Quantitative data on the dynamics of cell signaling induced by different stimuli requires large sets of self-consistent and dynamic measures of protein activities, concentrations, and states of modification. A typical process flow in these experiments starts with the addition of stimuli to cells (cytokines or growth factors) under controlled conditions of concentration, time, and temperature, followed at various intervals by cell lysis and the preparation of extracts. Microfluidic systems offer the potential to do laborious assays in a reproducible and automated fashion [1].

Figure 1 shows quantification of the stimulation of a T-cell line with antibodies performed in a micro-fluidic device with integrated cell lysis. The device is capable of resolving the very fast kinetics of the cell pathways, with protein activation levels changing 4-fold in less than 15 seconds [2]. The quantification of the lysate is currently performed off-chip using electrophoretic separation. To effectively extract meaningful data from cellular preparations, many current biological assays require similar labor-intensive sample purification steps.

Micro-electrophoretic separators have several important advantages over their conventional counterparts, including shorter separation times, enhanced heat transfer, and the potential to be integrated into other devices on-chip. However, the high voltages required for these separations prohibit using metal electrodes inside the microfluidic channel. A PDMS isoelectric focusing device with polyacrylamide gel walls [3] has been developed to perform rapid separations by using electric fields orthogonal to fluid flow. This device and its variants have been shown to focus organelles, low-molecular-weight dyes, proteins, and protein complexes (Figure 2a) in seconds. Simulations have driven the development of improved device configurations, such as tandem IEF stages (Figure 2b).

REFERENCES
Microreactors for Synthesis of Quantum Dots

S. Marre, J. Guan, J. Park, M.G. Bawendi, K.F. Jensen
Sponsorship: NSF, ISN, Rhodia

We have fabricated gas-liquid, segmented-flow reactors with multiple temperature zones for the synthesis and the overcoating of quantum dots (QDs). In contrast to single-phase flow reactors, the segmented flow approach enables rapid mixing and narrow residence time distribution, factors which strongly influence the ultimate QD size distribution. The silicon-glass reactors accommodate a 1-m-long reaction channel (hydraulic diameter ≈ 400 µm) and swallow side channels for multiple additional injections of precursors inside the main channel (Figure 1). Pressure-drop channels were added in order to avoid backflow into the side channels. Two temperature zones are maintained, a heated region (> 260 °C) and a cooled quenching region (< 70 °C). Measurements of the flow distribution (Figure 2a) show that this side manifold design results in very uniform distribution even at very low nominal flow rates. As a model system, monodispersed CdSe and CdSe/ZnS QDs were prepared using this reactor. For the preparation of CdSe QDs, cadmium and selenium precursor solutions were delivered separately in the cooled region and were thereafter mixed in the heated region. An inert gas stream is introduced further downstream to form a segmented gas-liquid flow, thereby rapidly mixing the precursors and initiating the reaction, as was shown in a previous work [1]. In the case of the synthesis of CdSe/ZnS QDs, CdSe cores are introduced directly inside the main channel, while Zn and S precursors are added through the side swallow channels, allowing the overcoating. The reaction is stopped when the fluids enter the cooled outlet region of the device. When we vary the process parameters (temperature, precursors flow rates), the size of the cores material can be tuned without sacrificing the monodispersity. In addition, the overcoating of CdSe cores allows shifting the absorbance spectrum (5 nm), due to the presence of the ZnS layering (Figure 2b).

---

**References**

Microfluidic Synthesis and Surface Engineering of Colloidal Nanoparticles
S.A. Khan, E.V. Loewer, K.F. Jensen

There has been considerable research interest over the last decade in fabricating core-shell materials with tailored optical and surface properties. For example, core-shell particles of silica and titania have drawn attention due their potential for trapping light at specific frequencies. This optical property depends on the formation of nanolayers on nano- or micro-cores. To obtain useful particles, these layers need to be uniform and even. These layered particles also need to be distinct and monodispersed. While nanolayer formation is successful in batch reactions, nonuniformity, agglomeration, and secondary nucleation often occur. We have developed microfluidic routes for synthesis and surface-coating of colloidal silica and titania particles.

The chief advantages of a microfluidic platform are precise control over reactant addition and mixing and continuous operation. Microfluidic chemical reactors for the synthesis and overcoating of colloidal particles are shown in Figures 1a and 1b, respectively [1-2]. Figure 2a is an SEM micrograph of silica particles synthesized in a microreactor (Figure 1a) operated in segmented gas-liquid flow mode. Figure 2b shows a silica nanoparticle coated with a thick shell of titania. We have also fabricated integrated devices combining synthesis and overcoating to enable continuous multistep synthesis of core-shell particles.

