# MICROFLUIDIC ASSEMBLY BLOCKS

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## Abstract

We propose a method for microdevice construction where non-expert users can assemble the blocks on glass slides to build their custom devices in minutes without any complicated fabrication steps. This approach involves prefabrication of individual microfluidic assembly blocks (MABs) in PDMS are pre-fabricated and readily assembled to form microfluidic systems. We describe the construction process, the assembly of the devices, and various bonding techniques to accomplish hermetic assembly. Finally, we demonstrate common microfluidic applications including laminar flow development, valve control, and cell culture.

## Introduction

Microfluidic systems for biological assays [1-5] benefit from reduced requirements for reagents, short analysis times, and portability. However, the impact of microfluidics has not yet been where it was initially envisioned. For microfluidic systems, a huge gap exists between the technology developers and potential users especially in the life sciences. The high cost and the level of expertise required for microfabrication deters such non-expert users from using microfluidic systems.

We demonstrate here a novel assembly approach for microdevice construction. This approach involves fabrication of microfluidic assembly blocks (MABs) in PDMS followed by the construction of a full functioning microfluidic system by assembling the blocks. Each MAB has an own unique function including inlet/outlets, valves, straight/curved/bifurcated channels, and chambers. Mass production of identical blocks is possible by microfabrication experts in a regular lab environment. The fabricated blocks then can be sent to non-expert users who can assemble devices with the blocks in minutes without the need for expensive design software or clean-room facilities.

## Materials and methods

### *Fabrication*

The prototypical MABs were manufactured using the standard soft-lithographic technique [6]. The proposed SU-8 master mold for MAB fabrication consists of thin patterns (~ 75 to 150 μm) for channel network and thick patterns (~ 500 to 1200 μm) for

grid walls. For demonstration purposes, the channel widths were chosen to be either 500 μm or 1000 μm because the majority of biological experiments in microfluidics would employ relatively wide channels. Once the SU-8 master mold was prepared, a mixture of PDMS prepolymer and curing agent (9:1 w/w, Sylgard 184, Dow-Corning) was cast against the multi-layered mold. We slightly tilted the mold and scratched the excessive PDMS solution off, using a commercial razor blade. After curing, each cured PDMS block was carefully removed with a sharp aluminum needle from individual cells separated by the grid walls.

*Assembly*

To prepare substrates on which blocks are assembled, glass cover slides (Dow Corning) were spincoated with a 10:1 PDMS mixture and cured to have a thin (~100 μm) PDMS layer on the glass side. In accordance with the design to be realized, we started with selection of proper MAB. The selected blocks then were carefully aligned and assembled together. Using a pair of tweezers, we put a block together as tightly as possible by horizontally pushing and releasing it toward the block that had been already placed on the substrate. Visual aids such as a high magnification stereoscope were utilized to further facilitate the alignment procedure.

We investigated a number of bonding techniques, using adhesive substances (the PDMS mixture used to fabricate the blocks, the PDMS curing agent, and a UV-curable glue) to increase the block/block bonding. The adhesive not only flows into the nanometer gap between the blocks and the substrate but also fills the inter-block gaps. The adhesive agent cannot be loaded onto the device in excess since the adhesive will then flow in the main channels of the device, and, if large gaps exist between block, capillary action will not be able to fill them.

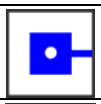
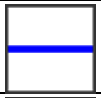
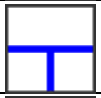
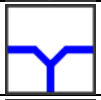
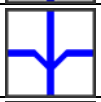
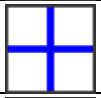
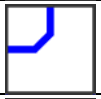
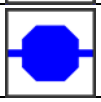
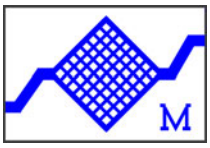
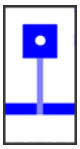
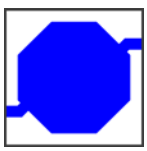
## Results and discussion

*MAB concept*

To construct a microfluidic device, MABs are selected from a standard set of components (Table 1) and then assembled to form the desired channel network, as shown in Fig. 1a. Noticeably, the majority of recent microfluidic needs in the life sciences requires a very simple design of channel network and relatively wide channels. Various MABs can be produced at low cost and in large quantities, and the custom devices rapidly can be designed, assembled, and tested.

Fabrication of the MABs involves a multi-step lithography to construct the SU-8 master mold. The mold consists of thin channel patterns and thick grid patterns up to 1200 μm in height. To achieve this thickness, multiple repetitions of spin-coating and pre-baking were incorporated [7]. The MAB mold is then used to form the individual PDMS assembly blocks. Figs. 1b-d show a photo of the constructed SU-8 master mold, the resulting square MABs, and a simple exemplary device assembled on a glass slide. The MABs are designed such that they can be rotated in 90° increments if a different orientation is needed.

Table 1. Exemplary Standard Microfluidic Assembly Blocks in the study

| Block Name | Schematic | Size | Function or Purpose |
|---|---|---|---|
| Inlet/Outlet |  | 1x1 | To connect the device to external tubing.<br>The size of a hole varies.<br>The width of a connecting channel varies. |
| Straight Channel |  | 1x1 | To form a plain straight channel.<br>The channel width and height may vary. |
| T Channel |  | 1x1 | To add a side stream to the main stream or divide an incoming stream into two outgoing streams.<br>The channel width and height may vary. |
| Y Channel |  | 1x1 | To merge two incoming streams to form a fused outgoing stream<br>The channel width and height may vary. |
| Ψ Channel |  | 1x1 | To merge three incoming streams to form a fused stream.<br>The channel width and height may vary. |
| Cross Channel |  | 1x1 | To merge or divide stream(s)<br>The channel width and height may vary. |
| 90° Curved Channel |  | 1x1 | To form a 90° turn in a stream.<br>The channel width and height may vary. |
| Chamber (small) |  | 1x1 | To collect samples or secure a reaction |
| Connector |  | 1x1 | To connect two blocks with channels of different widths |
| Spacer |  | 1x1 | To fill blanks between blocks or obstruct one end of a channel. |
| Zigzag Channel |  | 1x3 | To enhance advective mixing in the stream.<br>The channel geometry and width may vary.<br>Used in molecular gradient generators. |
| Culture Bed |  | 2x3 | To provide separate room for cell culture.<br>The size of a bed may vary.<br>Patterns in the chamber may vary. |
| Pneumatic Valve |  | 2x1 | To control flow or separate an adjacent compartment. The valve is closed at the normal condition. When vacuum is applied to the inlet, the valve will open. Dark blue represents the upper layer and light blue represents the bottom layer. |
| Chamber (large) |  | 2x2 | To collect samples or secure a reaction.<br>Used for on-chip PCR. |

