thin SiO_2 layer for higher chemical stability and inertness of the reactor compared to a pure silicon surface.

For flow distribution to the individual microreaction chambers, independent flow restrictors for each reaction chamber in the form of porous membranes are used (fabricated in wafer 2, see Fig. 3), as the pressure drop along the fluid flow path is the key for controlling the fluid flow rate. A considerable pressure drop can be generated depending on the pore number and the pore radius. In particular reduced pore radii result in a pronounced increase of the pressure drop. These microstructured membranes themselves consist of an arrangement of a defined number of short straight pores with a very small diameter. The functioning of this approach has been proven by computational fluid dynamics simulations [15]. By means of the pressure drop caused by the individual pore membranes at the inlet of every reaction chamber, a single feed stream is equally divided into sub-streams flowing through each reaction chamber. The top-down direction of fluid flow thus enabled, and the small footprint of a single microreaction chamber together allow the extension of the reactor in two dimensions resulting in a very high number of microreaction chambers on a small chip area. We designed and fabricated a 25 × 25 arrangement of microreaction chambers (625 parallel microreaction chambers) on an area of less than 50 mm × 50 mm on a total chip size of 70 mm × 70 mm.

As can be estimated from Fig. 3, the beads are held centrically in the microreaction chambers generating symmetrical flow conditions. This is achieved by combination of a pyramid frustum with the spherical bead. Another advantage of the pyramid is the tolerance to variations of size and form of the beads. A spherical bead cannot block the quadratic cross-section of the frustum. No special precautions need usually be taken to ensure the sphericity of the beads. Furthermore, different bead sizes can be employed, however, the bead size is usually kept constant for one experiment.

In direction of the flow, the cross-section of a single microreaction chamber varies from 150 μm × 150 μm at the inlet and the outlet to 1400 μm × 1400 μm in the center of the chamber. Accordingly, the annular distance between the bead and the wall of the chamber varies, resulting in different superficial flow velocities. In the catalytic zone of the well, the average distance between the wall and a 1000 μm bead is approximately 300 μm.

2.2. Operation mode

In standard operation mode, the single-bead reactor is filled with catalytic beads and then mounted into a stainless steel flange (see Fig. 4) that allows pressing of the second semi-system to the first one resulting in an encapsulation of each bead in a single, independent microreaction chamber and in avoiding fluidic cross-talk between adjacent reaction chambers.

The reactor is operated in continuous flow mode and under stationary conditions simultaneously for all 625 microreaction chambers, while the complete flange system and the feed gas is homogeneously heated to reaction temperature. The feed that may consist of a multicomponent gas mixture including vaporized liquid feedstocks (i) enters the reactor from the top, (ii) is divided into sub-streams by the individual flow restrictors at the entrance to each microreaction chamber, (iii) the sub-stream flows through the chamber contacting the catalytic bead and (iv) leaves the chamber through the corresponding product outlets at the bottom of the reactor, compared to Fig. 3. At those individual product outlets, the separate product streams are sampled and analyzed individually in an automated fashion, for instance, by scanning mass spectrometry [9]. Once all or all selected product streams are sampled and analyzed, a new set of operation conditions (e.g. different temperature, different gas composition and different space velocity) can be applied automatically [16], and the sampling procedure is repeated. Thus, it is easily possible to investigate the catalyst library at different operating conditions or to study time-on-stream behavior including regeneration cycles, etc.

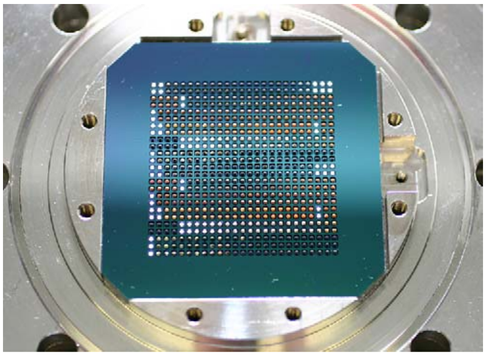


Fig. 4. Lower semi-system of single-bead reactor containing catalysts before closing and pressing with upper semi-system in stainless steel flange.

