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A simple micro check valve for microfluidic point-of-care diagnostics

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U.S. DEPARTMENT OF ENERGY

1. Overview

- **Purpose:** To develop passive, normally closed check valves amenable to integration in mass-produced thermoplastic microfluidic devices.
- **Methods:** We prepared valves by laser cutting or conventional machining, tested valve performance, and applied valves to enhance device functionality.
- **Results:** 1) Valves provide leak-free one-directional flow with adjustable opening pressure. 2) Valves enabled staged delivery, pumping, and NAAT.

2. Introduction

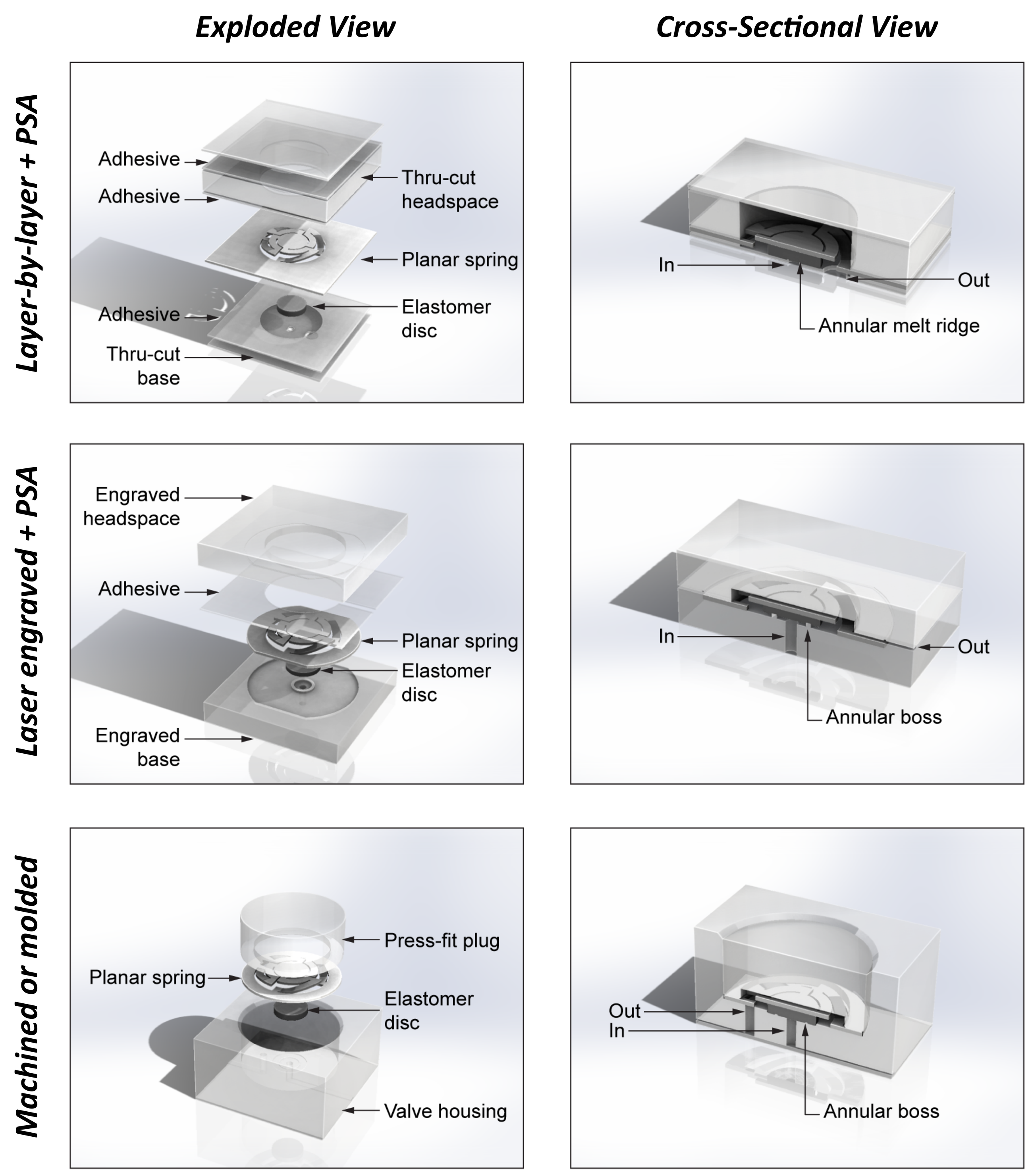
Microfluidic check valves enable automated sample processing for diagnostics at the point of care. However, there is an unmet need for a passive check valve that is compatible with rigid thermoplastic devices during all stages of development—from initial prototyping with a laser cutter to final production with injection molding. Here, we present simple designs for a passive, normally closed check valve that is manufactured from commonly available materials with a CO_2 laser and readily integrated into prototype and production thermoplastic devices. The check valve consists of a thermoplastic planar spring and a soft elastomeric pad that act together to seal against backflow. The valve's cracking pressure can be tuned by modifying the spring's planar geometry and thickness. Seal integrity is improved with the addition of a raised annular boss beneath the elastomeric pad. To demonstrate the valve's usefulness, we employ these valves to create a finger-operated on-chip reagent reservoir and a finger-actuated pneumatic pump. We also apply this check valve to passively seal a device to enable portable detection of RNA from West Nile virus in a laser-cut device with a smartphone.

3. Methods

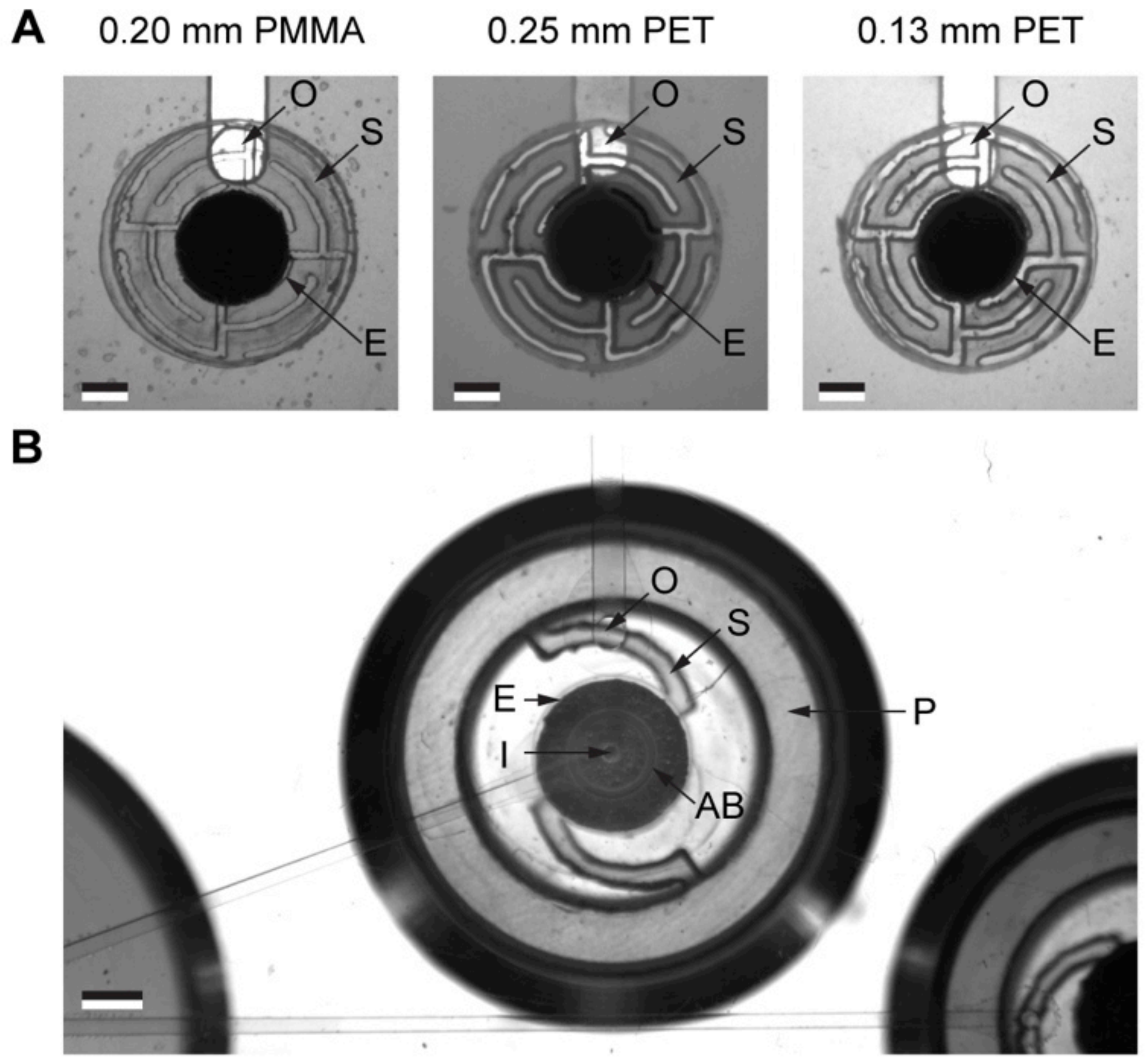
Valve components were cut with a CO_2 laser or prepared by conventional machining. Opening pressures were measured using compressed air. RT-LAMP detection of West Nile Virus was performed using previously published methods (Parida et al., J. Clin. Micro. 2004) and a proprietary fluorescence-based molecular detection technique.

4. Results

I. Valves are designed for all stages of production



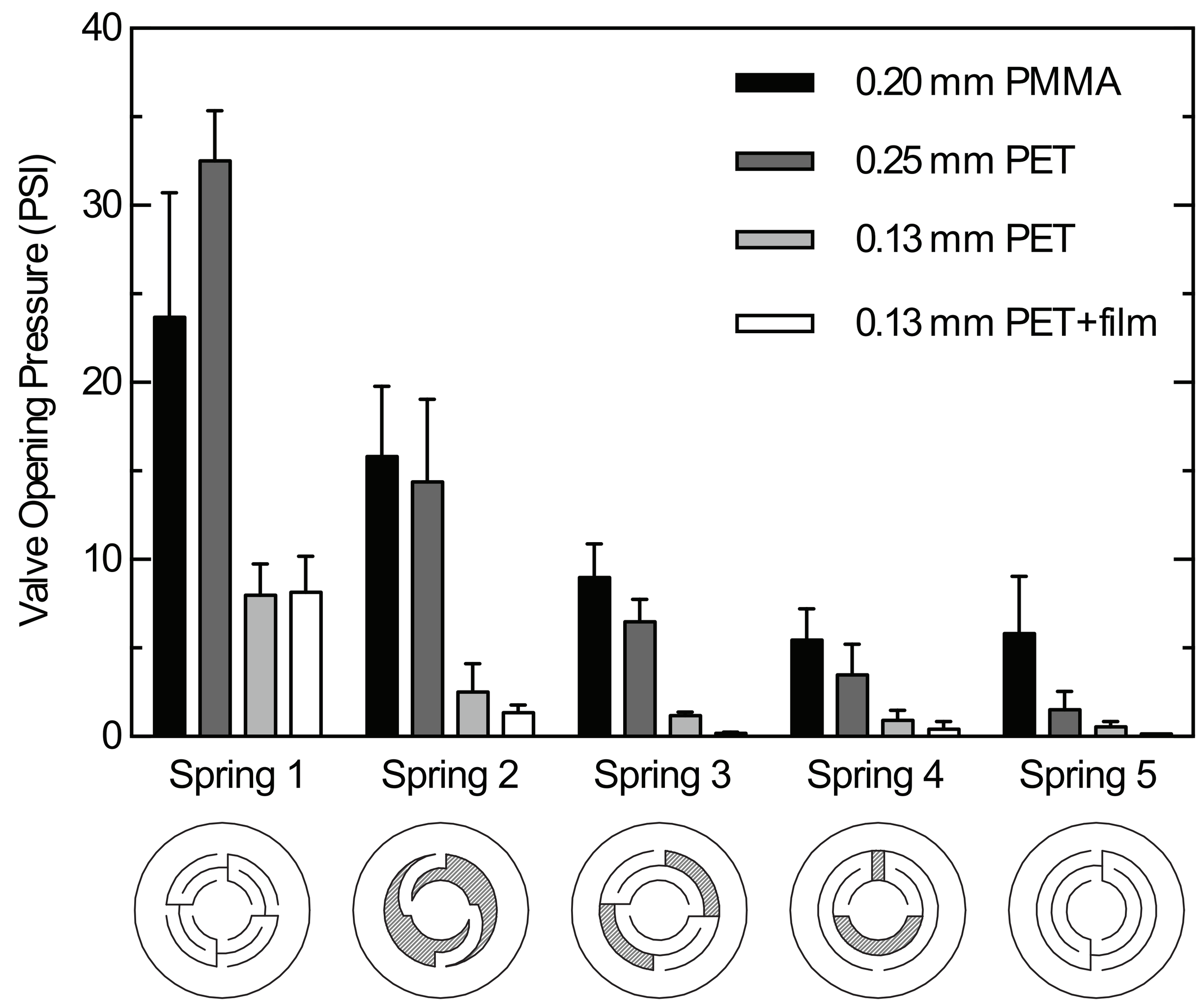
II. Valves integrate into prototype devices



O = Outlet, S = Spring, E = Elastomer, I = Inlet, P = Press-fit plug, AB = Annular Boss

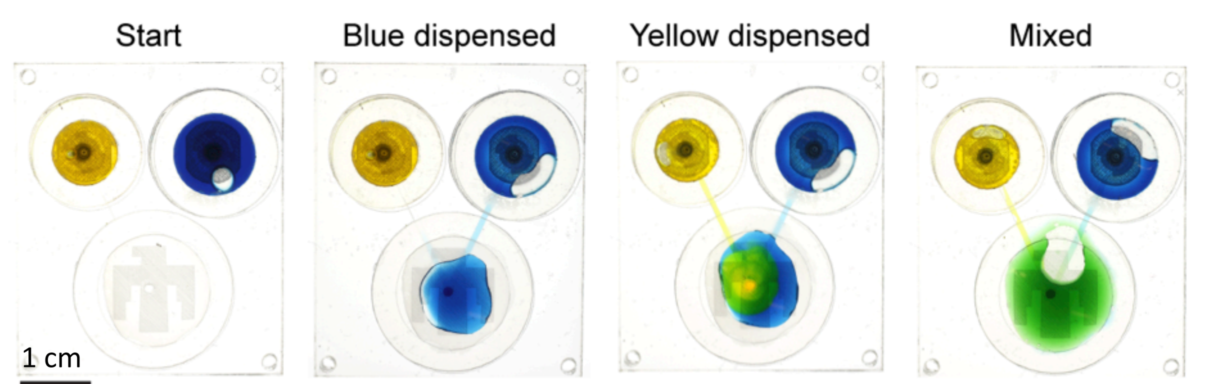
A. Stereoscopic images of valves assembled layer-by-layer from laser cut plastics and pressure sensitive adhesives.
B. Stereoscopic image of a valve assembled into a machined valve housing as part of a larger microfluidic device.

III. Valves feature broadly tunable opening pressure via the orthoplanar spring design



- Spring pattern can broadly tune opening pressure.
- Stiffer materials make stiffer springs, which open at higher pressures.
- Thicker springs open at higher pressures.

IV. Valves enable staged reagent delivery



Laser engraved PMMA device with check valves demonstrating finger-actuated, sequential delivery of different fluid volumes to a common mixing chamber.

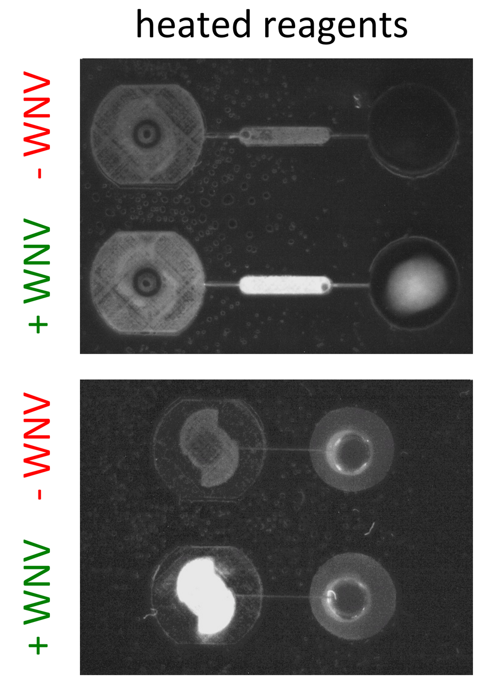
V. Valves enable pumping and pressurization