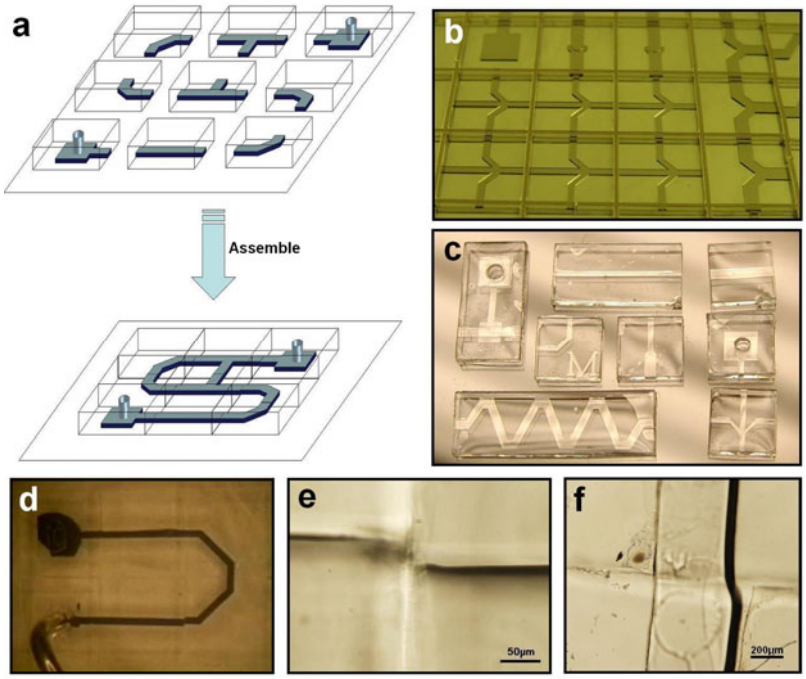



Figure 1. (a) A schematic of the basic concept of the MAB approach. Users build a custom device by assembling MABs on a plain glass slide. (b) A photo of the fabricated mold for various square blocks. (c) A photo of microfluidic assembly blocks before assembled. (d) Six square MABs were assembled on a PDMS-coated glass slide to build a basic U-turn channel, consisting of two inlet blocks, two straight blocks, and two 90˚ turn blocks. No post-treatment for bonding was applied. The sized of each block is 6mm x 6mm, and the channel width is 500μm. (e) MAB Alignments for various assemblies. Without any post-treatment for bonding, the inter-block gaps could be achieved under <5μm. (f) After the bonding with curing agent, the blocks were tightly sealed.

*Bonding and sealing*

We investigated two types of substrates where various MAB are assembled; a bare glass slide and a PDMS coated glass slide. The adhesion to both of these substrates is reversible and can withstand inside pressures up to 5 psi [8], a pressure high enough to perform typical pneumatically driven flow experiments in biochemical studies. With a simple tweezer manipulation, a fairly good contact between blocks (inter-block gap less than 5 μm) could be repeatedly achieved within seconds (Fig. 1e). In addition to the bonding between the blocks and the substrate, the inter-block bonding should be hermetic to prevent fluid loss. The loss of liquid from the channels is an important consideration in this and all PDMS devices. Even if every connection between blocks is hermetic, evaporation will still occur by diffusion through the top membrane of the channel. To address the time elapsed in evaporation through the PDMS, we introduced a dimensionless diffusion time to directly compare the evaporation results from various devices with different device thicknesses. The dimensionless time, $\tau$, is defined as,

$$\tau = \frac{t \cdot D}{h^2}. \qquad (1)$$

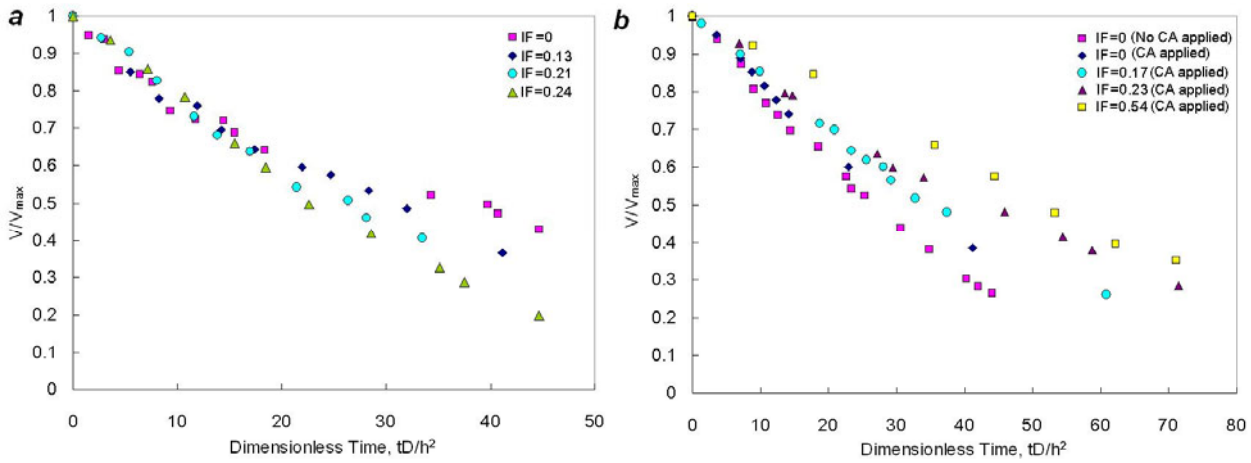



Figure 2. The effect of inter-block gaps on the evaporation rate. The device of IF=0 is a completely closed device while the devices of non-zero IFs have inter-block junctions. (a) No post-treatment for bonding has been applied. Open gaps expedites evaporation. (b) The devices have inter-block junctions filled with the curing agent except for the first device of IF=0. Gaps filled with the curing agent decreases evaporation rates.

