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TOPICAL REVIEW

A review of microvalves

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Abstract
This review gives a brief overview of microvalves, and focuses on the actuation mechanisms and their applications. One of the stumbling blocks for successful miniaturization and commercialization of fully integrated microfluidic systems was the development of reliable microvalves. Applications of the microvalves include flow regulation, on/off switching and sealing of liquids, gases or vacuums. Microvalves have been developed in the form of active or passive microvalves employing mechanical, non-mechanical and external systems. Even though great progress has been made during the last 20 years, there is plenty of room for further improving the performance of existing microvalves.

(Some figures in this article are in colour only in the electronic version)

1. Introduction

Since the first integrated circuit was invented by Kilby (the Nobel Prize winner in Physics in 2000) in 1958 [1], miniaturization has become an important research topic in both electronic and non-electronic devices. In the late 1970s, miniaturization was extended to mechanical devices with electronics, which is now known as microelectromechanical systems (MEMS) [2, 3]. During the last two decades, MEMS research has been largely encouraged by the first introduction of miniaturized total analysis systems by Manz *et al* [4] to the MEMS community. They are widely employed in areas from biomedical and drug delivery to space and fuel cell microfluidic systems [2–29]. These systems have been reduced in size to micro scale for the realization of a fully integrated microfluidic system, such as lab-on-a-chip (LOC) or a micro total analysis system (μTAS) [4–7]. Major advantages of miniaturization are the drastic decrease in chemical reaction time and less consumption of expensive chemical reagents, as well as enhancement of reliability.

With the recent success of the human genome project [8] and the huge potential of biotechnology, the microfluidic systems are promising to be a big commercial success in life science applications. The microfluidic systems will be powerful tools for handling biomolecules, such as cells, DNA, RNA, proteins or neurons. They have been applied to polymerase chain reaction (PCR) [9], DNA analysis and sequencing [10, 11], protein separation [12, 13], immunoassay [14] and cellular analysis [15, 16], ranging from disposable lab-on-chips to high throughput microfluidic systems.

However, from a practical solution standpoint, the successful miniaturization and commercialization of fully integrated microfluidic systems have been delayed due to the lack of reliable microfluidic components, i.e., micropumps and microvalves. Therefore, even though much attention has been paid to the development of the microfluidic components, they are still the most difficult task. The research on microfluidics, including micropumps [17, 18], micromixers [19] and world-to-chip microfluidic interfaces [20] has been thoroughly reviewed, but rarely that on microvalves [21]. In this review, we update recent microvalve solutions that have appeared in over 200 archival journal papers since Terry's microvalve was first reported in 1979 [3]. In addition to traditional MEMS-based microvalves, we focus on some of the

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Table 1. Classification of microvalves.

Categories				Sections
Active	Mechanical	Magnetic	External magnetic fields	2.1.1
			Integrated magnetic inductors	2.1.2
		Electric	Electrostatic	2.2.1
			Electrokinetic	2.2.2
		Piezoelectric		2.3
		Thermal	Bimetallic	2.4.1
			Thermopneumatic	2.4.2
			Shape memory alloy	2.4.3
		Bistable		2.5
	Non-mechanical	Electrochemical		3.1
		Phase change	Hydrogel	3.2.1
			Sol–gel	3.2.2
			Paraffin	3.2.3
		Rheological	Electro-rheological	3.3.1
			Ferrofluids	3.3.2
	External	Modular	Built-in	4.1.1
			Rotary	4.1.2
		Pneumatic	Membrane	4.2.1
			In-line	4.2.2
Passive	Mechanical	Check valve	Flap	5.1
			Membrane	5.2
			Ball	5.3
			In-line mobile structure	5.4
	Non-mechanical		Diffuser	6.1
		Capillary	Abrupt	6.2
			Liquid triggered	6.2
			Burst	6.2
			Hydrophobic valve	6.2

non-traditional microvalves for various applications including life sciences.

Microvalves found today can be roughly categorized as shown in table 1. Most of them generally fall into one of two major categories: *active* microvalves, using *mechanical* and *non-mechanical* moving parts, as well as *external systems*, and *passive* microvalves, using *mechanical* and *non-mechanical* moving parts. In this review, we intend to categorize *active* microvalves into three subgroups according to their actuation originality. Traditionally, (1) *mechanical* active microvalves are accomplished using the MEMS-based bulk or surface micromachining technologies, where mechanically movable membranes are coupled to magnetic, electric, piezoelectric or thermal actuation methods. Unconventionally, (2) *non-mechanical* active microvalves can be operated by the use of smart or intelligent materials. These non-mechanical active microvalves may hold movable membranes which are, however, actuated due to their functionalized smart materials such as phase change or rheological materials. In addition, (3) *external* active microvalves are actuated by the aid of external systems such as built-in modular or pneumatic means. Sometimes, passive microvalves are regarded as a part of micropumps in many other reviews [17, 18, 28, 29]. Additionally, based on their initial mode, microvalves can be divided into normally open, normally closed and bistable microvalves. In this review, we categorize the microvalves into five different groups: active microvalve—mechanical (section 2), active microvalve—non-mechanical (section 3), active microvalve—external (section 4), passive microvalve—mechanical (section 5) and passive microvalve—non-mechanical (section 6).

2. Active microvalves—mechanical

Various actuation principles are adopted to actuate mechanical moving parts in active microvalves. Figure 1 illustrates the actuation principles widely employed in microvalve structures (or microactuators including micropumps). Most active microvalves couple a flexible membrane to magnetic [3, 30–42], electric [43–55], piezoelectric [56–65], thermal [66–84] or other actuation methods [85–93] (table 2). Traditionally, these active microvalves are accomplished using MEMS-based bulk or surface micromachining technologies, which have been well established in the MEMS field during the last two decades.

2.1. Magnetic

2.1.1. External magnetic fields. In 1979, a miniaturized electromagnetic microvalve was accomplished by using a solenoid plunger, which was physically connected to a silicon micromachined membrane by Terry *et al* [3]. The microvalve was the first active micromachined valve, a component of an integrated gas chromatography system, as shown in figure 2. Yanagisawa *et al* [30] built a microvalve with a thin NiFe membrane as a cap inside a small tube and a solenoid coil mounted outside. The microvalve working as a gas flow regulator was driven by 0.1 to 100 Hz rectangular magnetic field and the flow rates were controlled between 66 and 5140 l min^{-1} at an input pressure of 3.5×10^{-12} kPa.