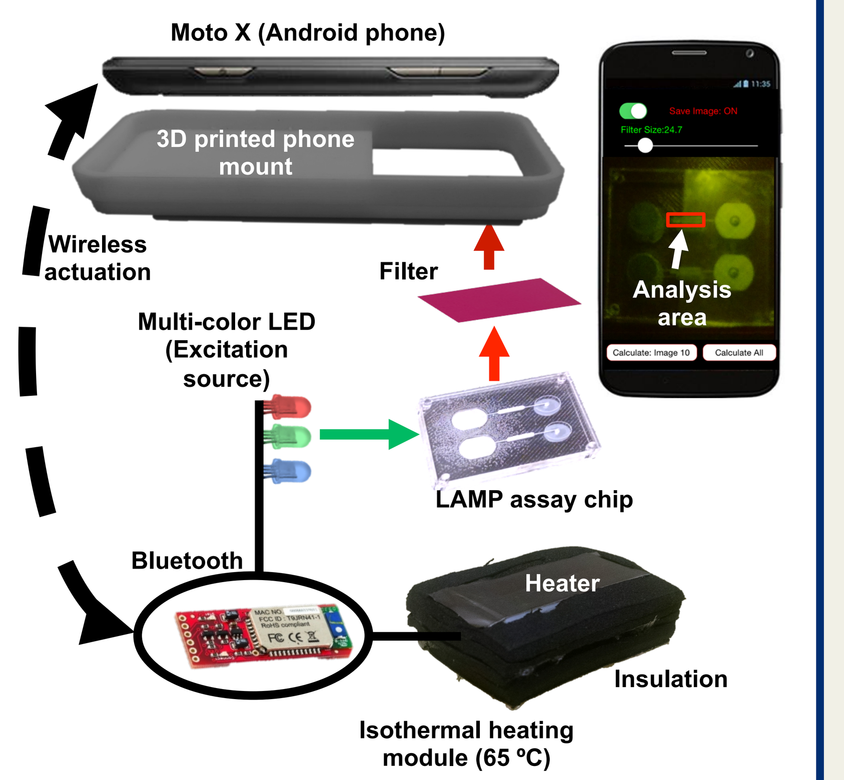
Check valves enable finger-actuated pumping of air and fluid into a "microfluidic frog's" throat. Air moves through the right nostril into the eyes, which are depressed to fill the throat with air.
Abbreviations: V_1 *= valve 1,* V_2 *= valve 2, E = elastomeric membrane.*

VI. Detection of West Nile virus using RT-LAMP and a smartphone enabled, 3D-printed detector

We used check valves to passively seal a chip for detection of RNA from West Nile virus by RT-LAMP, a nucleic acid amplification technique. The reaction occurs under pressure and is heated to 65°C for 30 minutes. A 3D-printed, portable, inexpensive smartphone detection system can provide real-time or endpoint detection of positive amplification (*see poster by Aashish Priye*).

Sample endpoint images of WNV assays using check valves to contain the pressurized and heated reagents





5. Conclusions

- Check valves are easily integrated into thermoplastic devices.
- Components are made from common materials.
- Valves require no external actuation.
- No minimum back pressure is required to seal against reverse flow, and valves hold >60 psi of back pressure without failure.
- Opening pressure is adjustable from 1-30 psi without changing form factor.
- Valve diameter (down to 3 mm), thickness (< 0.6 mm) and dead volumes (down to 4 µL) are small.
- Future work will demonstrate high-throughput manufacture with injection molding and die cutting.
- We plan to use these valves to enable fully automated biosurveillance for arbovirus targets within California.
- The valves reduce the complexity of microfluidic chip handling hardware, making automation simpler and more cost effective.

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