The Application of Microfluidic Systems to Chemical Synthesis

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Microfluidic systems are widely known as the systems containing a set of micron-sized channels. Basically, the size of channels is ranging from 10 to 300 μm. A microfluidic system is analogous to a microelectronic system in that it miniaturizes the conventional system (vacuum tube for a microelectronic system). Instead of electrons, fluids flow along these tiny channels controlled by either pressure or electric field.[1,2] Microfluidics holds promises to a broad spectrum of applications in biology, chemistry, physics, and engineering such as proteomics, genomics, high-throughput screening, and chemical synthesis[3] To date, several microfluidic systems have been launched to markets.[4]

Typically, a microfluidic system (device or chip) can be fabricated from various materials such as silicon, glass, metals, and polymers by a variety of techniques; for example, traditional photolithography and unconventional soft lithography. Photolithography is a technique used in microelectronic industry for integrated circuit fabrication. It requires clean room facilities and special equipment, which are of course expensive, for every single fabricated device. Soft lithography, however, enables faster and cheaper microfluidic fabrication by casting and curing elastomeric polymers, usually PDMS, against a master. Therefore, many devices can be replicated from just one master.[3]

Interest in chemical synthesis using the microfluidic approach has been rising significantly because of its high mass and heat transfer rates, large surface to volume ratio, safety in operation, and cost effectiveness.[5] Three examples are represented here. In 1999, Chambers and Spink performed fluorination on disulfide compounds using elemental fluorine in a microfluidic device made of Ni block.[6] Next, Kobayashi *et al* demonstrated gas-liquid-solid hydrogenation reaction of different compounds in a glass microfluidic device. The efficiency of mass transfer between phases was enhanced by immobilizing Pd catalyst at the wall of the microchannel, controlling the fluid flow so that substrate solution flowed along the inner wall while gas flowed through the center of the channel (see Figure 1). The reaction product was detected at the reaction time of two minutes.[7]

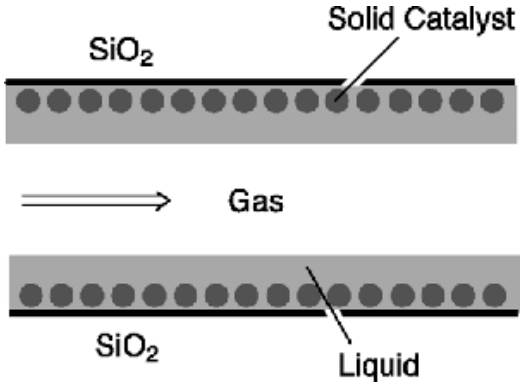

Figure 1: Ideal configuration for multiphase reactions[7]

Recently, Quake *et al* successfully synthesized 2-deoxy-2-[^{18}F]fluoro-D-glucose (2-FDG), a radiolabeled imaging probe used in positron emission tomography (PET), in a PDMS integrated microfluidic device.[8] Five processes (see Figure 2) were done chronologically within a single chip with the assistance of multilayer soft lithography (MSL) to fabricate on-chip microvalves,[9] a rotary pump,[10] and an ion exchange column (see Figure 2). These processes were completed within fourteen minutes compared with fifty minutes in commercial synthesizers.[8]

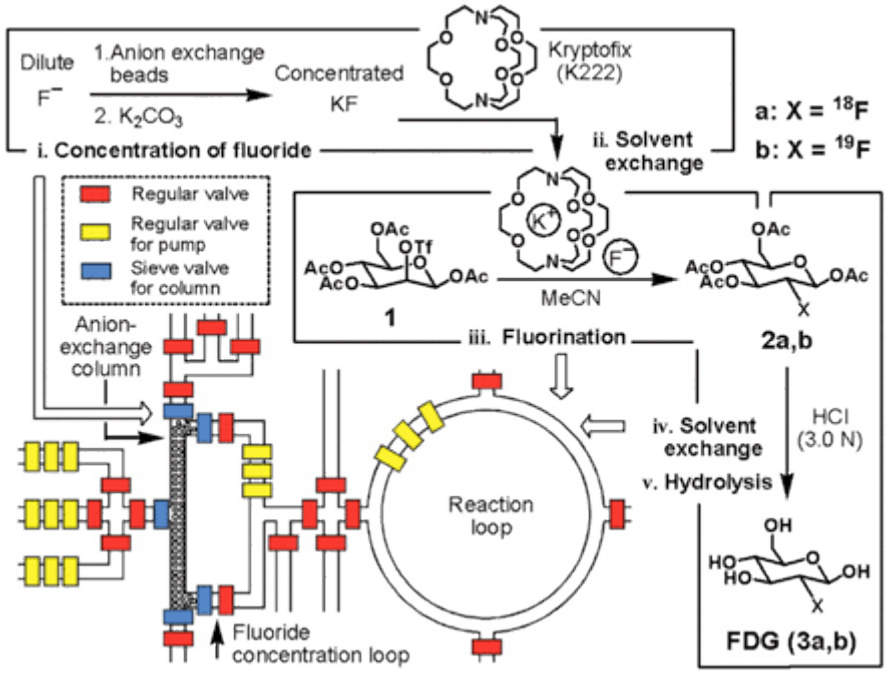

Figure 2: A schematic diagram of the integrated microfluidic device and synthetic steps used in 2-FDG production[8]

Although many successes have been achieved, there are still some issues that must be considered. For example, PDMS can swell in a variety of organic solvents.[11] Finally, the application of microfluidic systems to chemical synthesis is still in the beginning era. Further studies must be continued.

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