MECs: Building Blocks for Custom Microfluidic Diagnostics in the Developing World*

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***Abstract*— Microfluidic diagnostics for use in the developing world face a number of unique challenges. Doctors and nurses in developing countries are best suited to addresses these challenges, but they lack the resources and training needed to develop their own microfluidic diagnostics. To address this need, we are developing a system of *Multifluidic Evolutionary Components* or MECs, "building blocks" that can be snapped together by healthcare providers in resource-limited settings to build custom diagnostic instruments. MECs operate on multiple scales of fluid volumes (from nanoliters to milliliters) and include not only fluidic but also optical, mechanical, and electronic functions. In this work we share several prototype MECs and use them to build a demonstration instrument capable of measuring the pH of a sample.**

I. INTRODUCTION

Each year, around 13 million people die from malaria, respiratory and enteric infections, AIDS, and tuberculosis, and over 95% of these deaths occur in developing countries [1]. Clearly there is an urgent and unmet need for diagnostics for infectious diseases in the developing world. However, existing diagnostic tools used in the developed world are not always suitable for use in resource-limited settings. The World Health Organization's "ASSURED" criteria [1] summarize the basic requirements for a diagnostic test to be useful in the developing world:

- **Affordable** by those at risk of infection.
- **Sensitive** (few false-negatives).
- **Specific** (few false-positives).
- **User-friendly** (simple to perform and requiring minimal training).
- **Rapid** (to enable treatment at first visit) and **Robust** (does not require refrigerated storage).
- **Equipment-free**.
- **Delivered** to those who need it [1].

Many common diagnostic tools in first-world hospitals fail the ASSURED criteria and are unsuitable for use in third-world settings, and researchers in the developed world struggle to design diagnostic tools that satisfy the unique and complex requirements of the developing world.

We believe that the persons most qualified to design diagnostics for use in the developing world are the healthcare providers who are working in the developing world. Doctors and nurses in third-world countries know firsthand what does and does not work in their clinics and hospitals. But while they know what tools they need, caregivers in resource-limited settings may lack the infrastructure and training needed to make these tools themselves. This is particularly true of microfluidic diagnostics, which often require specialized equipment and training for their fabrication and use.

To address this need, we are developing a system of "building blocks" with which a doctor or nurse can build custom instruments in the field for their own unique needs. We call these building blocks *Multifluidic Evolutionary Components*, or MECs. The term "Multifluidic" indicates that MECs operate on multiple scales of fluid volumes (from nanoliters to milliliters) and include multiple disciplines (not just fluidics but also electronics, mechanics, and optics). In addition, MECs are "evolutionary" because they are designed

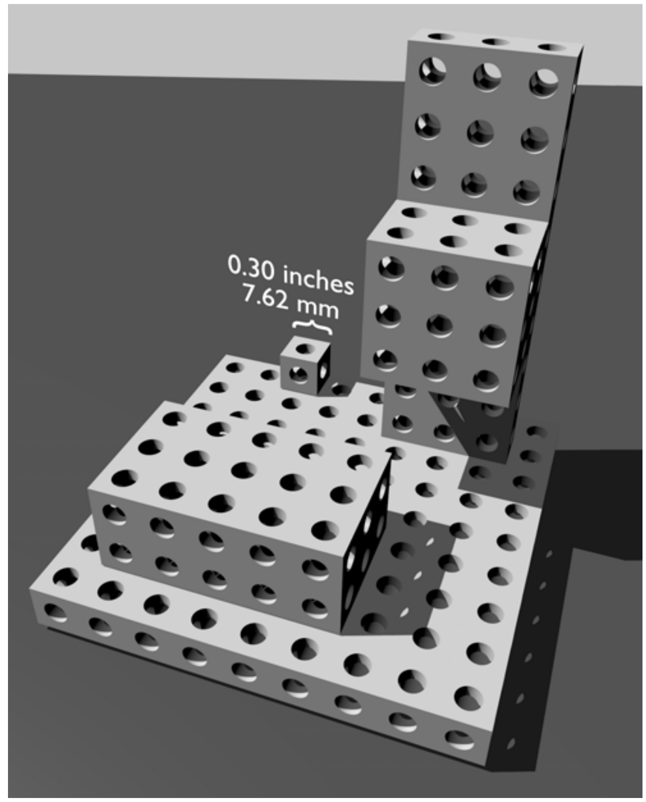

Fig. 1. The three-dimensional grid design of Multifluidic Evolutionary Components. MECs connect to each through circular openings that contain fluidic, electronic, mechanical, or optical interfaces.

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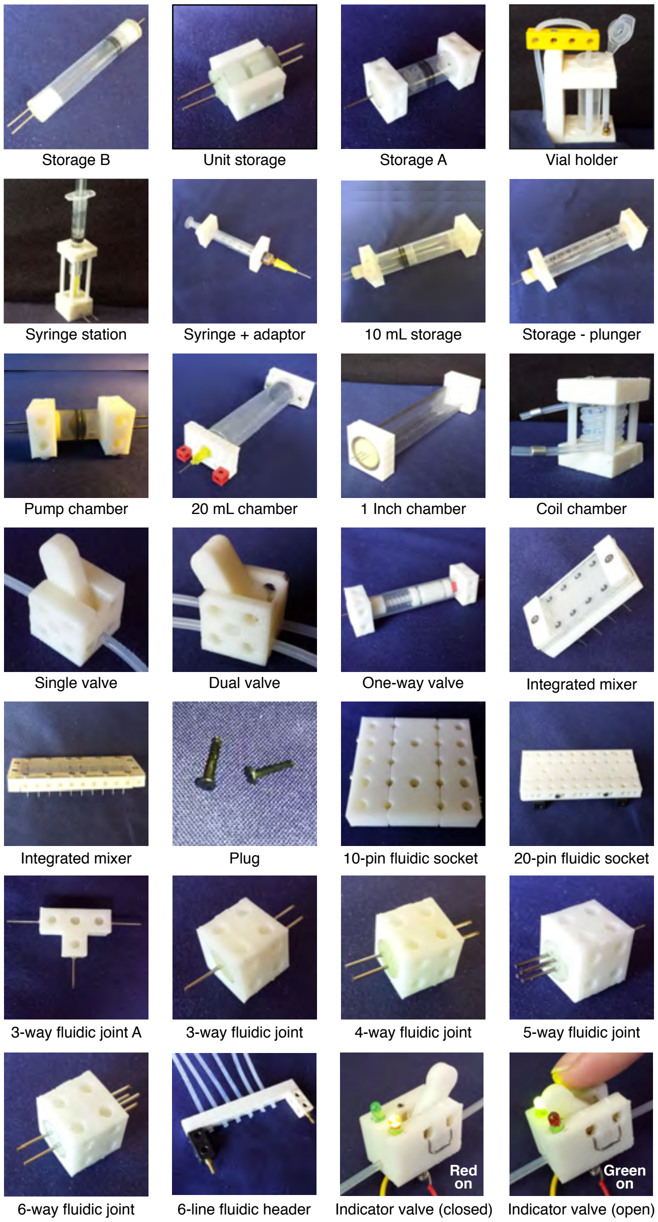

Fig. 2. Selected fluid-control MECs. Each MEC performs a fundamental function like fluid storage, sample introduction, valving, or pumping. The indicator valve (bottom row) includes LEDs for operator feedback.

to adapt to new applications quickly and easily. Using a library of MECs, a doctor or nurse could literally "snap together" a new fully-functional diagnostic instrument (or easily adapt an existing MEC-based instrument).

Other researchers have already recognized the potential value of component-based microfluidics. For example, Rhee and Burns' "microfluidic assembly blocks" each perform a basic microfluidic function like pumping or mixing [2], and Yuen *et al.* demonstrated pluggable connections between blocks [3]. By combining blocks like these in different ways, different microfluidic operations can be performed. However, these existing component-based microfluidic systems are purely microfluidic and do not operate on multiple scales

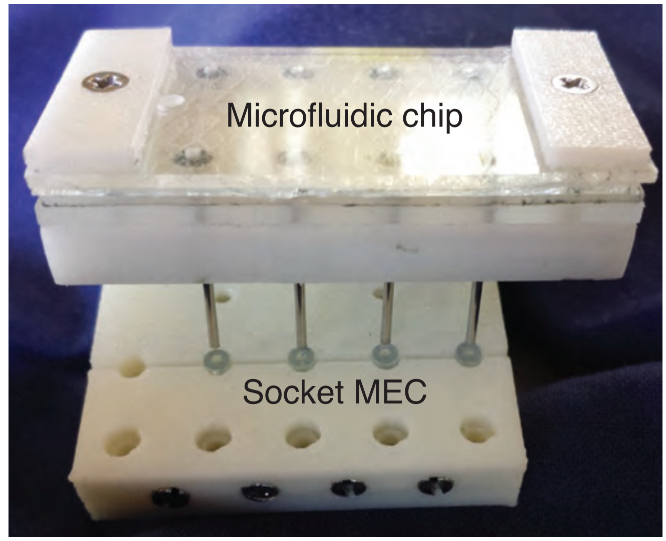

Fig. 3. The socket MEC creates a pluggable interface between any microfluidic chip and the MEC system.

of fluid volumes or include operations from other fields like electronics and optics. Since many diagnostic applications require more than just fluidic operations, existing component-based microfluidics are limited in their ability to build complete and functional diagnostic instruments.

II. MULTIFLUIDIC EVOLUTIONARY COMPONENTS

All Multifluidic Evolutionary Components adhere to the design standard shown in Figure 1. Circular connections on each face contain fluidic, electronic, mechanical, and optical interfaces. MECs can be made using a variety of different fabrication methods. The prototype MECs presented here were made using rapid prototyping (3D printing), CNC machining, PDMS casting, and glass etching.

Figure 2 shows a selection of fluidic and electronic MECs. Each MEC performs a fundamental function needed in many diagnostic instruments. Several MECs contain milliliter-scale volumes of fluid for storing samples or reagents in a diagnostic assay. Other MECs interface to standard external fluid reservoirs like syringes or vials. MECs with pneumatically-driven plungers pump fluid between components. Manualy-operated pinch valves control the flow of fluid through a MEC-based instrument. Indicator valves (bottom of Figure 2) also contain electronic components, red and green LEDs. When controlled by a microprocessor MEC, the indicator valve's LEDs tell the operator when to open or close a given valve. This combination of computer guidance with manual control reduces the likelihood of operator errors while keeping overall component cost low.

For applications that need to control fluid on a smaller scale (nanoliters to microliters), the special socket MEC in Figure 3 is used to interface microfluidic chips to other MECs. The microfluidic chip is packaged in a MEC "shell" that provides standard connections for fluidic input/output. By enabling any microfluidic chip to connect to other MECs,

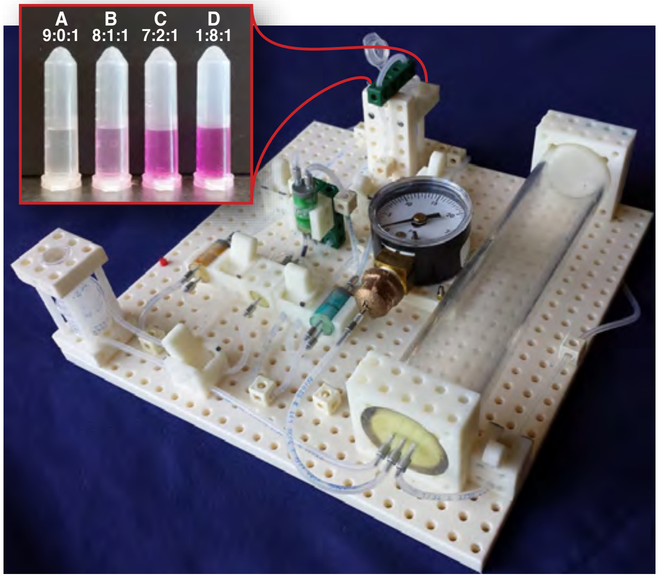

Fig. 4. A MEC-based instrument for performing acid-base titrations. By toggling the manual valves, an operator instructs the instrument to deliver any desired volumes of sodium hydroxide solution, phenolphthalein solution, and water to a vial. Vial A received these fluids in a ratio of 9:0:1 (final concentration 0% NaOH); Vial B received a ratio of 8:1:1 (final concentration 0.0005% NaOH), Vial C received a ratio of 7:2:1 (0.001% NaOH), and Vial D received a ratio of 1:8:1 (0.004% NaOH). The colors of the solutions (from clear in Vial A to magenta in Vial D) confirm the increasing pH of the solutions from A to D.

the socket facilitates connections between the library of off-the-shelf MECs and custom microfluidic chips.

III. MEC-BASED INSTRUMENTS

To demonstrate the utility of MECs, we used them to build several demonstration instruments. Shown in Figure 4 is a MEC-based instrument capable of performing conventional acid-base titrations. Onboard reservoirs are filled with water, sodium hydroxide solution (0.005%), and phenolphthalein solution (0.1% in 50% ethanol). By toggling the manual valves, any combination of these solutions can be delivered to the vial holder. The observed colors of the solutions (ranging from clear in Vial A to bright pink in Vial D in Fig. 13) confirm the increasing pH and increasing sodium hydroxide concentration from Vial A to Vial D. By comparison with the colors of these vials, the pH of an unknown solution could be estimated. Alternately, using an optical absorption MEC currently under development, the pH of an unknown solution could be determined by the optical absorbance of the fluid.

A more complex MEC-based instrument is shown in Figure 5. This fluidic routing system contains over one hundred individual parts from over 30 different kinds of MECs. It is capable of mixing fluids in volumes ranging from milliliters (using the MECs shown in Figure 2) down to microliters and nanoliters (using a custom PDMS microfluidic chip plugged into the socket MEC from Figure 3).

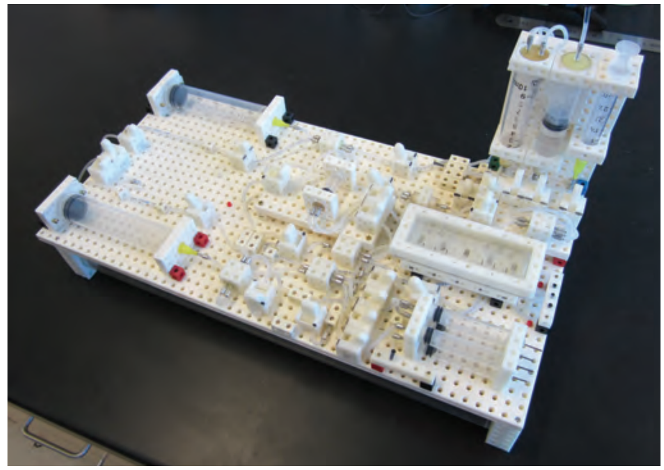

Fig. 5. A MEC-based fluidic router containing over 30 different types of MECs and over 100 individual parts. By toggling the manual valves, fluids from several reservoirs can be mixed in volumes ranging from nanoliters to milliliters.

IV. CONCLUSIONS

We have demonstrated the MEC system, a prototype set of components that could be used by doctors and nurses in developing countries to build custom diagnostic instruments. In future work we will attempt to further enhance the manufacturability and decrease the cost of these components, two crucial improvements that will be necessary before MECs can be deployed in resource-limited settings.

Along with applications in the developing world, MECs can be used in the developed world to create custom instruments. Researchers with no specialized fabrication equipment or training could use MECs to construct an instrument for their unique needs. Finally, we are also pursuing educational applications for MECs. For example, the titration instrument in Figure 4 could be built by students in a chemistry class and used to learn about acid-base equilibria.

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