In the previous equation, $t$ is the elapsed time, $D$ is the estimated diffusion coefficient of water vapor through PDMS membrane (D ~ $10^{-3}$ $mm^2/s$), and $h$ is the membrane thickness corresponding to the difference between the device thickness and the channel thickness (h ranges from 300 to 1100 μm). To address leakage out of imperfections in block-to-block bonding, we used a ratio of exposed interface area per fluid volume (IF) as a parameter:

$$IF = \frac{\sum_i A_i}{V} \quad where\ A_i = g_i \times (w + 2d)\ and\ V = lwd \qquad (2)$$

.

In this equation, $A_i$ indicates the interfacial area exposed to air at the i-th junction and $V$ represents the total volume of fluid sample. $A_i$ is calculated using the average gap distance ($g_i$), the channel width ($w$), and the channel thickness ($d$). Likewise, the fluid volume is calculated from the drop length ($l$) of fluid sample and the channel dimensions. Larger IF values indicate more exposure to air at junctions. Fig. 2a shows the effect of inter-block gaps on the evaporation rate and confirms that the gaps introduced by the MAB assembly procedure have only a minor effect on the evaporation rate.

In addition to the inherent adhesion of placing MABs on a substrate described above, we also investigated a number of other bonding techniques (See the supporting online material). We used three adhesive substances (the PDMS mixture used to fabricate the blocks, the PDMS curing agent, and a UV-curable glue) to increase the block/block bonding. When placed around the device in contact with the blocks, the adhesive substances flow into the interfacial gap between the device and the substrate due to capillary action. Curing the adhesive then resulted in strong bonding between the

surfaces. Interestingly, the curing agent filled in inter-block gaps appeared to exhibit another advantage of further reducing the evaporation rate as shown in Fig. 2b.

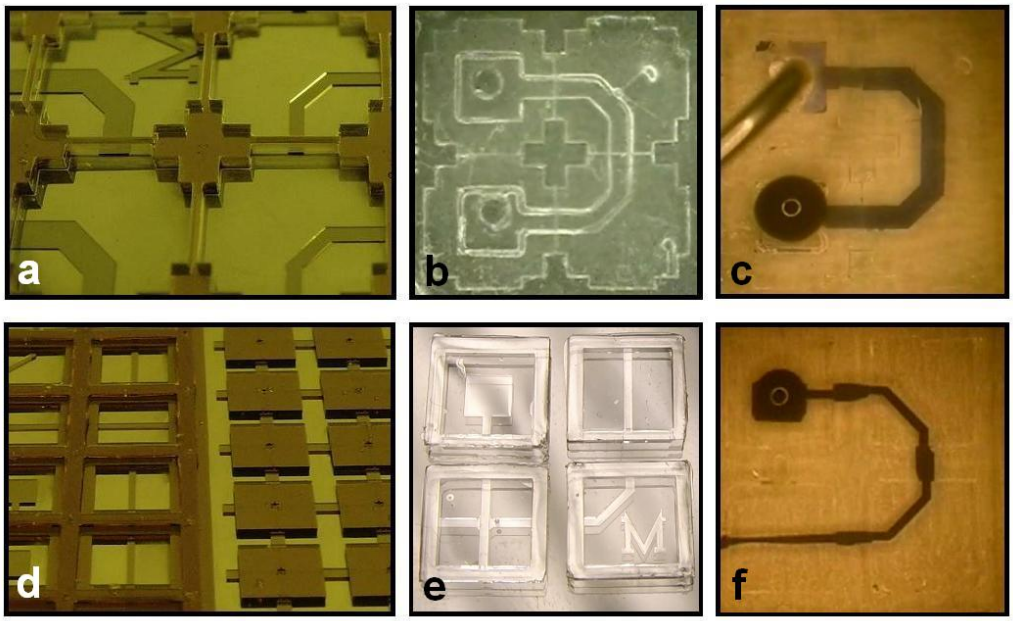



Figure 3. Photos of (f) the fabricated mold for the cross alignment key system, (g) the assembled device, and (h) a fluidic test. Photos of (i) the fabricated mold for the roofed blocks (left) and the channeled base (right), (j) roofed blocks. and (k) a fluidic test on an assembled device.

*Block Shapes*

The square block system proposed in this study has several obvious strengths in its application, the greatest of which is that the fabrication, mold design, and block removal is straightforward. Moreover, since there are no features added to the block for such purposes as alignment, the entire block surface area can be used for fluidic structures, thus minimizing dead volume. Additionally, these square blocks are designed to have minimal interface area when two blocks are connected. As the interface area decreases, the assembly will be more straightforward and thus require less elaborate techniques to bond.

One drawback of the assembly methodology with square blocks rather comes from the lack of alignment keys. Slight deviations in just a few blocks may cause an overall alignment problem, especially for a large assembly task. One applicable method for improved assembly is to constrain the blocks in pre-defined areas. The areas are created in PDMS by separately constructing a base structure that can carry a certain number of blocks. Fig. 3a-c show one of the block-and-base approaches using cross-shaped alignment posts in PDMS and SU-8. Such alignment posts tightly confine the block position to enhance alignment. Fig. 3d-f illustrate another block-and-base approach with a channeled base and roofed blocks. This channeled base not only defines the position of blocks by PDMS grid walls but also has interconnecting channels for each block in four directions. The resulting areas can hold the blocks in alignment but the interface area will be increased by twice, since the blocks will interface with the channeled wall rather than contact each other. The roof structure on a block acts as a

cover to seal the interconnecting channel. Despite its unique merit of improved sealing, this system has an inherent limitation that one can never incorporate multi-block modules in the base, since each base area can contain only one isolated block. Moreover, the roofed blocks cannot be assembled independently without a base structure; users must always use the corresponding base for assembly.

*Applications*

Some of most frequently used microfluidic devices have been prototyped using MABs. In addition to fluidic channels, a common component used in microfluidic systems is a PDMS pneumatic valve to control fluid flow [9]. We developed an MAB of two square-block size containing a microvalve that was designed according to previous reports [10-11]. Figs. 4a-d demonstrates the use of working valve blocks; the valve in this MAB is closed at rest and open when vacuum is applied. To verify its function when embedded in a device, we demonstrated a simple mixing channel network consisting of three inlet/outlet blocks, a Y-channel block, and two valve modules.
As another example, we used MABs to construct a microculture system for bacterial cells. The system used two inlet blocks for sample/media injection and a cell culture module occupying the space corresponding to six square blocks. Fig. 4e shows the successful culture results of *E. Coli* cells in the assembled microculture system. Increases in the number of grown cells were clearly shown in Fig. 4f.

In a micro-scale environment, the addition of two streams in laminar flow results in a clean boundary between streams. A complex system using the zigzag modules to generate molecular gradients is conceptualized in Fig. 5a. To show the working

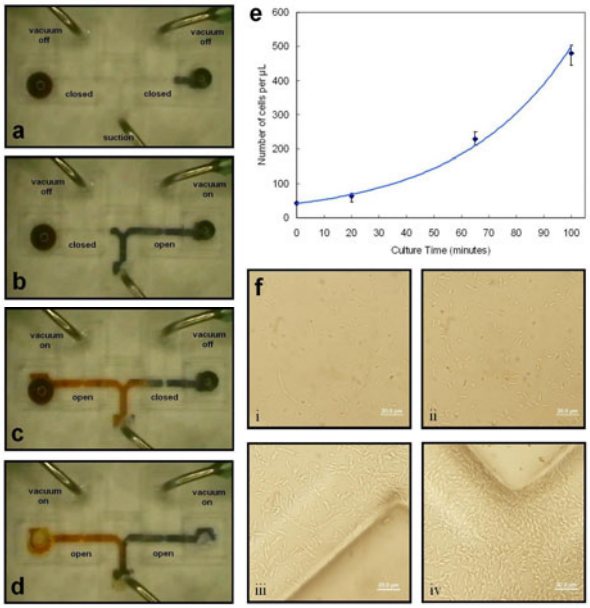



Figure 4. (a) Demonstration of the valve module working in an assembled device. A drop of an orange solution is placed at the left inlet while a blue drop at the right inlet. When both valves are closed, both the orange and blue drops will not move. (b) When the right valve is open in the presence of applied vacuum, the blue solution passes through the valve to the outlet where the suction exists. As the valve is closed, a portion of the fluid will stop and not be drawn further. (c)

After the left valve opens, the orange solution is drawn to the outlet. (d) When both valves are open, both solutions are aspirated. (e) *E. Coli* cell culture results in the MAB assembled device. (f) Photos of the grown cells in the device at different culture times.

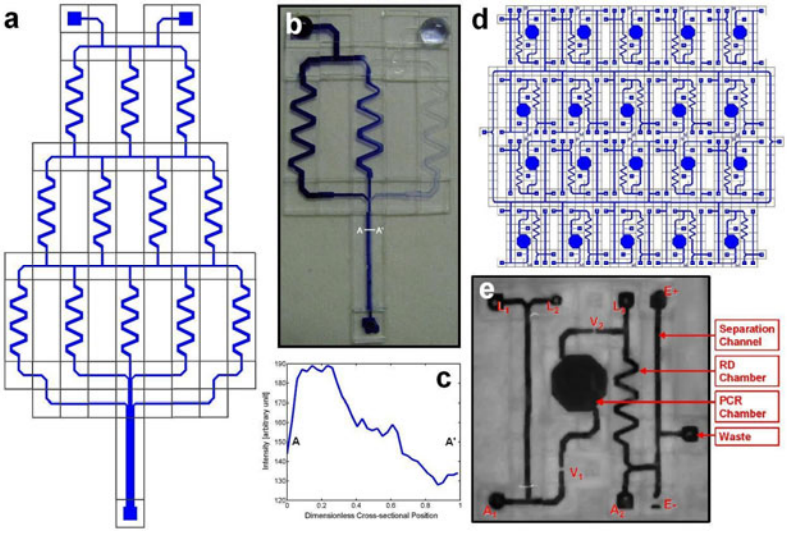



Figure 5. Exemplary systems for complex biochemical assays. (a) A conceptualization of a molecular gradients generator using the zigzag channel modules and other MABs that can generate five different concentration levels of the two-samplemixture. (b) Demonstration of a simpler system that mixes the blue dye and water into the outgoing stream with three different concentration levels. (c) The cross-sectional profile of blue dye concentrations at A-A' showing the concentration gradients. (d) A conceptualization of a large-scale integration of a complex system that can perform twenty independent assays simultaneously from one sample. (e) Visual demonstration of an independent assay unit similar to that in the integrated device in (d). Each unit device can perform reagent mixing, PCR, restriction digest reaction, and a separation. There are three liquid entries ("L"), two pneumatic air controls ("A"), two valves ("V"), and two electrode positions ("E").

principles of such assembly, a simpler system is illustrated in Fig. 5b that mixes the blue dye and water into an outgoing stream. The cross-sectional profile in Fig. 5c shows a distinct gradient of blue dye concentrations at AA'. The use of MABs can be also extended to complex biochemical assays. The conceptualized large-scale integration in Fig. 5d illustrates a system that can perform twenty independent assays simultaneously from one sample. An independent assay unit similar to that in the above integrated device is shown in Fig. 5e.

## Conclusions

The proposed assembly approach provides a simple yet robust way for non-fluidic researchers to construct custom microfluidic devices. There are several unique advantages of the MAB approach for microfluidic device constructions. The MAB approach is also ideal for selective surface modification or treatment limited to a specific section of the total device. The MABs fabricated in PDMS exhibit enough durability that the blocks could be used multiple times. Most importantly, the developers of MAB can manufacture a standard set of MABs that can be assembled into various custom devices. The MAB allows for full flexibility in planar configuration. The exemplary assembled devices demonstrated that the technology can be able to be used in a wide

variety of applications. Consequently, the proposed MAB methodology would be suitable for the recent needs since such devices with a simple configuration can be constructed within minutes in a regular laboratory environment.

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