References
Organic Synthesis in Microreactor Systems
J.P. McMullen, N. Zaborenko, H.R. Sahoo, K.F. Jensen
Sponsorship: Pacific Scientific, Microchemical Systems Consortium

Enhanced heat and mass transfer, reduced reaction volume, and the ability to run several experiments in parallel render microreactors powerful instruments for scanning and optimizing chemical reaction conditions. Furthermore, the high mechanical strength and thermal conductivity of silicon microreactors permit the exploration of organic syntheses at higher temperatures and pressures than can be achieved with conventional bench-scale equipment. An example of these benefits is demonstrated in the aminocarbonylation reaction study [1]. Traditionally, these reactions are performed at atmospheric conditions and with temperatures at or below the boiling point of the solvent (toluene, 110°C). However, in silicon microreactors (Figure 1), it is possible to reach pressures exceeding 100 bar [2] and temperatures above 800°C [3]. Exploration of the aminocarbonylation reaction offers information that can be useful for the optimizing selectivity of the synthesis; higher CO pressures enhance α-ketoamide formation and increased temperatures favor amide formation.

Once the chemical reaction is complete, it is desirable to separate the toxic gas from the liquid phase. Although negligible on the macro-scale, surface forces play a dominant role in microfluidics. Creating a capillary-based system (Figure 2) [4] makes it possible to take advantage of these forces. The liquid phase wets the capillaries and prevents the gas from penetrating the capillary matrix through the proper adjustments of pressure drops across the separator. Similarly, this concept can be applied to heterogeneous reactions that involve two immiscible liquids. Due to this microtechnology, microreactor systems can be assembled for multi-step synthesis and separation that could not easily be achieved in traditional laboratory environments. As a result, high throughput experiments can be performed and entire chemical processes can be optimized efficiently with microreactor systems.

Figure 1: Silicon microreactor. Photograph, F. Frankel.

Figure 2: Capillary system for gas-liquid separation.

REFERENCES
Autothermal Catalytic Micromembrane Devices for Portable High-purity Hydrogen Generation

K. Deshpande, M.A. Schmidt, K.F. Jensen
Sponsorship: ARO MURI

The high efficiency and energy density of miniaturized fuel cells provide an attractive alternative to batteries in the portable-power-generation market for consumer and military electronic devices [1-3]. The best fuel cell efficiency is typically achieved with hydrogen, but safety and reliability issues remain with current storage options. Consequently, there is continued interest in reforming of liquid fuels to hydrogen. The process typically involves high-temperature reforming of fuel to hydrogen combined with a low-temperature PEM fuel cell, which implies significant thermal loss. Owing to its high hydrogen content (66%) and ease of storage and handling, methanol is an attractive fuel. However, partial oxidation of methanol also generates CO, which can poison the fuel cell catalyst [1].

Previously [4] we have successfully demonstrated hydrogen purification using thin (~200 nm) Pd-Ag membranes using electrical heating. Further, integration of these devices with LaNiCoO₃ catalyst allowed methanol reforming at 475°C with 47% fuel conversion [5]. In the current work, we fabricate a novel autothermal reformer for hydrogen generation and purification using bulk micromachining techniques. This device combines the reforming unit with a catalyst loaded microreactor for combustion of hydrogen not recovered through the Pd-Ag membrane, generated CO, and unreacted methanol. The energy from the combustion heats the reformer to the operating temperature (~450°C). High thermal conductivity of silicon ensures efficient heat transfer from combustor to reformer. In the first phase, Pd-Ag membrane stability post-fabrication was tested; results indicated a pin-hole- and crack-free layer. Further, we successfully demonstrate high-pressure operation (up to 1.6 atm) of the device for enhanced hydrogen flux. The microburner has also been characterized with hydrogen oxidation over platinum catalyst. Work on reforming methanol for hydrogen generation and characterization of thermal responses is currently under progress.

Figure 1: Fabricated reformer-burner unit with palladium membranes.

Figure 2: Hydrogen flux comparison as a function of applied feed pressure.

REFERENCES
Thermal Management in Devices for Portable Hydrogen Generation

B. Blackwell, M.A. Schmidt, K.F. Jensen
Sponsorship: ARO MURI, Lincoln Laboratory

The development of portable-power systems employing hydrogen-driven solid oxide fuel cells continues to garner significant interest among applied science researchers. The technology can be applied in fields ranging from the automobile to personal electronics industries. This work focuses on developing microreaction technology that minimizes thermal losses during the conversion of fuels—such as light-end hydrocarbons, their alcohols, and ammonia—to hydrogen. Critical issues in realizing high-efficiency devices capable of operating at high temperatures have been addressed: specifically, thermal management, the integration of materials with different thermophysical properties, and the development of improved packaging and fabrication techniques.

A new fabrication scheme for a thermally insulated, high-temperature, suspended-tube microreactor has been developed. The new design improves upon a monolithic design proposed by Arana et al. [1]. In the new modular design (Figure 1), a high-temperature reaction zone is connected to a low-temperature (~50°C) package via the brazing of pre-fabricated, thin-walled glass tubes. The design also replaces traditional deep reactive ion-etching (DRIE) with wet potassium hydroxide (KOH) etching, an economical and time-saving alternative. A brazing formulation that effectively accommodates the difference in thermal expansion between the silicon reactor and the glass tubes has been developed. Autothermal combustion of hydrogen, propane (Figure 2), and butane has been demonstrated in ambient atmosphere and in a vacuum.