Magnetic microvalves can often be hybrid-integrated with permanent magnets to increase magnetic forces with less power consumption: movable membranes integrated with coils (in this case, the permanent magnet is fixed) [31, 65, 93]

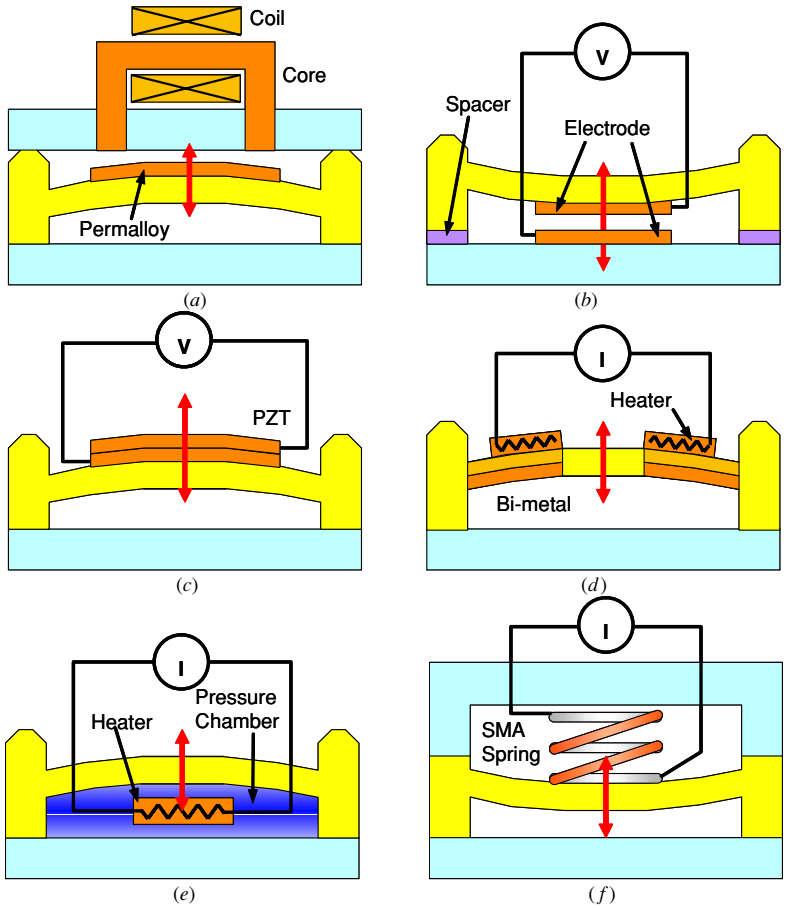

Figure 1. Illustrations of actuation principles of active microvalves with mechanical moving parts: (*a*) electromagnetic; (*b*) electrostatic; (*c*) piezoelectric; (*d*) bimetallic; (*e*) thermopneumatic and (*f*) shape memory alloy actuation.

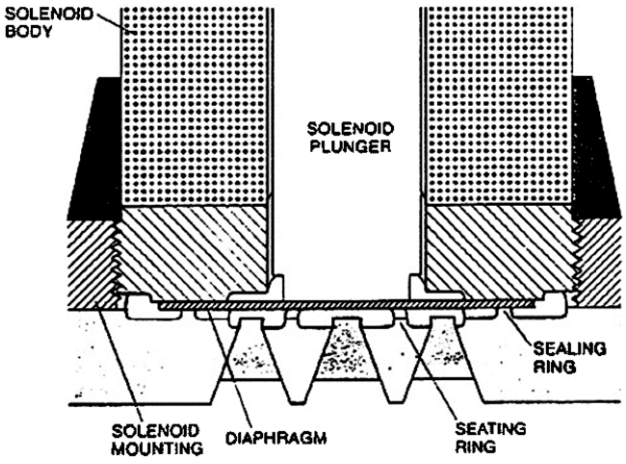

Figure 2. The microvalve with a solenoid plunger as a component of an integrated gas chromatography system by Terry *et al* [3].

or mounted with permanent magnets (the permanent magnet is free to move by actuating external coils) [32, 33, 66]. Meckes *et al* [31] developed a microvalve with an integrated gold coil defined on the movable membrane, which was deflected by the magnetic force between the current within the planar coil and an external permanent magnet. A closing force of 0.8 mN to deflect the membrane over an inlet valve seat was produced by applying a dc current of 25 mA. Bae *et al* [32, 33] designed a pressure regulating microvalve with a permanent magnet attached to a micromachined membrane and an external solenoid coil for glaucoma implant. Current pulse operation of the microvalve produced deflection of the membrane, thereby modulating the pressure release rate. An intraocular pressure of 2.3 kPa was obtained with an applied current of 60 mA.

Various types of active ball-type microvalves making use of magnetic actuations [34–36] were reported. Krusemark *et al* [34] reported a ball-type microvalve using a spherical metal ball, which stayed on the circular valve seat of an outlet orifice to stop the fluidic flow and actively moved upward by an external magnetic force to open the fluidic flow. Oh *et al* [35] realized an in-line micro ball valve through polymer tubing, consisting of a biomedical grade silicone tube (625 μm ID and 1190 μm OD), a nickel ball with a diameter of 760 μm and a Teflon tube for housing. The valve structure was symmetric so that it could be operated bidirectionally and could be easily connected with other microfluidic systems. At an input pressure of 2.1 kPa, there was an abrupt increase in flow rate at an applied current of around 500 mA. The device showed a leakage flow rate of about 30 μl min^{-1} at 2.1 kPa. Fu *et al* [36] developed another micro ball valve using iron balls with a diameter of 3 mm as the moving part driven by an external solenoid. The normally open microvalve switched up to 200 kPa differential pressure with an initial current of 300 mA. In addition, the valve could be operated as a

Table 2. Mechanical active microvalves.