The reactor is typically operated at ambient pressure, although higher pressures are possible. Typical residence times are in the range of 50–200 ms, although this range is mainly determined by the analysis technique. The scanning mass spectrometer, for instance, requires a minimum product flow rate of approximately 0.5 ml/min, which corresponds to a maximum residence time of 200 ms with the reactor geometry presented in Fig. 3.

The current reactor configuration contains no special means for controlling the temperature in individual reaction chambers. The temperature homogeneity is therefore typically estimated from reference experiments, where identical catalysts are mounted at different positions in the reactor and comparing the corresponding catalytic results. Small deviations in the catalytic results then imply a good temperature homogeneity over the complete 25 × 25 reactor area [14].

2.3. Anodic bonding of filled reactor

Typically, one semi-system of the reactor is filled with beads, then the other semi-system is pressed against it during reaction which achieves fluidic separation between adjacent reaction chambers, because the manufactured semi-systems are designed to be completely symmetrical. However, it is also possible to combine these in a non-detachable manner by two bonding processes. In that case, the beads need to be inserted into the reactor before the final bonding step. Therefore, a bonding process must be used that does not alter the catalytic properties of the beads. In our case, the connection was realized by a two-step anodic bonding process. First, an anodically bondable glass wafer (Borofloat), structured by micro powder blasting, was bonded onto one semi-system. After cleaning and adjusting the wafers to each other the two bond partners were inserted into the bond device and heated up to 400 °C (see Fig. 5). Thereby, the Borofloat wafer becomes electrically conductive. By applying an electric field an electrostatic attraction and an exchange of ions at the interface takes place leading to a hermetically sealed connection.

Secondly, beads were inserted in the resulting wafer assembly (semi-system plus Borofloat wafer) which was then covered with a second semi-system by anodic bonding again. No bonding problems that could have potentially been caused

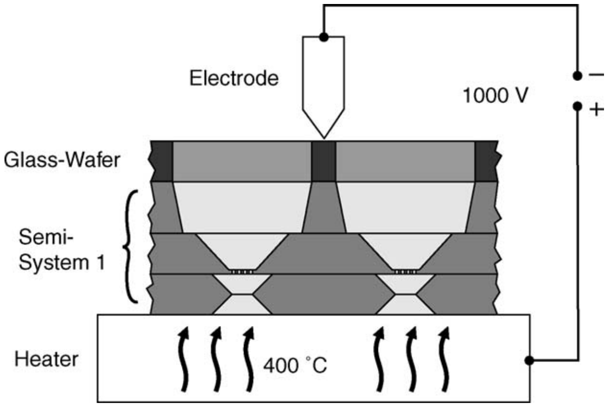


Fig. 5. Principle of the anodic bonding process applied to bond a structured glass wafer to a silicon semi-system of the single-bead reactor.

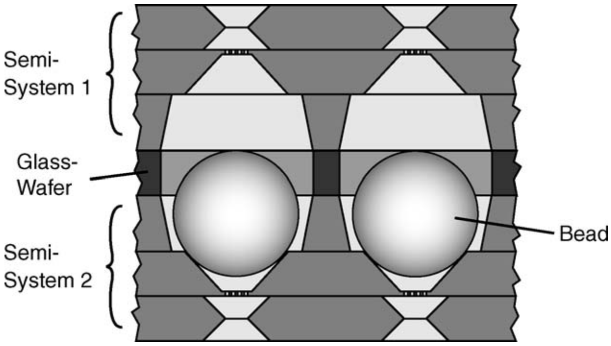


Fig. 6. Cross-section of two parallel microreaction chambers of an anodically bonded single-bead reactor. The bead diameter is 1 mm.

by the contained catalysts could be observed. The cross-section of the final device (see Fig. 6) differs from the original cross-section (shown in Fig. 3) by the additional glass wafer that is bonded between the two semi-systems. Thereby, the volume of the microreaction chambers is increased according to the thickness of the applied glass wafer. A photograph of the bonded 625-parallel single-bead reactor system that allows the parallel testing of 625 catalysts is shown in Fig. 7.