---

**REFERENCES**

Microscale Singlet Oxygen Generator for MEMS-based COIL Lasers
Sponsorship: DARPA, MDA, AFRL

Conventional chemical oxygen iodine lasers (COIL) offer several important advantages for materials processing, including short wavelength (1.3 µm) and high power. However, COIL lasers typically employ large hardware and use reactants relatively inefficiently. This project is creating an alternative approach called microCOIL. In microCOIL, most conventional components are replaced by a set of silicon MEMS devices that offer smaller hardware and improved performance. A complete microCOIL system includes microchemical reactors, microscale supersonic nozzles, and micropumps. System models incorporating all of these elements predict significant performance advantages in the microCOIL approach [1].

Initial work is focused on the design, microfabrication, and demonstration of a chip-scale singlet oxygen generator (SOG), a microchemical reactor that generates singlet delta oxygen gas to power the laser. Given the extensive experience with microchemical reactors over the last decade [2], it is not surprising that a microSOG would offer a significant performance gain over large-scale systems. The gain stems from basic physical scaling: surface-to-volume ratio increases as the size scale is reduced, which enables improved mixing and heat transfer. The SOG chip being demonstrated in this project employs an array of microstructured packed-bed reaction channels interspersed with microscale cooling channels for efficient heat removal [3]. To date the device has produced oxygen concentrations of 10^17 cm^-3, yields approaching 80% and molar flowrates in excess of 600×10^-4 moles/L/sec [4]. The yield and molar flowrates indicate a significant improvement over the macroscale SOG designs.

![Figure 1: A – View of chip surface showing glow resulting from singlet-oxygen production; B – View of packaging and optics surrounding microSOG; C – Photograph of microSOG.](image)

![Figure 2: The IR spectra measured at the µSOG gas outlet versus time. The peak at 1268 nm indicates the spontaneous decay of singlet oxygen into its triplet state.](image)

REFERENCES
Microfabricated Thin-film Electrolytes and Electrodes for Solid Oxide Fuel Cells

Sponsorship: DOD MURI, NSF, DOE

There is growing interest in the microfabrication of electrodes for solid oxide fuel cells (SOFCs) in microionic devices [1]. Recently, we reported the fabrication of Pt/(Zr,Y)O2 (YSZ) nanocomposite electrodes by reactive magnetron co-sputtering [2]. Use of X-ray diffraction and X-ray photoelectron spectroscopy (XPS) characterization show these composites to be a two-phase system with no change of oxidation state from the constituent compounds. Electrical characterization via impedance spectroscopy demonstrated promising electrochemical properties at low temperatures; an area-specific resistance of 500 Ω cm² was achieved at 400°C.

To test whether microfabricated thin-film electrolytes may suffer from degradation due to grain boundaries acting as short-circuiting diffusion pathways, sputtered NiO diffusion source films were in-diffused along grain boundaries into nanocrystalline CeO2 thin films grown by pulsed laser deposition (PLD), at temperatures from 700-800°C. The diffusion profiles were measured by Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS) at the Institute for Physical Chemistry at RWTH Aachen University, Germany. These SIMS spectra, shown in Figure 2, point to a single diffusion mechanism, believed to be grain boundary diffusion, at these relatively low temperatures. Further work to systematically determine the unique opportunities and challenges associated with microstructured SOFCs is currently underway.

Figure 1: Photograph of a Pt/YSZ composite microelectrode device fabricated by reactive magnetron sputtering. Five microelectrodes lie on the surface and the counter electrode is visible through the transparent YSZ substrate.

Figure 2: The ToF-SIMS spectra of Ni diffusion in CeO2. The as-deposited profile is shown, as are profiles resulting from anneals at 700 and 800°C for 5 hours. In the 800°C sample, Ni has diffused through the entire film.

REFERENCES
Microfabricated solid oxide fuel cells were investigated for portable power applications requiring high energy densities [1]. The thickness of the electrolyte, the travel length of oxygen ions, was reduced down to ~150nm. The tri-layers (yttria-stabilized zirconia (YSZ) as an electrolyte and platinum-YSZ cermet as cathode/anode) were sputter-deposited on a silicon wafer, and then they were released as square plates by KOH etching the silicon through patterned silicon nitride masks on the back side. High intrinsic and extrinsic (thermal) stresses due to fabrication and operation (25-600°C) [2], respectively, require careful thermomechanically stable design of μSOFCs.

First, material properties of the ultra-thin YSZ were characterized experimentally and found to be significantly different than those of bulk YSZ [3]. Second, based on the obtained properties, maximum stresses in the plates at 625°C were analyzed using non-linear von Karman plate theory [4]. The stresses showed three regions with sidelength variation: an un-buckled regime, a buckled regime with high stresses, and post-buckling regime with lower stresses (see Figure 1). The μSOFCs were fabricated in the post-buckling regimes with ~80-~180μm sidelength and total ~450nm thickness. With the plates buckled as shown in Figure 2, the μSOFCs produced power output of 0.008mW/cm, lower than the expected power from their electrochemical test. Given the high-performance predicted for the underlying nano-structured ultra-thin electrolyte, anode, and cathode layers, additional studies are needed to improve specimens and test setup and to assess μSOFCs’ long-term operational stability.

REFERENCES: