Teaching Microfluidic Diagnostics Using Jell-O® Chips

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Using Inexpensive Jell-O Chips for Hands-On Microfluidics Education

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As the field of microfluidics continues to grow, there is an increasing demand for public education about this technology. This article presents a quick, simple, safe, and inexpensive method for teaching microfluidics to younger students and the general public. (To listen to a podcast about this article, please go to the Analytical Chemistry multimedia page at pubs.acs.org/page/ancham/audio/index.html.)


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Most of us, being educators or researchers in science and technology, remember a defining moment in our adolescent years that sparked a life-long interest and passion in this field. It may have been performing an oxidation-reduction reaction; it may have been building an electronic circuit; or it may have been watching cells divide under a microscope. Regardless of the subject matter, one thing these pivotal moments have in common is that they are all examples of hands-on education.

Hands-on science education is a very effective method of teaching because students learn better when they are active, thinking, and having fun. The most wonderful demonstrations clearly deliver the important scientific knowledge and concepts in a distilled and easy-to-understand format. Other factors including low cost, safety, and simplicity are also of great value because they increase the number of students who have access to the demonstration.

The accelerating rate of scientific discoveries is driving the integration of science and technology into everyday life. In addition to developing groundbreaking technologies, those in the scientific field must focus on communicating the most important developments to the public and science students in a timely and efficient manner. Hands-on education can effectively contribute to this task. Our most recent contribution to this effort is a simple and low cost method for educating young students about a technology featured regularly in *Analytical Chemistry*, microfluidics.

MICROFLUIDICS AND SOFT-LITHOGRAPHY: A GROWING APPLICATION SPACE

The interdisciplinary field of microfluidics develops miniaturized technologies for manipulating the flow and reaction of small amounts of fluids.[1] Microfluidics has the potential to revolutionize modern biology and medicine because it offers the advantages of working with smaller reagent volumes and shorter reaction times, which greatly reduce the cost required for an analysis.[2,3] Current efforts are being made to integrate an entire laboratory's worth of analytical instrumentation onto a single chip to produce "lab on a chip" systems.[4] Microfluidics has been applied to solve problems in diverse areas in both basic and applied sciences,[5−9] and highly parallelized microfluidic systems are also being actively explored to improve existing technologies.[10,11] Currently, highly integrated microfluidic chips with a thousand or more detection chambers can be produced and implemented easily.[12−14]

Many types of materials are used to fabricate microfluidic channels and chips. Among these, PDMS elastomer has been extensively used in microfluidics because of its low cost, optical transparency, relatively simple processing, and biocompatibility.[15] PDMS chips are usually fabricated using soft lithography,[16] typically in three steps: rapid prototyping, replica molding, and

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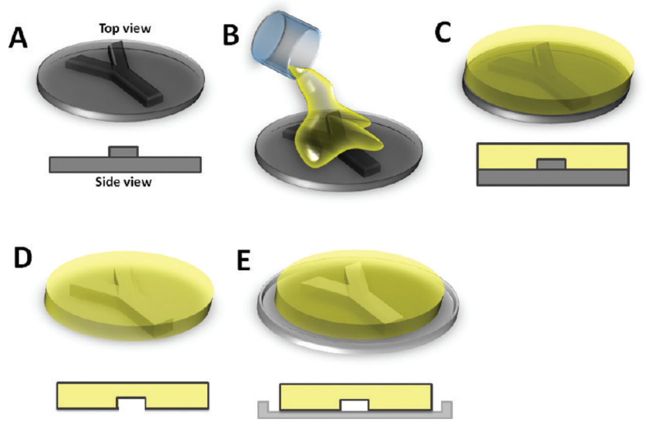

Figure 1. Scheme for producing Jell-O chips using soft lithography. (A) A negative mold is made with desired features. (B) Liquid chip material is poured onto the mold. (C) Mold with liquid material is cured. (D) Solidified chip is peeled off and (E) placed on a rigid substrate for experiments.

sealing. Rapid prototyping produces the silicon mold; replica molding produces a solid PDMS chip from its liquid precursor; and sealing produces a seal between the PDMS and a rigid substrate, forming enclosed microfluidic channels.[16] In addition, the PDMS surface can be chemically modified[17] and used in multiple applications including protein separation[18] and biological studies.[19] Figure 1 presents the general workflow of the soft lithography fabrication process.

IMPORTANCE OF MICROFLUIDICS EDUCATION

Currently, many universities around the world have facilities and resources dedicated to teaching microfluidics to undergraduate and graduate students. But as this field continues to grow, younger students and the general public must also understand this technology that will become an integral part of their daily lives. Some educational and experimental demonstrations introducing soft lithography, photolithography, and microfluidics have been previously published.[20,21] Berkowski et al. presented a technique incorporating polymer chemistry to demonstrate the concepts of photolithography-based microchip fabrication to junior high or high school students. In this experiment, a glass microscope slide was layered with photoresist and covered with a negative photo-mask. Subsequently, the slide was illuminated with UV light to polymerize the photoresist in the exposed area, which formed a shape. Concepts including photolithography, crosslinking density, photopolymerization, and rapid prototyping can be easily conveyed with this method.[21] However, bringing the PDMS chip fabrication process outside of a laboratory is a challenging task because of the toxicity and cost of fabricating molds and the toxicity of PDMS elastomer and curing agent. Thus, the goal of this project was to create a simple and inexpensive process using easily obtainable and non-toxic materials to teach microfluidics principles to high school or grade school students in a few class periods. Three Jell-O chips have been developed to achieve this goal.

Some gelatin-based microfluidic devices have been previously developed.[22−24] For example, Paguirigan and Beebe developed a method for fabricating microfluidic devices using gelatin crosslinked by the enzyme transglutaminase. Cells were cultured in these microfluidic devices to study the effects of soluble factors and extracellular matrix on cellular morphology.[23,24] However, the advantage of the Jell-O chip fabrication method presented here is the accessibility of the starting materials. Jell-O powder and other materials are readily available, the chips and mold materials are easily disposed of, and the experimental demonstrations are directly visible without a microscope. The total cost required to make a single Jell-O chip is <$2 CAD. Therefore, this method provides educators with a fast, inexpensive, fun, and hands-on way to introduce microfluidics principles and various science and engineering concepts to students.

A NEW TEACHING TOOL WITH THE CLASSIC WIGGLE

For detailed information regarding how to make Jell-O chips, please refer to the Supporting Information section. The main materials used to create the molds were foam plates, wooden coffee stirrers, and double-sided tape. The coffee stirrers were cut into different shapes and sizes depending on the purpose of the mold and were then taped onto a foam plate using double-sided tape, creating a specific pattern. To produce a smoother surface on the wooden sticks, single-sided tape was adhered onto their surfaces. We produced three types of molds for the experiments described here: a "JELLO" mold, a Y-channel mold, and a pH sensor mold. The chips themselves were made by pouring a liquid Jell-O and gelatin mixture onto the molds; these were left to cure for two days in a refrigerator. The chips were then removed from the refrigerator, peeled from the molds, and placed in aluminum dishes for demonstrations. The high sugar content from the Jell-O and gelatin mixture provided a natural seal on the aluminum dishes suitable for the low pressure applications demonstrated here. A general workflow for fabricating these Jell-O chips is shown in Figure 2.

TEACHING METHODS

The purpose of this work was not only to develop the Jell-O chips, but also to test them in educational situations with a variety of learners. This was achieved through high school workshops conducted in the Michael Smith Laboratories as well as a one-day workshop for grade-school and high-school science teachers from around the Vancouver area. From these workshops, consensus on the best approaches to teaching microfluidics using Jell-O emerged. The protocols below represent our consolidated understanding of these approaches, divided into modules for younger (grade-school) and more mature (high-school, general public) learners.

To conduct the demonstrations, instructors should allocate two one-hour class periods. The first class period (preferably on a Friday so the chips can be cured over the weekend) is dedicated to introducing microfluidics and soft-lithography, making the molds, preparing the Jell-O and gelatin mixture, pouring the liquid onto the molds, and transferring the plates to the refrigerator. After the chips are cured for two days, the second class period is focused on conducting the hands-on experiments, observing the results, explaining the theory, and discussing some relevant microfluidic applications. For more mature audiences, the learners should conduct both parts of the demonstration (chip fabrication and experimentation). For younger students, the mold and the chips are better made in advance by instructors. However, the students should still be responsible for manipulating the chips to

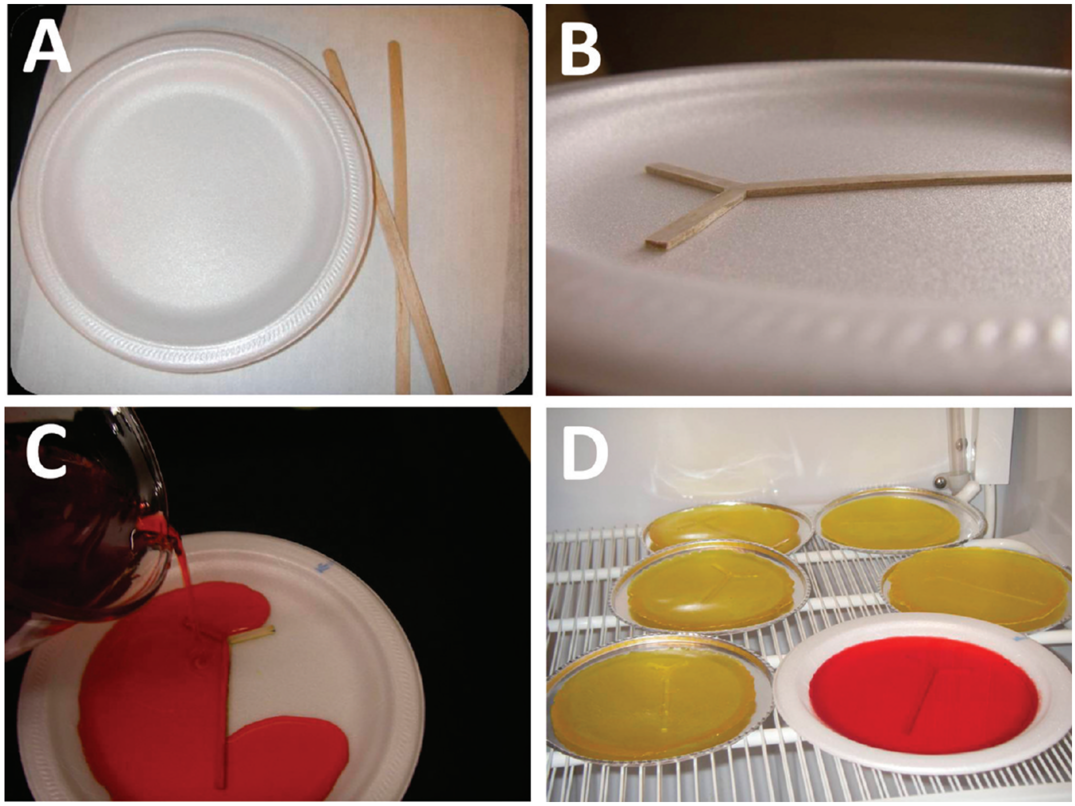

Figure 2. General workflow for producing Jell-O chips using soft lithography approach. (A) Foam plate and wooden coffee stirrers are starting materials for making the mold. (B) A negative mold is made with desired features using double-sided tape. (C) Jell-O and gelatin liquid mixture is poured onto the mold. (D) The molds with liquid material are left to cure in a 4 °C refrigerator. Solidified chips are peeled off and placed on aluminum pans for experiments at room temperature.

form a seal on an aluminum pan, as well as conducting the experiments. This article introduces three teaching modules for varying age groups. The main points are summarized in Table 1 below.

Module I: Pressure-Driven Flow. For a detailed list of materials required and mold fabrication guide for Module I, please refer to the Supporting Information section. Figure 3 shows a chip that has been patterned with the letters "JELLO", which is used in this set of experiments.

After carefully peeling the "JELLO" chip off of the mold, the hollow channel was naturally and reversibly sealed against an aluminum pan. An inlet hole was punctured at the letter "J", and an outlet hole was punctured at the letter "O" with a round drinking straw using a gentle twisting motion. A few drops of concentrated green food coloring dye were added to a small vial of purified water. The green water was loaded into a disposable transfer pipette and injected into the channels by gently squeezing the pipette bulb. The resulting fluid flow was directly visualized without the help of any imaging apparatus.

The answers to the learning questions can be addressed using the introductory materials presented above. All students should be able to peel the Jell-O chips off of the mold and seal them against aluminum pans for experiments. Recalling that a typical PDMS chip is produced in three steps, the differences between Jell-O chip and PDMS chip fabrication can be highlighted using this demonstration. For example, negative molds for PDMS chip fabrication are produced using photolithography; the PDMS pre-polymer is cured in an oven at 60 °C; and the feature sizes of PDMS microfluidic chips are usually a few micrometers in width.[16] However, the general fabrication concepts and PDMS soft lithography can be easily demonstrated using the Jell-O chip fabrication process.

During or after the demonstration, instructors can also explain the concept of pressure-driven flow. In applying pressure to the inlet, we are applying pressure to the colored water and observing fluid flow. As soon as we release pressure from the pipette bulb, the fluid motion stops. In addition, if there is only an inlet and no outlet, the fluid cannot flow through the channel as air present in the channel has no place to escape. If a larger pressure is exerted on the fluid in this system, the reversible seal between Jell-O and aluminum pan will break. Thus, the outlet provides a convenient "exit" path for the air inside the channel, allowing the fluid to flow.

The final key learning outcome that can be taught using this demonstration is the level of creativity that can be demonstrated in designing microfluidic chips to achieve a specific purpose. Depending on our specific needs, we can fabricate molds with different features that perform various tasks. Current microfluidics research is focused on making PDMS chips that can perform different functions and address issues in diverse areas. The following two demonstrations will introduce other types of Jell-O chips that can be made to achieve specific purposes.

Module II: Dimensionless Parameters. After the lesson on pressure-driven flow, another Jell-O chip can be fabricated to teach the principles of dimensionless numbers. As shown in Figure 4, there are two inlets in the Y-channel chip: one for clear water and one for colored water. When both fluids are introduced into

Table 1. A summary of Learning Outcomes for Module I: Pressure-Driven Flow, Module II: Dimensionless Parameters, and Module III: pH Sensing and Parallelization

Parameter	Module I	Module II	Module III
Target Learners	Grade school science students	High school science students	High school science students
Mold Fabrication Difficulty	Medium	Medium	Easy
Experimental Difficulty	Easy	Medium	Medium
Learning Objectives	Basics of microfluidic fabrication	Visualization of laminar flow	Differences between acids and bases
	Soft lithography	Differences between laminar flow and turbulent flow	Fundamentals of pH sensing
	Concept of pressure-driven flow	Significance of dimensionless parameters	Concept of parallelization
	Diversity, complexity, and flexibility of designs	Current microfluidic applications of laminar flow	Current microfluidic parallelization applications
Questions to be Answered	What is microfluidics and how are microfluidic chips made?	Why do the two solutions not mix in this Jell-O chip?	What are acids and bases?
	How are channels formed in microfluidic chips?	What is the difference between turbulent flow and laminar flow?	How can we determine the pH of solutions using pH papers?
	How do liquids flow in microfluidic chips?	What are dimensionless numbers?	What is parallelization?
	Can fluid be passed through the chip with only one inlet and no outlet?	How can dimensionless numbers help us to build our devices?	What are current microfluidic applications of parallelization?

the channels simultaneously, turbulent mixing does not occur and the two liquids remain separate due to laminar flow.

For a detailed list of required materials and mold fabrication guide for Module II, please refer to the Supporting Information section. After carefully peeling the Y-channel chip from the mold, the hollow channels were sealed against an aluminum pan. Two inlet holes and an outlet hole were punctured with a round drinking straw using a gentle twisting motion. Two small vials of purified water were prepared, and a few drops of concentrated blue food coloring dye were added to one. Two 10-mL syringes

Figure 3. A chip made into the letters “JELLO” and filled with green colored water demonstrates the ease of making complex patterns with the Jell-O technique.

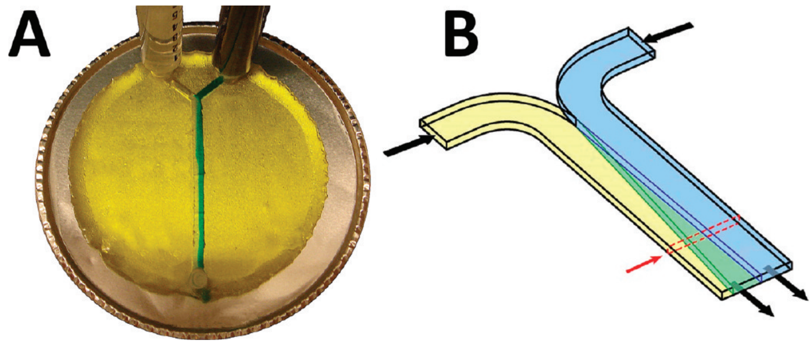

Figure 4. (A) A Jell-O Y-channel chip with a Reynolds number of 30. The injection of colored water to one inlet and clear water to the second results in the classic laminar flow profile, in which both streams remain separate and mix solely by diffusion along the length of the channel. (B) Diagram of laminar flow diffusive mixing occurring at the interface between two different fluids along the channel length. This phenomenon is governed by the Péclet number (adapted from Kamholz).[25] Part B courtesy of Paul Yager: http://faculty.washington.edu/yagerp/microfluidicstutorial/tsensor/tsensor.htm.

were used: one was loaded with blue water and the other one with clear water. Clear water (left channel) and blue water (right channel) were injected simultaneously. The resulting fluid profile was directly visualized.

The most evident benefit of this demonstration is that the students can directly visualize laminar flow without the use of a microscope. In addition, by changing the flow rate of one solution through the channel, students can observe the movement of the interface between colored and uncolored water. That fluids don't mix in the Y-channel chip is counterintuitive; this demonstration provides an interesting starting point for discussing the difference between laminar flow and turbulent flow. More advanced students can be introduced to dimensionless parameters for a more comprehensive understanding.

Dimensionless parameters do not have a physical unit, and they are usually defined as a ratio of properties (these may have units individually, but when combined, the units cancel out).[26] Reynolds number (Re) is one such dimensionless parameter, relating inertial to viscous forces in fluid flows:

$$\mathrm{Re} = \rho \mathrm{U}_0 \mathrm{L}_0 / \eta \qquad (1)$$

where ρ is the fluid density, U_0 is the characteristic velocity, L_0 is the typical length scale, and η is the shear viscosity.[2,26] A high Re implies that inertial forces are dominant whereas a low Re implies that viscous forces are dominant. Therefore, Re is used to differentiate between laminar and turbulent flows. Using water as the working fluid ($\rho = 1.0$ g/cm^3 and $\eta = 0.010$ g/cm·s) with a velocity of 1.0 cm/s and a channel radius of 0.30 cm yields Re = 30. Typically, the transition from laminar to turbulent flow in round pipes occurs at Re = 2000−3000,[26] so Re = 30 indicates that the flow is within the laminar flow regime.

In addition to the Reynolds number, more advanced students may learn about another dimensionless parameter, the Péclet number (Pe), which is defined as

$$\mathrm{Pe} = \mathrm{U}_0 \mathrm{L}_0 / \mathrm{D} \qquad (2)$$

where U_0 is the characteristic velocity, L_0 is the typical length scale, and D is the diffusion coefficient. For a molecule with an unknown diffusivity, this value can be modeled as a spherical solute

$$\mathrm{D} \approx \mathrm{k_B T} / 6\pi\eta a \qquad (3)$$

where $\mathrm{k_B}$ is the Boltzmann constant, T is the temperature, η is the shear viscosity, and a is the molecule size.[26] The diffusion coefficient of typical food coloring dye is about 200 μm^2/s;[27] therefore, calculation yields Pe = 150,000 in our Jell-O chips. This large Pe indicates that convective mass transfer dominates and little diffusion along the length of the channel occurs (Figure 4A). However, as the typical length scale decreases (such as in the case of research microfluidic systems), intermediate Pe is achieved, and the differences in solute diffusion rates will become more pronounced (Figure 4B).

Understanding of Pe requires an understanding of diffusion. Elementary diffusion explanations can be initiated using the Jell-O chips described here, as laminar flow is an ideal flow regime in which to demonstrate the effects of diffusion. Although one cannot achieve reliable separation of analytes based solely on diffusion or molecular size in these devices, such work has been conducted in smaller microfluidic systems. For example, diffusive mixing has been employed in microfluidic T-sensors for chemical concentrations measurements[28] and for rapid determination of diffusion coefficients of large and small molecules.[29] This work is available as an extension to the discussion of convection and diffusion should time and educational level allow.

In general, learning how to use dimensionless numbers is an important skill for scientists and engineers. Dimensionless numbers allow calculation of the dominant forces in our fabricated microfluidic devices. Using Re, we can calculate if the devices have laminar or turbulent flow; using Pe, we can determine whether convective mass transfer or diffusion dominates. We can also change a parameter to change the analytical regime. Similarly, we can use dimensionless numbers to help us design microfluidic chips. For example, if the properties of the fluid to be used are known and the chip must demonstrate turbulent flow, determining the typical length scale and the characteristic velocity is possible.

Finally, after developing the fundamental understanding of laminar flow, some current applications of the Y-channel design can be highlighted. Microfluidic devices use the phenomena of laminar flow and diffusive mixing to achieve different aims. In

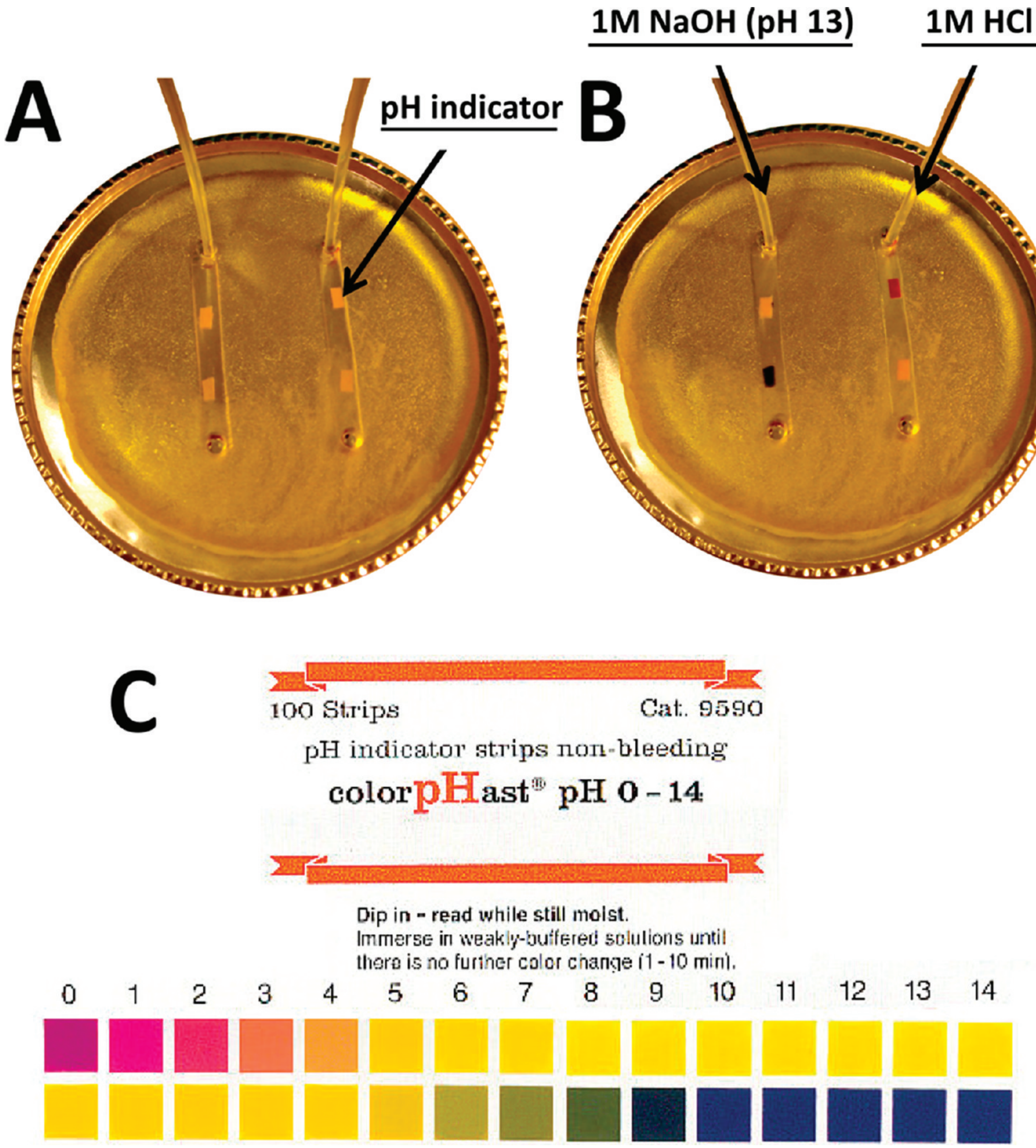

Figure 5. Dual Jell-O chip pH sensor. (A) Two different pH sensing regions per channel can be used to detect different solutions. (B) The addition of either acidic or basic solutions to each channel results in a distinct pattern of color change visible to the naked eye. (C) pH indicator chart for reference (adapted from EM-Reagents).

addition to the two examples mentioned previously, laminar flow is used in Y-shaped fuel cells to keep the anode and cathode streams separated without using a polymer electrolyte membrane.[30−32]

Module III: Fundamentals of pH Sensing and Parallelization. Figure 5 presents the third Jell-O chip that we have developed for teaching the fundamentals of pH sensing and parallelization.

For a detailed list of materials required and mold fabrication guide for Module III, please refer to the Supporting Information section. After carefully peeling the pH sensor chip off of the mold, the hollow channels were sealed against an aluminum pan. Two inlet holes and two outlet holes were punctured with a round drinking straw using a gentle twisting motion, forming two separate channels. In both channels, a piece of acid-sensing pH paper was placed near the inlet and a piece of base-sensing pH paper was placed near the outlet. Double-sided tape was used to tape the small pieces of pH paper onto the aluminum pan. Small vials of 1M HCl and 1M NaOH were prepared (both ~30 mL). (Caution must be exercised when working with high concentrations of acids and bases: proper protective clothing such as a lab coat, gloves, and goggles should be worn. Safer acids or bases, such as vinegar and sodium bicarbonate, could also be used for this experiment.) Two disposable transfer pipettes were used: one was loaded with NaOH and the other loaded with HCl. The NaOH (left channel) and HCl (right channel) were injected simultaneously, and the resulting color changes were directly visualized.

When 1M NaOH is introduced in the left channel, the pH paper nearest the channel outlet, which detects basic solutions, turns blue. Similarly, the acid-sensing indicator strip nearest the channel inlet turns purple when 1M HCl is injected into the right channel. As a result, distinct patterns of color changes can be observed. Using this setup, the basics of chemical sensing can be simply explained. In a more integrated learning activity, one could also combine the method used in this module with the lessons from

Module II by injecting both a weak acid and a weak base over a pH sensing strip in a Y-channel chip and readily observe distinct regions of color change on the same pH sensing strip as a result of the laminar flow pattern previously observed.

The concept of parallel analysis can also be introduced with this chip. For instance, assuming that the indicator strips near the inlet represent areas that contain a type of ligand that only detects analyte A and the other areas contain a second type of ligand that specifically detects analyte B, when two unknown fluid samples are introduced, the analyte in each solution can be determined. Similarly, the channels can be modified with four different ligands, and four independent tests can be conducted in parallel using only one fluid sample. Therefore, this simple demonstration can promote the current efforts in microfluidics research to conduct multiple experiments in parallel by modifying the surface with different ligands.[33,34]

CONCLUSIONS

Using the Jell-O fabrication technique, microfluidics may be more easily demonstrated in a hands-on approach to convey current research topics to younger students and the general public. Our experience is that when students learn about science at a young age, they will become more attracted to pursuing an engineering or science degree in their post-secondary education. To encourage this process, three types of Jell-O chips have been fabricated: a "JELLO" chip, a Y-channel chip, and a pH sensor chip. Using these demonstrations, elementary and high school students, as well as the general public can learn about how microfluidic chips are made; learn microfluidics concepts, including dimensionless scaling factors, diffusion coefficients, and pH sensing; make the connection to current microfluidics research; and become excited about scientific research.

The fabrication method is fast, simple, and inexpensive, allowing Jell-O chip demonstrations to enter a wide variety of learning environments not accessible to current microfluidics methods. Other types of chips (including bubble and droplet generators, not shown) can also be fabricated, suggesting that this technique possesses an enormous educational potential. Experiments with other naturally-occurring gels also indicate that this method could be extended to developing regions of the world to provide microfluidic technology both for education and diagnostics. Finally, we are also currently developing fabrication techniques for bonded and functional multilayer Jell-O chips to further extend the applications of this fabrication method. We hope that this work will serve as a model for future educational endeavors in science.

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SUPPORTING INFORMATION AVAILABLE

Additional information as noted in text. This material is available free of charge via the Internet at http://pubs.acs.org.

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