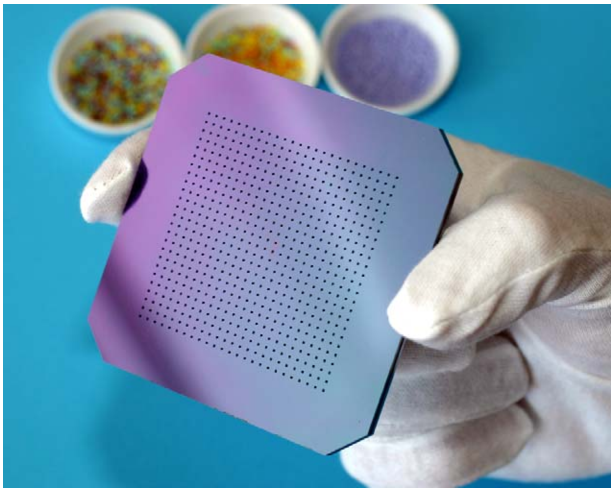


Fig. 7. Photograph of an anodically bonded single-bead reactor having 625 parallel microreaction chambers containing different solid catalysts. The outer dimensions of the 625-parallel single-bead reactor are 70 mm × 70 mm.

3. Results

3.1. Comparison of pressed and bonded reactor

For a comparison of the performances of a pressed and an anodically bonded single-bead reactor, a number of 26 catalyst batches were prepared with the target being the preparation of differently active catalysts in order to allow good discrimination and comparison. SASOL Alumina Spheres 1.0/160 with a diameter of 975 ± 25 μm were used as catalyst support. Single-component and two-component catalysts of Co, Fe, Mn, Pd, Pt, Rh and Ru with a total metal content of 1 wt% or 3 wt% were prepared in separate porcelain dishes placed on a shaker by incipient wetness of 1 g of support material for each batch utilizing a standard liquid handling robot. As precursor solutions, the aqueous solutions of the corresponding nitrates were used. All catalysts were dried for 16 h at 80 °C and then calcined for 4 h at 420 °C in air. Then, individual beads of each catalyst batch were taken and filled according to a predefined pattern into the two reactors. Thereby, it could be ensured that both reactors contain identical catalysts, i.e. individual beads from the same preparation batch. The second reactor was bonded according to the procedure described in Section 2.3 before use.

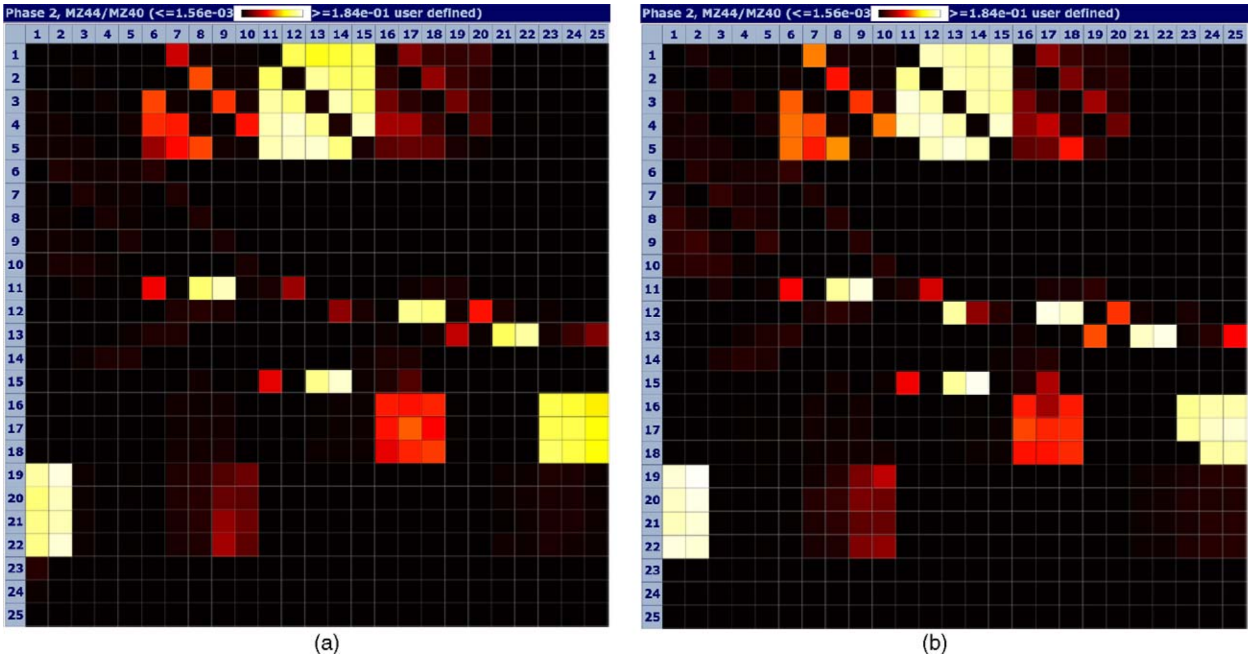
The catalyst libraries of both reactors were subsequently tested for catalytic activity in CO oxidation as a model reaction. Preceding the test, the catalysts were activated for 2 h at 300 °C in hydrogen flow. The operating conditions were set to 170 °C, a flow rate of 1.5 ml/min per bead (corresponding to a residence time of approximately 60 ms), a pressure of 1 bar and a gas composition of 1% CO, 1% O_2, 5% Ar (as internal standard) in N_2. For product analysis, fast-sequential scanning mass spectrometry [9] with an analysis time of 30 s per sample was used. The results are shown in Fig. 8, expressed as color-coded MS intensity signals for CO_2, normalized to the signal of the internal standard. Therefore, light colors mean high conversion degrees to CO_2, dark colors mean low conversion degrees.

As can be seen, the resulting color patterns are the same, hence the same results are obtained with both reactor configurations. There are only three exceptions to this general observations, namely at row 5/column 11, row 12/column 13 and row 18/column 23. However, those exceptions are related to errors when manually filling the reactor before anodic bonding. Without those three exceptions, the correlation between both reactor types equals to $R^2 = 0.983$.

The most active catalysts in these libraries are Ru/Al_2O_3 catalysts, followed by Pd/Al_2O_3 and Rh/Al_2O_3. Less activity was also observed for $Pt\text{-}Fe/Al_2O_3$ catalyst.

3.2. Accuracy and reproducibility of single-bead synthesis

For the comparison between a single-bead synthesis and conventional laboratory scale batch synthesis of supported



(a)

(b)

Fig. 8. Comparison of the performance of (a) a pressed and (b) an anodically bonded single-bead reactor configuration, expressed as color-coded MS intensity signals for CO_2, normalized to the signal of Ar. *Reaction conditions*: 170 °C, 1.5 ml/min per bead, 1 bar, 1% CO, 1% O_2, 5% Ar as internal standard, N_2 balance.

catalysts by wet impregnation, a number of reference catalysts were prepared.

For all catalysts, γ-Al_2O_3 beads SASOL Alumina Spheres 1.0/160 were used as support material. The beads were sieved carefully in order to work with a very narrow bead diameter distribution of 975 ± 25 μm. The main parameters of the prepared catalysts are listed in Table 1. As precursor solutions, the aqueous solutions of the corresponding metal nitrates were used.

For the single-bead synthesis, a single-bead reactor semi-system was filled with empty beads that were then impregnated automatically on an inkjet-type pipetting robot applying an incipient wetness method. The dispensing volume for each bead was set to 400 nl that was dispensed in four steps with a droplet size of 100 nl each.

Table 1
Preparation parameters of the Ru/Al_2O_3 and Ru-Fe/Al_2O_3 catalysts used for comparison of single-bead and batch synthesis

Catalyst	Method	Metal content		Comments
		Ru (wt%)	Fe (wt%)	
B1	Batch	3	0	Incipient wetness
B2	Batch	3	0	Excess solution
B3	Batch	3	0	Incipient wetness, PEG addition
B4	Batch	3	0	Excess solution, PEG addition
B5	Batch	2	1	Incipient wetness
B6	Batch	2	1	Excess solution
B7	Batch	2	1	Incipient wetness, PEG addition
B8	Batch	2	1	Excess solution, PEG addition
S1	Single-bead	3	0	
S2	Single-bead	2	1	
R		0	0	Pure Al_2O_3 support, inert reference

PEG: polyethylene glycol.

For the standard conventional batch synthesis, the catalysts were prepared in separate porcelain dishes placed on a shaker by incipient wetness of 1 g of support material for each batch utilizing a standard liquid handling robot. Deviations from that procedure were the addition of PEG to the impregnation solution to improve wetting behavior and the application of a wet impregnation procedure with excess solution that was removed by filtration after impregnation, as indicated in Table 1.

All catalysts were dried for 16 h at 80 °C and then calcined for 4 h at 420 °C in air. Several catalytic beads of each type were mounted into a 625-parallel single-bead reactor. Preceding the test, the catalysts were activated for 2 h at 300 °C in hydrogen flow. The operating conditions were set to 160 °C, a flow rate of 1.5 ml/min per bead (corresponding to a residence time of approximately 60 ms), a pressure of 1 bar and a gas composition of 1% CO, 1% O_2, 5% Ar (as internal standard) in N_2 in order to allow appropriate comparison of the catalysts at a CO conversion degree in the range of 50–60%. For product analysis, fast-sequential scanning mass spectrometry [9] with an analysis time of 30 s per sample was used. Product sampling was done in randomized mode, i.e. with random selection of the catalyst to be sampled.

The results of the experiment are shown in a standard Box-Whisker plot (see Fig. 9). In the plot, the distribution of the measured conversion degrees on the individual beads of the particular catalysts is visualized. No CO conversion is measured on the inert reference R, which is also an indication of almost no cross-talk between adjacent microreaction

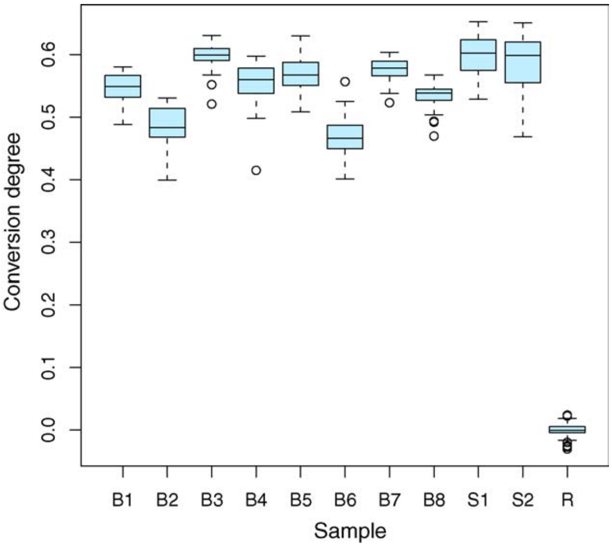


Fig. 9. Box-Whisker plot of the activity of different Ru/Al_2O_3 and Ru-Fe/Al_2O_3 catalysts prepared by batch or single-bead synthesis according to Table 1, given as conversion degree of CO. *Reaction conditions*: 160 °C, 1.5 ml/min per bead, 1 bar, 1% CO, 1% O_2, 5% Ar as internal standard, N_2 balance.

chambers. The activity of the other catalysts is typically in the range of 50–60%, with differences between the catalysts of different type. Regarding the catalysts prepared by conventional batch synthesis, a significantly narrower distribution of the measured conversion degree can be observed for catalysts that were prepared with addition of PEG to the aqueous impregnation solution. Furthermore, catalysts prepared in excess solution generally show less activity. The catalysts S1 and S2 prepared by the single-bead incipient wetness method show comparable activity to the best batch catalysts (B3 and B7), but with a slightly broader distribution. However, they were not prepared with PEG addition that could have narrowed the distribution, as can be seen from the different batch catalysts, e.g. B1 versus B3 and B5 versus B7.

Table 2 summarizes the results from the experiment for the average conversion degree and the corresponding standard deviation. The smallest standard deviations for the batch catalysts are in the range of 3% (catalysts B3 and B7), while it is in the range of 4–6% for batch catalysts prepared without addition of PEG. For the single-bead incipient wetness method, slightly larger standard deviations in the range of 5–7% are observed for those catalysts. Thus, the single-bead incipient wetness method is almost as accurate and reproducible as the conventional batch preparation method.

Table 2
Average activity and corresponding standard deviation measured for different Ru/Al_2O_3 and Ru-Fe/Al_2O_3 catalysts prepared by batch or single-bead synthesis according to Table 1

Catalyst	N	X_{average}	σ (%)
B1	36	0.548	4.08
B2	36	0.485	6.21
B3	36	0.597	3.48
B4	36	0.555	5.97
B5	48	0.570	5.01
B6	48	0.469	6.4
B7	48	0.577	2.86
B8	48	0.533	3.45
S1	36	0.598	5.6
S2	48	0.585	7.76

Reaction conditions: 160 °C, 1.5 ml/min per bead, 1 bar, 1% CO, 1% O_2, 5% Ar as internal standard, N_2 balance. N: number of beads of that type in the reactor; X_{average}: average CO conversion degree; σ: standard deviation of calculated conversion degree.

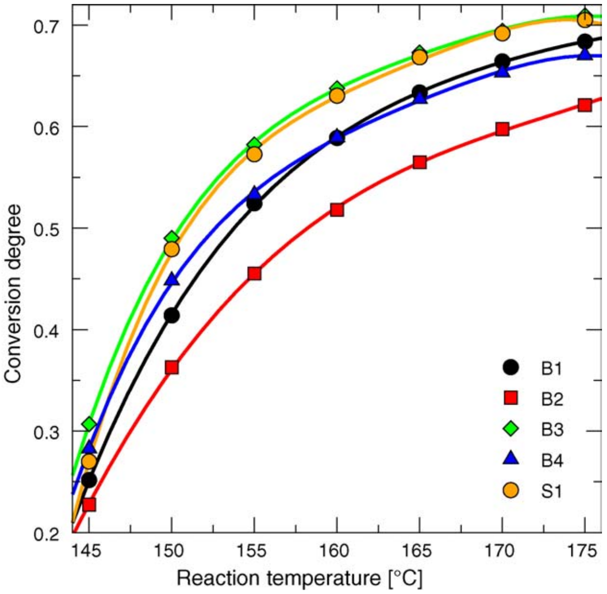


Fig. 10. Activity of catalysts B1, B2, B3, B4 and S1 at different temperatures, given as conversion degree of CO. Reaction conditions: 145–175 °C, 1.5 ml/min per bead, 1 bar, 1% CO, 1% O_2, 5% Ar as internal standard, N_2 balance.

The single-bead architecture and the chosen experimental approach allow convenient and fast testing of the catalysts at different reaction conditions with automatic control of the reaction parameters and the sampling and analysis process. As an example, Fig. 10 shows the temperature–activity curves for the Ru/Al_2O_3 catalysts of Table 1. Plotted are the average values for the measured CO conversion degree on catalytic beads of the different types in a temperature range of 145–175 °C. Within that temperature window, the observed conversion degrees increase from approximately 20% to approximately 70%. The conversion-over-temperature curves can be accurately interpolated by polynomials. As expected, the same relative behavior of the catalysts compared to Fig. 9 is observed for the temperature variations. The example shows that the time-resolved sampling permits an in-depth testing of all or of selected catalysts at different reaction conditions in a fast-sequential mode while the different runs could be preceded by regeneration steps, if necessary. In principle, all process variables can be included in such a sensitivity study, as shown for feed concentrations and flow rates in Ref. [14]. It has to be noted that the testing at different reaction conditions is much more difficult in screening systems where the product samples are accumulated over time to get suitable signal intensities, such as for the sorbent and color detection approach described in Ref. [10].

4. Discussion

We have demonstrated the possibility to anodically bond a single-bead reactor filled with supported catalysts resulting in a hermetically closed reactor assembly. The bonding process enables excellent fluidic properties within the separate microreaction chambers, as fluid cross-talk between the chambers can be efficiently eliminated by the bonding process. In general, such an anodic bond process (as all other comparable bond processes) benefits from clean bond surfaces. That cleanliness of the bond surfaces can easily be ensured with the single-bead approach, as the beads can be prepared and calcined in a device having the same format as the reactor with parallel transfer of the beads to the reactor before bonding. During that transfer step, contact of the beads with the bond surfaces can easily be avoided.

From the results shown in Fig. 8 it becomes clear that the bonding process in our approach does not damage the catalysts in any way, hence the original catalytic properties of the catalysts are preserved in the bonding process. The test results between the bonded and the pressed reactor assembly in the model reaction are almost identical. That means of course, on the other hand, that the bonding has no clear advantage over the pressing of the reactor for the particular application, as the same results can be generated. The problem of cross-talk, however, is usually more pronounced in more demanding applications, such as reactions at much higher temperatures, e.g. up to 500 °C. In those cases, a bonded reactor assembly can be beneficially applied. Beyond that, a bonded reactor assembly has a number of additional advantages compared to the pressed system, as it significantly facilitates handling of the single-bead reactor, including mounting, dismounting, archiving, regeneration and re-use of the reactor, and protection of the beads.

It has to be noted that such a bonding process would be much more difficult in the case of catalysts coated to the reactor or specific regions on a substrate, as shown in Fig. 1. All the preparation and calcination steps have to be performed in the device itself while any contamination (either by the solution phase chemistry or just by dust particles) of the bond surfaces needs to be avoided. This would essentially require very accurate robotic solution phase chemistry under clean-room conditions when working with coatings.

We believe that working with single beads in individual microreaction chambers has a number of advantages for high-throughput screening of supported catalysts compared to working with catalyst coatings. With beads, we can benefit from well-established preparation methods for those beads, a number of different materials are furthermore commercially available. That means that we can work with industrially used materials in a miniaturized reactor format. Potential scale-up risks are therefore significantly reduced. When working with coatings, on the other hand, one has to apply special preparation methods for the support on the reactor or substrate with a number of important boundary conditions, such as satisfactory adhesion, requiring changes to the preparation recipe.

Beads are very efficient with regard to required chip space. In general, spherical beads offer a much larger geometrical catalyst surface area and catalyst volume per chip area than coatings. For instance, a cylindrical coating with the same geometrical surface area as a 1 mm diameter bead would require a minimal chip area with a diameter of 2 mm compared to 1 mm for the bead. Assuming the same distances between adjacent coatings as for the 625-parallel bead reactor, an arrangement of only 17 × 17 catalysts compared to 25 × 25 would be possible. This reduces the capacity on the same chip area to 46%. This effect is even more pronounced if we compare catalyst volumes for beads and cylindrical coatings. A coating with a thickness of 100 μm but the same volume as a 1 mm bead would reduce the number of catalysts to 14 × 14 on the same chip area, hence a reduction to 31% capacity. A reduction of the coating thickness, which may be more realistic, reduces the capacity to 16% for a 50 μm thick coating (10 × 10 arrangement of 100 catalysts) and to 4% for a 10 μm thick coating (5 × 5 arrangement of 25 catalysts). Thus, only beads enable massively parallel reactor approaches, as shown with our 625-parallel single-bead reactor.

Regarding the comparison of a single-bead, non-contact incipient wetness preparation method with the corresponding conventional laboratory scale catalyst synthesis procedures, it became clear from Fig. 9 that the miniaturized single-bead synthesis is almost as accurate and reproducible as the conventional approach. The deviations in catalytic activity for catalysts prepared the single-bead way, although this is not fully optimized, are only slightly larger than the deviations found between catalytic beads originating from the same conventionally prepared batch. The standard deviation of the individually prepared single-bead catalysts could be quantified to be in the range of 5–7%, while it is in the range of 3–6% for conventionally prepared catalysts. This standard deviation comprises all experimental errors, including synthesis, flow distribution and potential temperature inhomogeneities.

Both reactor bonding feasibility and single-bead synthesis accuracy have important influences on the overall screening workflow. This workflow is schematically shown in Fig. 11. Statistical design of experiments is done for both the catalyst composition and, to a lesser extent, for variation of process and operation parameters. The most often used mixture designs that may span several 625-member libraries, may already deal with a potential masterbatch synthesis, as this proved to be a very efficient starting point before diversification in the actual library synthesis. Of course, all designs are completely randomized before execution, and reference samples are added. After preparation and heat treatment, the reactor is optionally bonded before screening. This, incidentally, allows geographic separation of library synthesis and library screening, as the synthesis may be performed in a dedicated, experienced and appropriately equipped facility with mass fabrication capabilities, while the fully assembled reactor may be shipped to another laboratory for screening. A vital part of the workflow is powerful data management and statistical data analysis that, as well as the other workflow steps, are fully supported by our software tools [16]. The throughput of the single-bead preparation method is by far sufficient for the corresponding 625-parallel single-bead reactor. If, however, the

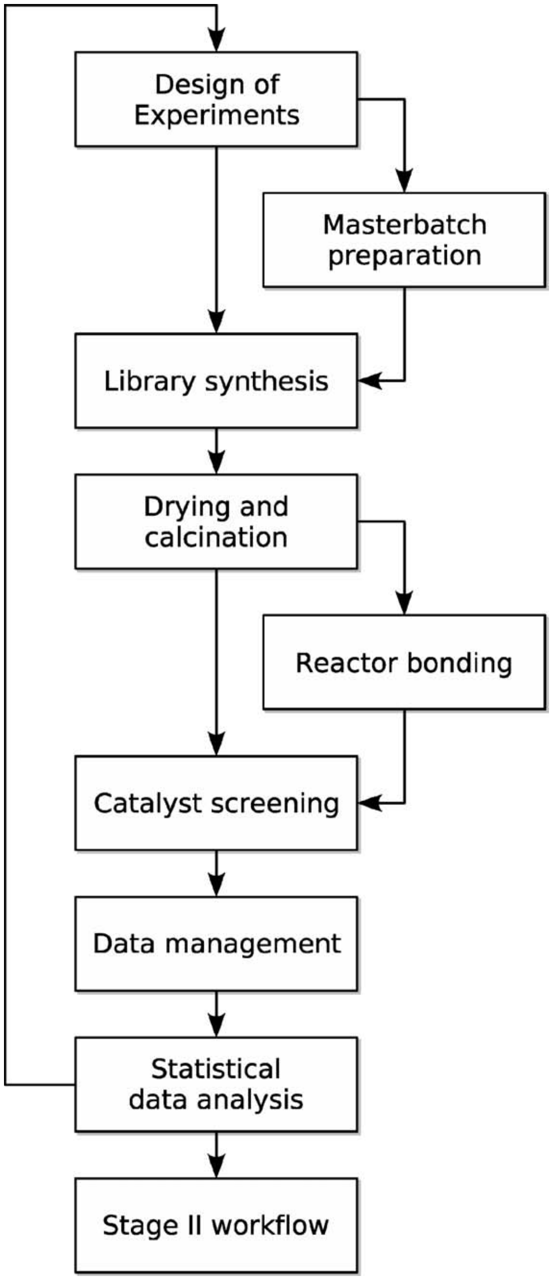


Fig. 11. Workflow for the single-bead reactor technology.

throughput needs to be significantly increased in the future, new preparation methods, such as Split & Pool [17], together with well-adapted screening methodologies [18] are available.

5. Conclusion

We have discussed a number of critical issues in massively parallel stage-I screening of heterogeneous catalysts that have important implications for efficiency of the whole screening workflow. We have demonstrated the possibility to anodically bond a 625-parallel single-bead reactor filled with supported catalysts resulting in a hermetically closed reactor assembly. The bonding process enables excellent microfluidic properties by eliminating fluidic cross-talk between adjacent microreaction chambers. The bonding significantly facilitates handling of the reactor assembly, including mounting, dismounting, archiving, regeneration and re-use of the reactor, and protection of the catalytic materials. We have shown that bonding is more difficult when working with catalytic coatings, hence such approaches could not benefit from the named advantages. Furthermore, the single-bead approach is very efficient regarding required chip size, thus enabling *really* high-throughput screening.

Regarding the comparison of a single-bead, non-contact incipient wetness preparation method with the corresponding conventional laboratory scale catalyst synthesis procedures, we have shown that the miniaturized single-bead synthesis is almost as accurate and reproducible as the conventional approach. The standard deviations of the observed conversion degree of the individually prepared single-bead catalysts in CO oxidation as a model reaction could be quantified to be in the range of 5–7%, while it is in the range of 3–6% for conventionally prepared catalysts. This single-bead preparation can be fully automatically performed for large numbers of beads and thus seamlessly integrated into a complete stage-I catalyst screening workflow.

Together with the standardized reactor format, the complete massively parallel single-bead concept may be a very accurate, elegant and last but not least highly competitive approach for high-throughput catalyst screening workflows.

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