									On/off switching		Flow regulation				Leakage	
Reference	Type	Mechanical part	Material	Mode	Application	Fluid	Experimental or theoretical data	Valving time (ms)	Max pressure (kPa)	On/off power	Generated force/pressure/ deflection	Measured flow (μl min^{-1})	Applied power	Applied pressure (kPa)	Measured leakage (μl min^{-1})	Applied pressure (kPa)
Terry *et al* [3]	EM	M	Si	NC	S	G										
Yanagisawa *et al* [30]	EM	M	NiFe	NO	R	V	E							7.5 E–13		
Meckes *et al* [31]	EM	M	Au/P-Si	NO	R	G	E				0.8 mN		0.025 A			
Bae *et al* [32, 33]	EM	M	PDMS	NO	R	L	E				2.3 kPa		0.06 A			
Krusemark *et al* [34]	EM	Ball	Metal	NC	S	G										
Oh *et al* [35]	EM	Ball	Ni	NC	R	L	E					1300 000	1.0 A		1	21
Fu *et al* [36]	EM	Ball	Fe	NO	R	G	E	10				500 000	0.2 A	50		
Oh *et al* [37, 38]	EM	Pinch	Silicone	NC	S	L	E		207	0.12 A		836 000	0.16 A	8.2	0	207
Ahn's group [41]	EM	Integrated	NiFe	NC	R	G	E			0.25 A					5.6	4.8
Ahn's group [41]	EM	Integrated	NiFe	NC	R	DI	E			0.25 A					3.9	4.1
Shikida *et al* [43, 44]	ES	M	NiFe	NO	R	G	E			200 V		1 000		0.1		
Goll *et al* [45]	ES	M	PI/Au/PI	NO	S	N_2	E			60 V	25 μm	12 000		110		
Robertson and Wise [46]	ES	M	Si	NO	R	G	T	0.1		80 V		0.87		0.75		
Schailble [47]	ES	M	Si	NC	R		E	1								
Wijngaart *et al* [48]	ES	M	Si	NC	R	Air	T				15 μm		366 V	500		
Wijngaart *et al* [48]	ES	M	Si	B	R	Air	T				5 μm		24 V	100		
Yobas *et al* [49, 50]	ES	M	P-Si	NO	R	Air	T		82.7							
Yang *et al* [54]	ES	M	Si	NC	S	N_2	E					45 000	136 V	900		
Yang *et al* [54]	ES	M	Si	NC	S	He	E								6	170
Roberts *et al* [56, 57]	PE	M	SOI	NC	R	G	E				17 μm	12 600	500 V	260		
Rogge *et al* [58]	PE	M	PI	NC	S	N_2	E	2	193	245 V	50 μm				30	200
Rogge *et al* [58]	PE	M	PI	NC	S	DI	E								0.013 3	100
Shao *et al* [59]	PE	M	Polymer	NC	R	N2	E	0.7				70 000		50		
Peirs *et al* [60]	PE	Ball	Steel	NO	R	DI	E				140 N 6 μm		100 V		420	600
Chakraborty *et al* [61]	PE	M	Si	NC	S	Air	E				10 μm					
Yang *et al* [62]	PE	M	Si	NC	R	He	E					52 000	10 V	2070	5	550
Waibel *et al* [63–65]	PE	Lip	Santoprene	NC	R	Ink	E				80 μm	190	140 V		0.002	1
Jerman [66]	BM	M	Al/Si	NC	R	N_2	E					150 000		350	30	34.5
Barth [67]	BM	M	Ni/Si	NC	S	Air	E	200	1035			1000 000	1.03 W			
Rich and Wise [68]	TP	M	Si	NO	S	G	E	1 s	7.4 Pa	0.34 W	0.016 kPa		0.5 W			
Rich and Wise [68]	TP	M	Si	NO	S	G	E					400 000		0.011 3	1	
Ruzzu *et al* [69]	TP	M	Polymer	NO	S	G	E			0.04 W				20	9600	20
Takao *et al* [70]	TP	M	PDMS	NO	S	DI	E	5 s (O) 8 s (C)		0.2 W				20	1	30

Table 2. (Continued.)

									On/off switching		Flow regulation				Leakage	
Reference	Type	Mechanical part	Material	Mode	Application	Fluid	Experimental or theoretical data	Valving time (ms)	Max pressure (kPa)	On/off power	Generated force/pressure/ deflection	Measured flow (μl min^{-1})	Applied power	Applied pressure (kPa)	Measured leakage (μl min^{-1})	Applied pressure (kPa)
Yang *et al* [71, 72]	TP	M	Silicone	NO	R	DI	E				134 μm			28.3		
Yang *et al* [71, 72]	TP	M	Silicone	NO	R	N_2	E					1000 000	0.04 W	228		
Baechi *et al* [73, 74]	TP	M	PDMS	NO	S	L	E	150 (C)			3.5 μm		0.24 W			
Kim *et al* [75]	TP	M	PDMS	NO	S	DI	E	25 s (O) 20 s (C)		0.2 W	40 μm		0.025 W			
Kohl *et al* [80]	SMA	M	NiTiPd	NO	R	G	E	22			20 μm	360 000	0.22 W	250		
Reynaerts *et al* [82]	SMA	Pinch	NiTi	NC	S	L	E	660 (O)		0.12						
Pemble and Towe [83]	SMA	Pinch	NiTi	NC	S	L	E	1 s (O) 2.5 s (C)	207			16 800	0.398 W	20.7		
Tamanaha *et al* [84]	SMA	Pinch	PDMS	NC	S	A	E				2.35 N 406 μm					
Goll *et al* [88]	Thermal	M	Polymer	B	S	G	E		47							
Ren and Gerhard [89]	EM	Cantilever	NiFe	B	S	A	E	0.3 (C)		1.25 A	5 mN 100 μm					
Bohm *et al* [90]	EM	M	Si	B	S	DI	E				200 μm					
Bosh *et al* [93]	EM+ES	M	Si	B	S	G	E	0.4		0.2 A (O) 30 V (C)		3 000		16		

EM, electromagnetic; ES, electrostatic; PE, piezoelectric; BM, bimetallic; TP, thermopneumatic; SMA, shape memory alloy; NC, normally closed microvalve; NO, normally open microvalve; B, bistable; G, gas; L, liquid; DI, deionized water; V, vacuum; R, flow regulation; S, on/off switching; O, opening; C, closing; PI, polyimide; P-Si, poly-silicon; SOI, silicon-on-insulator; M, membrane; E, experimental data; T, theoretical data.

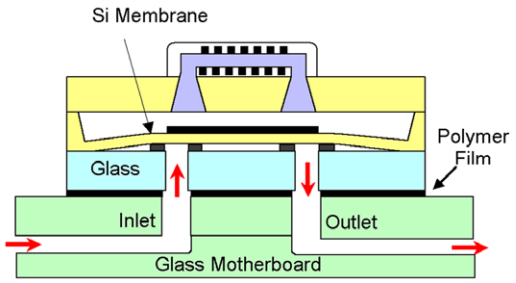

Figure 3. The normally closed magnetic microvalve with an integrated magnetic inductor by Oh *et al* [42].

proportional valve to regulate the outlet pressure ranges from 0 to 112.5 kPa at an input pressure of 200 kPa. The microvalve was closed at a current of 200 mA with a leakage flow rate of 0.5 l min^{-1} at 50 kPa.

Among the other types of valves, pinch-type valves are often favored because they can provide zero leakage flow, zero dead volume, fast response, high flow range and easy replacement of tubing. Although some pinch valves are commercially available (from Bio-Chem Valve, Boonton, NJ), a miniaturized pinch-type valve using a conventional solenoid compliant with a surface mountable scheme on an integrated microfluidic biochemical detection system for magnetic bead-based immunoassay has been reported by Ahn's group [37, 38]. The pinch valve included a solenoid, a spring loaded plunger and a silicone tube (735 μm ID and 940 μm OD). Due to the compressive spring force, the plunger pinched down the silicone tube, making the valve to operate in a normally closed mode.

2.1.2. Integrated magnetic inductors. Ahn's group also developed active microvalves consisting of an integrated inductor, a deflectable silicon membrane with an NiFe thin film and a stationary inlet/outlet valve seat [39–42]. A schematic representation of the microvalve mounted on a glass motherboard is shown in figure 3. The magnetic inductor, valve components and the glass motherboard were fabricated individually and then bonded together using a low temperature bonding technique to accomplish the microvalve [42]. The inductor acted as a flux generator and produced sufficient forces to pull the silicon membrane by magnetically coupling with the NiFe permalloy electroplated on the silicon membrane. The membrane pulled up and removed itself from the valve seats. The valve thus opened and fluids flew from the inlet to the outlet because of the pressure difference in between. The achievable flow rate increased quickly after an applied current of about 250 mA for N_2 gas. The measured leakage flow rates were 20.5 μl min^{-1} at an input pressure of 12.4 kPa, 9.4 μl min^{-1} at 7.6 kPa and 5.6 μl min^{-1} at 4.8 kPa. The leakage flow rates increased with inlet pressure. For the case of DI water the leakage flow rates were around 10.5 μl min^{-1} at 8.3 kPa and 3.9 μl min^{-1} at 4.1 kPa [41].

2.2. Electric

2.2.1. Electrostatic. Electrostatic microvalves have been reported with flexible membranes [43–45] or rigid silicon membranes [46–52]. Most microvalves were employed for gas flow regulations rather than liquid flow controls due to electrolysis of liquids at high voltages [43–50, 52]. Shikida *et al* [43, 44] developed a gas microvalve consisting of a pair of planar electrodes with a separation of 2.5 mm, sandwiching a conductive film in the middle. The 5 μm Ni–Fe film was elastically bent in an S-shape and the S-bend moved back and forth as the voltage was alternately applied between each of the electrodes and the film. The propagation speed was 4.0 m s^{-1} at an applied voltage of 150 V. The microvalve was applicable to molecular beam epitaxy (MBE) apparatus in the order of 1 ml min^{-1} at 0.1 kPa. Goll *et al* [45] presented a microvalve with a flexible three-layer membrane consisting of two insulating layers with a conductive gold layer in between. The 3 μm thick layer was attracted by an electrostatic force toward one of the electrodes in the upper or the lower chamber with a separation of 25 μm, thus opening or closing the inlet of the microvalve. Voltages of 60–150 V enabled the membrane to close the valve. At a differential pressure of 110 kPa, an N_2 gas flow rate of 12 ml min^{-1} was obtained.

A gas modulator that integrated electrostatically actuated microvalves with a micromachined 3 μm thick silicon beam was designed by Robertson and Wise [46]. The gas flow modulator was theoretically capable of delivering a gas flow of 0.87 μl min^{-1} at 0.75 Pa. An estimated response time was less than 0.1 ms with a voltage of 80 V. A normally closed microvalve with a micromachined silicon plate and membrane, regulating pressure ranges between 50 and 1600 kPa with a response time of 1 ms, was realized by Schaible *et al* [47]. A large stroke electrostatic microvalve for high pressure control by a pressure balancing concept was simulated by Wijngaart *et al* [48]. The simulation showed that it was possible to control a 500 kPa air pressure, while ensuring a 15 μm gas flow gap at 366 V, alternatively to control a 100 kPa pressure with a 5 μm flow gap using only 24 V. Yobas *et al* [49, 50] introduced an electrostatic microvalve for the purpose of enabling a pneumatic refreshable Braille display system. The normally open microvalve was electrostatically closed against a differential pressure of 82.7 kPa with an applied voltage of 68 V, between a fixed silicon substrate with an inlet port of 70 μm × 70 μm and 20 deflectable wheel-like beams with a length of 665 μm. Teymoori and Abbaspour-Sani [51] designed and simulated a peristaltic micropump serially connected with electrostatic silicon microvalves for medical applications. In addition, a group from MIT has developed microengines for much higher power and energy densities than other compact power sources [52–54]. The micro gas turbine engine required an integrated fuel-metering device for graded fuel modulation that was achieved with an array of electrostatic on/off microvalves [54]. The microvalve opened against a differential pressure of 900 kPa with 136 V and delivered an N_2 gas flow rate of 45 ml min^{-1} at room temperature. At 170 kPa upstream pressure, the helium leakage rate was measured to be 6 μl min^{-1}.

2.2.2. Electrokinetic. In addition to electrostatically actuated microvalves, electrokinetic actuation principles, which are widely used to move liquids and particles in microchannels, can be applicable to the development of active microvalves. Kirby *et al* [55] showed a voltage addressable electrokinetic microvalve consistent with the pressures and solvents engaged for high pressure liquid chromatography. Mobile plugs

with diameters and lengths close to 60 μm, formed by photopatterning of polymer monoliths inside microchannels, were opened and closed by electrokinetically induced pressures. The microvalves showed a ratio of open/closed flow rates ranging from 10^4 to 10^6 over pressure ranges of 150–7000 kPa with a working fluid of acetonitrile–water (90:10). The pressure–leak relationship showed potential uses for valving of flow through packed or monolithic chromatography columns. The photopatterned polymer monoliths were also used as mobile structures in microchannels for passive in-line microvalves [197, 198].

2.3. Piezoelectric

Piezoelectricity is the ability of certain crystals to produce mechanical stress or stretching with an applied electric field. Piezoelectric actuations are widely used in micropumps, since the piezoelectric effect can generate both extremely big bending force (several MPa) and small displacements (with less than 0.1% strain). There are several commercially available MEMS-based micropumps based on these piezoelectric principles (from thinXXS Microtechnology, Zweibrücken, Germany and Star Micronics, Shizuoka, Japan). Although large force is available using piezoelectric actuators, large stroke is a challenging issue even for large voltages. The drawback of small strokes has been overcome by the hydraulic amplification of the piezoelectric [56–59], stacked piezoelectric discs [60–62] or piezo bimorphs [63–65]. Large strokes with a 40-fold hydraulic amplification with high bulk modulus silicone oil were obtained in [56, 57]. A maximum average flow rate of 12.6 ml min^{-1} for a 1 kHz sinusoidal driving voltage of 500 V with a stroke of 17 μm against a differential pressure of 260 kPa was measured. Rogge *et al* [58] developed a normally closed microvalve for gases and liquids with a 25-fold hydraulic amplification, achieving a valve stroke of 50 μm. The microvalve was able to produce driving voltages of up to 300 V with a response time of 2 ms. The leakage flow rate was 30 μl min^{-1} at a pressure of 200 kPa for N_2 gas and 0.0133 μl min^{-1} at a pressure of 100 kPa for water. Shao *et al* [59] operated a polymer microvalve with a 6 nl dead volume and a switching time of 0.7 ms for exact dosing of small amounts of liquids and gases. The maximum N_2 gas flow rate was 70 ml min^{-1} at a pressure difference of 50 kPa.

Peirs *et al* [60] presented a miniature robotic manipulator with piezoelectric and electromagnetic microvalves for a self-propelling endoscope application. A piezoelectric stack of 1.4 mm × 3 mm × 9 mm generated a maximum stroke of 6 μm and a maximal force of 140 N at 100 V. The leakage flow rate of water was 420 μl min^{-1} at 600 kPa. Chakraborty *et al* [61] reported a 10 mm high laminated piezo stack producing at most 10 μm defection. Yang *et al* [62] developed a leak-tight normally closed piezoelectric microvalve for microspacecraft applications, consisting of a piezoelectric stack actuator (8.4 mm × 5 mm × 6 mm) bonded onto silicon valve components, such as the seat, boss and tether. A static flow rate of 52 ml min^{-1} at 2070 kPa with a voltage of 10 V and a helium gas leakage flow rate of 5 μl min^{-1} at 550 kPa were obtained.

Waibel *et al* [63] developed a fountain pen integrated with a liquid level senor, a microvalve actuated with a piezo bimorph [64, 65] and an ink reservoir filled with capillary forces and hydrostatic pressure differences. The microvalve was fabricated by precision injection molding including a highly elastic membrane resistant against a wide range of mechanical loads. The piezo bending microvalve with a maximum deflection of 80 μm was achieved with a voltage of 140 V. The maximum leakage flow rate of 0.002 μl min^{-1} at 1 kPa was attained.

2.4. Thermal

2.4.1. Bimetallic. The use of thermally actuated microvalves, such as bimetallic [66, 67], thermopneumatic [68–75] and shape memory alloy actuations [76–82], considerably increases the force available from microstructures while simultaneously achieving large strokes. Although drawbacks include relatively slow actuation speed and high power consumption due to temperature changes, thermal actuation schemes are attractive because of the simplicity in microstructures. Jerman [66] developed a bimetallically driven microvalve with an 8 μm thick silicon membrane and a 5 μm thick aluminum layer. The microvalve provided fully proportional control of flows in the range of 0–0.15 l min^{-1} at input pressures between 7 and 350 kPa with a leakage flow rate of 30 μl min^{-1} of N_2 gas at 34.5 kPa. Barth [67] demonstrated a bimetallic microvalve with a 30 μm thick Ni film deposited on a silicon membrane. This Ni/Si bimetallic microvalve opened against 1035 kPa and flowed more than 1 litre min^{-1} of air with a power consumption of 1.03 W in 0.2 s.

2.4.2. Thermopneumatic. Thermopneumatic microvalves are operated by volumetric thermal expansion coupled to membrane deflection. Rich and Wise [68] reported a microvalve featuring a cavity sealed with a volatile fluid below a corrugated membrane. Polysilicon heater grids were 9 μm above the cavity floor, and the cavity was partially filled with pentane to increase thermal efficiency. The microvalve generated a 16 Pa pressure rise with 500 mW, while closing of the membrane was maintained with a 30 mW steady input power. The microvalve generated a flow rate of 400 ml min^{-1} under 11.3 Pa differential pressure and leakage flow rates as low as 1 μl min^{-1}. Ruzzu *et al* [69] presented a catheter tip with an integrated positioning system consisting of a thermopneumatic three-microvalve system to switch three microballoons inside a blood vessel. The microvalve with freely suspended nickel heaters and a deflectable polyimide membrane required a power of 40 mW at 20 kPa to blow up the microballoons.

Takao *et al* [70] presented a thermopneumatic microvalve, employing a PDMS membrane for large stroke and high sealing performance. In addition, the PDMS material was used as an adhesive layer between glass and silicon in the structure. Leakage flow rates of liquids were less than 1 μl min^{-1} at 30 kPa. With an inlet pressure of 20 kPa, the power to close was 200 mW while the power to reopen was 85 mW, showing hysteresis due to sticking of PDMS. Yang *et al* [71, 72] developed a normally open microvalve using a composite membrane and 3M Fluorinert fluids for thermopneumatic actuation as shown in figure 4. The composite membrane comprising silicone rubber and Parylene

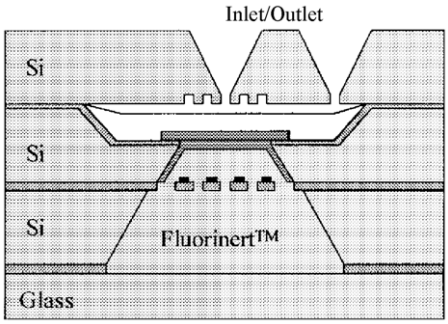

Figure 4. The thermopneumatic valve with composite silicone rubber/Parylene membrane by Yang *et al* [72].

C showed great impermeability for an effective vapor barrier and flexibility for large strokes with a membrane deflection of 134 μm at 28.3 kPa. Less than 40 mW was required to switch an N_2 gas flow rate of 1 litre min^{-1} at 228 kPa and 100 mW for water due to the cooling effect of the liquid.

Baechi *et al* [73, 74] significantly increased in-line microvalve densities up to 600 valves cm^{-2} by thermopneumatic actuation with a thin PDMS membrane and reduced thermal crosstalk by water cooling. The microchannel network system was designed for the manipulation of biological cells or bacteria with a size between 0.1 and 5 μm. The PDMS membrane, an area of 130 μm $\times$ 30 μm and a thickness of 3 μm, was deflected up to 3.5 μm with 240 mW power, closing the microchannels in 150 ms. Flow velocities in a channel of 5 μm depth and 25 μm width were 5.75 mm min^{-1} in an open mode and 0.5 mm min^{-1} in a closed mode. Kim *et al* [75] also fabricated a normally open thermopneumatic in-line microvalve with a deflectable PDMS membrane, an area of 400 μm $\times$ 40 μm. The 70 μm thick membrane was deflected up to about 40 μm with an ITO heating power of 25 mW. The microvalve with a 170 μm thick membrane was switched on/off with an applied power of 200 mW in 20 s for closing and 25 s for opening.

2.4.3. Shape memory alloy. The shape memory effect is an attractive actuation principle for the development of microvalves, since it allows simple and compact structures with high output forces, which are capable of controlling high pressure differences and flows [76, 77]. Kohl *et al* [78–80] developed gas microvalves actuated by microfabricated shape memory alloy (SMA) thin films. The NiTiPd SMA microvalves worked in a normally open mode that allowed the control of pressure differences below 250 kPa corresponding to a gas flow of 360 ml min^{-1} with a stroke of about 20 μm. Power for NiTiCu and NiTi microvalves was 110 mW, and 220 mW for NiTiPd microvalves. The NiTiPd SMA microvalve with high phase transformation temperatures allowed a cooling time of 22 ms at room temperature resulting in a maximum operation frequency of 30 Hz [81].

Reynaerts *et al* [82] reported a pinch-type microvalve using shape memory alloy wires for an implantable drug delivery system. An NiTi SMA wire with a diameter of 120 μm was used to pinch down a silicone rubber tube with an inner diameter of 0.6 mm and an outer diameter of 1 mm, withstanding a pressure up to 200 kPa. The microvalve opened in 0.66 s with a power consumption of 120 mW. Pemble and Towe [83] miniaturized a normally closed pinch-type microvalve employing NiTi shape memory alloy wires with a diameter of 0.15 mm to control flows in silicone tubing. At a differential pressure of 20.7 kPa the microvalve permitted a maximum flow rate of about 16.8 ml min^{-1} with a power consumption of 398 mW. The maximum withstanding pressure was 207 kPa with an opening time of 1 s and a closing time of 2.5 s. By locally compressing a flexible PDMS membrane, fluid flows were blocked in a manner analogous to the pinch-type valves [84]. The normally closed microvalves were an array of cantilevers operated by shape memory alloy wires, producing 2.35 N with a displacement of 406 μm.

2.5. Bistable

A drawback of typical active microvalves is that continuous power has to be applied to keep the microvalves open in normally closed microvalves or closed in normally open microvalves. This problem can be solved by bistable actuations that require power only in a transient mode between two stable positions. Bistable microvalves using thermal buckling of membranes have been reported [85–88]. Goll *et al* [88] presented a microvalve with a bistable polyimide membrane. The microvalve was closed tight against an inlet gas pressure of up to 47 kPa. Buckling of the membrane with a compressive stress was induced by thermal treatment and mechanical loading. Because of the bistability of the microvalve, only a short pressure rise and a short pressure drop were obtained by controlling an electric current through a resistive heater in the actuator chamber. The short pressure rise to close the valve was generated by quickly heating the air in the actuator chamber.

Ren and Gerhard [89] fabricated a bistable magnetic actuator, consisting of an in-plane magnetic conductor with two pole pieces, a flux-conducting cantilever, trip coils and a permanent magnet. By means of a current pulse in the trip coils, the cantilever was excited and switched from one stable position to the other. A current pulse of 1.25 A with a duration of 0.3 ms on the 60-turn coil was needed to produce a switching distance of 100 μm with a closing force of 5 mN. Bohm *et al* [90] designed a bistable electromagnetic microvalve as shown in figure 5. The microvalve incorporated a NeFeB permanent magnet, an 800-turn solenoid coil with a soft magnetic circuit and a spring-biased armature to achieve bistable actuation with a large stroke of 200 μm. When a positive current was applied to the coil, the holding force of the armature with the magnet was reduced and hence the spring force pushed the armature downward and closed the microvalve. A negative current pulse could open the valve. A bistable microvalve with the combination of forces generated from coil-to-coil and magnet-to-coil was presented by Capanu *et al* [91].

In addition, combination of the actuation mechanisms, such as pneumatic–electrostatic or electromagnetic–electrostatic, enables bistable active microvalves. Wagner *et al* [92] suggested a bistable electrostatic microvalve with pneumatic coupling. A lower active chip of the valve contained two silicon membranes which were buckling due to intrinsic compressive stress. The cavities below the membranes were air-sealed in order to operate in

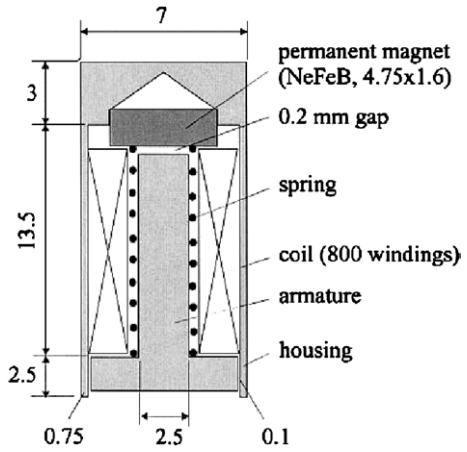

Figure 5. The bistable electromagnetic microvalve with an integrated magnet, a spring and a solenoid coil by Bohm *et al* [90].

counteraction. Each membrane was electrostatically switched down using an underlying driving electrode. By switching one membrane down the sealed air pushed the second membrane up. Bosh *et al* [93] combined electromagnetic and electrostatic actuations in a bistable silicon microvalve for gas flow regulation. A membrane part with an integrated planar coil, which was bonded to another part to locate the flow channel beneath the membrane and defined as an electrode, was placed between permanent magnets. A current pulse of 200 mA was applied to provide an impulsive magnetic force to the membrane; while an electrostatic voltage of 30 V dc was required to keep the valve in a closed mode. The valve could be operated against a static gas pressure of 16 kPa and flow rates up to 3 ml min^{-1}.

3. Active microvalves—non-mechanical

In this section, selected examples of active microvalves with non-mechanical moving parts will be discussed. The examples include actuation principles based on electrochemical [94–98], phase change [99–123] and rheological materials [124–129]. Phase change actuation mechanisms such as hydrogel [99–112], sol–gel [113, 114], paraffin [115–122] and ice [123] will be described. In addition, electro-rheological materials [124] or ferrofluids [127–129] can be used for the non-mechanical active microvalves (table 3). These phase change microvalves are relatively new and cheap compared to the traditional mechanical active microvalves. These non-mechanical active microvalves are of particular interest in terms of their simple device structure and disposability, making them well suited for applications in life sciences.

3.1. Electrochemical

An electrochemical valving concept with a deflectable membrane due to oxygen gas generation by electrolysis was suggested by Neagu *et al* [94, 95]. When the microvalve was driven at 1.6 V and 50 μA, a pressure of 200 kPa could be obtained within seconds, causing membrane deflections in the ranges of 30 to 70 μm. Electrochemically (or sometimes thermally) generated bubbles in a capillary microchannel, by using its geometries or surface properties, can be used as an actuation force in active check valves [96–98]. Suzuki and Yoneyama [96] constructed a microfluidic system consisting of an on-chip micropump and an active check valve by means of a hydrogen bubble generated electrochemically. The growth and shrinkage of the bubble were controlled by working electrode potentials. The critical pressure was smaller than the 3 kPa normally required in other types of valves. With its sequential opening and closing the valve controlled the flow passages of two different solutions in the microchannel in the order of several seconds. Hua *et al* [97] built an eight-way multiplexer with valves generating electrochemical bubbles inside the channel. Whereas bubble inflation rates increased with applied voltages, small microfluidic dimensions accelerated bubble deflation rates.

3.2. Phase change

3.2.1. Hydrogel microvalves. Stimuli-responsive or smart hydrogel is able to change its volume reversibly and reproducibly by more than one order of magnitude even with very small alterations of certain environmental parameters [99]. The volume change of smart hydrogels can be induced in response to a variety of inputs, such as pH [100–103], glucose [103] temperature [104–106], electric field [108, 109], light [110], carbohydrate [111] and antigen [112].

Beebe *et al* [100] presented a hydrogel-based microvalve concept for autonomous flow control inside microfluidic channels corresponding to different pH values. The hydrogel components were fabricated inside the microchannels using a liquid phase *in situ* photopolymerization process. A 3D hybrid microvalve that coupled a flexible PDMS membrane to the hydrogel actuator was designed [101]. The hydrogel actuator expanded as the pH 11 solution was flowing in the upper channel. The membrane deformed and completely blocked the orifice with a displacement of up to 185 μm. A maximum differential pressure of 184 kPa was recorded if the lower channel height was 75 μm. The shut off time response of the 3D hybrid valve was 19 s.

Since the response time using hydrogels is relatively slow, hydrogel microvalves are appropriate for drug delivery applications. Eddington and Beebe [102] reported a microdispensing device using an array of pH-responsive hydrogels to deform a flexible membrane above a fluid reservoir chamber as shown in figure 6. When the microvalve was open, the deformation of the membrane reduced the volume of the reservoir chamber and pushed fluids through the microvalve at an average flow rate of 2 μl min^{-1}. When the microvalve was closed, the expanding hydrogel array generated a storable pressure source of up to 35 kPa that resulted in fluid dispensing at an average flow rate of 540 μl min^{-1} once the microvalve was opened. Baldi *et al* [103] made a microvalve consisting of a hydrogel disc sandwiched between a stiff porous membrane and a flexible silicone rubber membrane. The swelling of the hydrogel that was produced by diffusion of chemical species through the porous membrane resulted in the deflection of the silicone membrane and closure of the valve inlet orifice. The microvalve was based on a phenylboronic acid hydrogel responding to changes in glucose concentration and pH.

Table 3. Phase change microvalves.

Reference	Type	Reversible/ irreversible	Phase change material	Valving channel	Mode	Fluid	Time	Pressure (kPa)	Power	External system
Liu *et al* [101]	Hydrogel (2D)	Reversible	pH sensitive hydrogel	In-line PDMS	NO	pH buffers	12 s	390		pH buffers (pH 3, pH 11)
Liu *et al* [101]	Hydrogel (3D)	Reversible	pH sensitive hydrogel	In-line PDMS	NO	pH buffers	19 s	184		pH buffers (pH 3, pH 11)
Baldi *et al* [103]	Hydrogel	Reversible	Glucose sensitive hydrogel	PDMS membrane with a Si bump	NO	Glucose	32 min (O) 18 min (C)			Glucose buffers
Baldi *et al* [103]	Hydrogel	Reversible	pH sensitive hydrogel	PDMS membrane with a Si bump	NO	pH buffers	7 min (O) 13 min (C)	5.9 5.9		pH buffers (pH 7.4)
Richter *et al* [105]	Hydrogel	Reversible	Temperature sensitive hydrogel ($T_c = 34$ °C, swelling at $T < T_c$)	In-line Si	NC	Methanol	0.3 s (O) 2 s (C)	840	0.2 W	
Yu *et al* [106]	Hydrogel	Reversible	Temperature sensitive hydrogel ($T_c = 32$ °C, swelling at $T < T_c$)	In-line glass	NC	Water	3.5 s (O) 5 s (C)	1380		Thermoelectric cooler
Liu *et al* [113]	Sol–gel	Irreversible	Pluronics sol–gel ($T_c = 5$ °C, liquid at $T < T_c$)	In-line PC	NC	PCR mixture		138		Thermoelectric cooler
Tashiro *et al* [114]	Sol–gel	Reversible	Methylcellulose sol–gel ($T_c = 55$ °C, liquid at $T < T_c$)	In-line glass/Si	NO	Methyl-cellulose	1 s		2 W	IR laser
Carlen and Mastrangelo [115]	Paraffin	Reversible	Logitech bonding wax ($T_m = 72$ °C, volume expansion)	Parylene membrane	NO	Gas			0.05–0.15 W	
Selvaganapathy *et al* [116]	Paraffin	Reversible	Logitech bonding wax ($T_m = 72$ °C, volume expansion)	Parylene membrane	NO	DI	15 ms	160	0.04 W	
Klintberg *et al* [119]	Paraffin	Reversible	Paraffin ($T_m = 45$ °C, volume expansion)	Corrugated silicon membrane	NO	Gas				
Pal *et al* [120]	Paraffin	Reversible	M1595 wax ($T_m = 85$ °C, phase change)	In-line glass/Si	B	PCR mixture	2 s	1725	0.015 W	Pneumatic air/ vacuum
Liu *et al* [121, 122]	Paraffin	Irreversible	Paraffin ($T_m = 70$ °C, phase change)	In-line PC	B	PCR mixture	10 s	275		
Gui *et al* [123]	Ice	Reversible	Water (phase change)	In-line	NO	Water	15 s (C)		5 A	Thermoelectric cooler
Yoshida *et al* [124]	Electro-rheological	Reversible	ER fluids (viscosity change)	In-line	NO	ER	0.2 s	60% of supply pressure	4 kV mm^{-1}	
Hartshorne *et al* [127, 128]	Ferrofluid	Reversible	Ferrofluids (600 cP)	In-line	NO	DI	15–30 s	12		Permanent magnet
Oh *et al* [129]	Ferro-wax	Reversible	Paraffin-based ferrofluids ($T_m = 68 \sim 74$ °C, phase change)	In-line	B	DI	3 s	345		Permanent magnet

NC, normally closed microvalve; NO, normally open microvalve; B, bistable; ER, electro-rheological material; DI, deionized water; O, opening; C, closing.

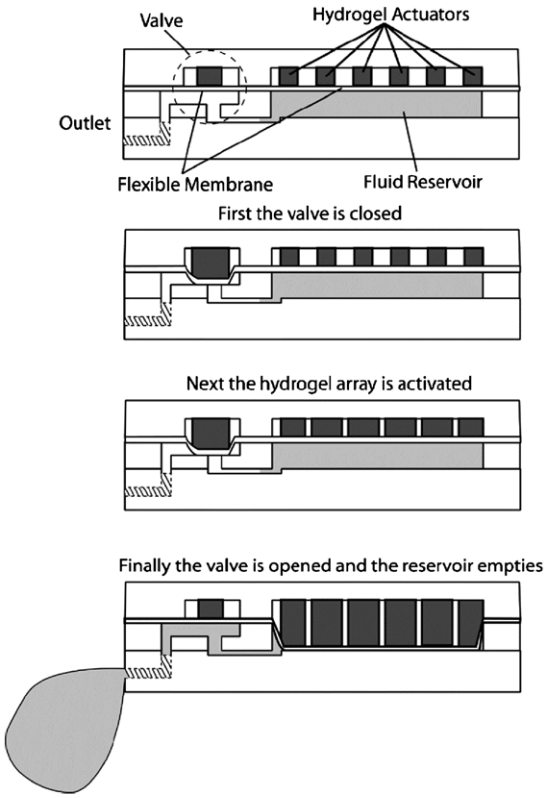

Figure 6. The microdispensing device with pH-sensitive hydrogel microvalves by Eddington and Beebe [102].

However, the response time was comparatively slow, with the most rapid time response achieved being 7 min, using a 30 μm thick hydrogel and a 60 μm porous membrane.

Richter *et al* [104, 105] reported a normally closed in-line microvalve based on temperature sensitive hydrogels. The hydrogel actuators were directly placed in a flow channel by a photopolymerization process. The phase transition temperature of the hydrogel was 34 °C. The switching time of the electronically controllable microvalves was 0.3 s for opening and 2 s for shut off. Also, Yu *et al* [106] fabricated monolithic gel plugs with a phase change temperature of 32 °C by photopolymerization within the channel of the microvalve. The time required to open and close the valve was 3.5 and 5.0 s, respectively. And the normally closed microvalve at 17 °C resisted pressures of up to 1380 kPa.

3.2.2. Sol–gel microvalves. Pluronics sol–gel phase change valves for micro PCR were demonstrated by Liu *et al* [113]. The Pluronics sol–gel material was PCR compatible, and 30% Pluronics polymer valves provided enough holding pressure of up to 138 kPa to ensure a successful PCR amplification. The sol–gel polymer formed self-supporting cubic liquid crystalline gels at room temperature. By reducing the temperature to 5 °C by a Peltier TE cooler device, Pluronics valves were liquefied and opened. Tashiro *et al* [114] fabricated a microfluidic gel valve using a reversible sol–gel transition. The methyl cellulose solution was injected into a microchannel and locally hardened at a specific part of the microchannel by an IR laser. The microfluidic valve operation for cell sorting was demonstrated by irradiating the IR laser on both outlet channels of a Y-branch-type microchannel. The switching time was 1 s in both open-to-closed and closed-to-open states.

3.2.3. Paraffin microvalves. Using paraffin materials has been attractive due to the phase change nature of the material. The phase change material can be used either as a propellant for a membrane or as a meltable plug. Since the volume expansion associated with the solid-to-liquid phase transition of paraffin is 10–30%, the propellant scheme can be incorporated for the deflection of the membrane. Mastrangelo's group realized the propellant scheme in a normally open microvalve for gas regulation [115] and an in-line microvalve for liquid regulation [116]. The microvalves having a flexible Parylene membrane or microchannel were fabricated using a surface micromachining process. The in-line microvalve was completely closed with a power of 40 mW and a response time of 15 ms and the microvalve was resistible up to 160 kPa. Also, Klintberg *et al* [117–119] fabricated paraffin-actuated membranes in a ring-shaped silicon cavity, a polycarbonate structure and a corrugated silicon caddy suspended in springs for valve applications. The stroke of 15 μm on each side of the corrugated caddy was attained by the volume expansion of paraffin.

Two groups reported thermally actuated paraffin microvalves as the meltable plug in microchannels: a reversible microvalve with external pneumatic air/vacuum systems [120] and an irreversible microvalve without external pneumatic air/vacuum systems [121, 122]. The plug changed phase from solid to liquid by thermal heating and moved in the microchannel by the pressures from the upstream liquid flow (figure 7(*a*)) or the external pneumatic air/vacuum systems (figure 7(*b*)). The paraffin plug is essentially leakproof because of the phase change nature of the material; once the plug is solidified, it forms a solid seal. For the reversible microvalve no leakage flows were detected over a period of 15 min up to 1725 kPa. For the irreversible microvalve the maximum hold-up pressure was about 275 kPa. The time response (2–10 s) of the paraffin-based microvalves was relatively slow compared to that of many active microvalves (∼ms), as shown in figure 8. However, it is believed that the paraffin-based microvalves are practical and useful in some applications where rapid valving time is not critical, such as micro PCR devices.

3.3. Rheological

3.3.1. Electro-rheological (ER). Electro-rheological (ER) fluids whose viscosity was controlled by electric fields were used for the regulation of ER fluids by Yoshida *et al* [124]. Miniaturized ER valves were realized by using micromachining technologies. A static viscosity change rate of 4.5 was achieved with an electric field strength of 5.0 kV mm^{-1}. The controllable pressure change rate was 0 to 60% of supply pressure depending on the electric field strengths and the response time was 0.2 s. Since the ER fluids are used as working fluids in the microchannel, it may not have wide applications where carrier fluids are not ER fluids.

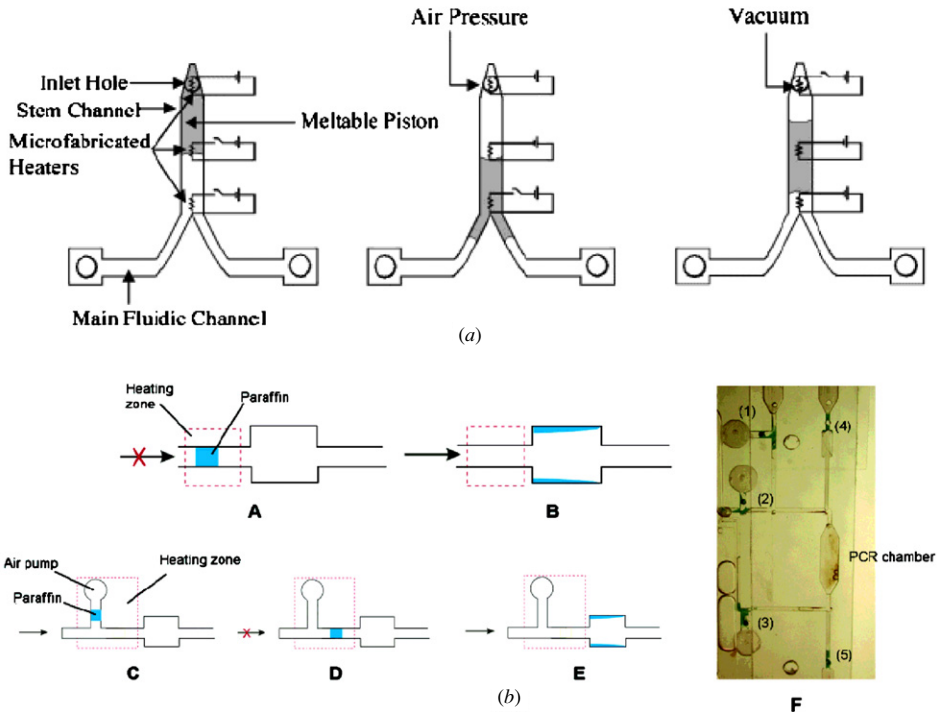

Figure 7. (*a*) The reversible microvalve with external pneumatic air/vacuum systems by Pal *et al* [120] and (*b*) the irreversible microvalve without external pneumatic air/vacuum systems by Liu *et al* [121, 122].

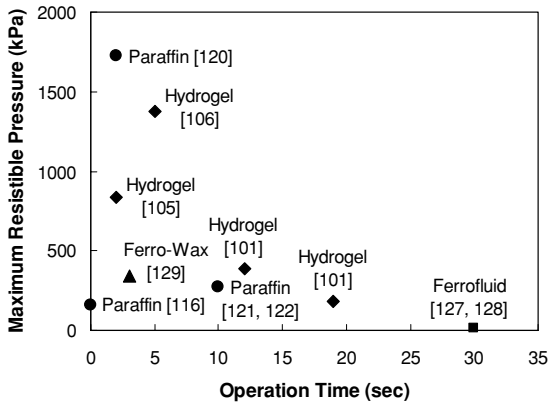

Figure 8. Graph of operation times versus maximum resistible pressures for selected non-mechanical active microvalves.

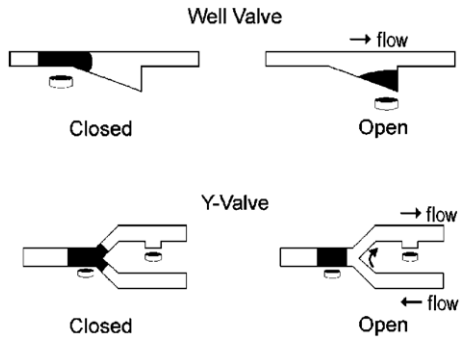

Figure 9. The ferrofluid-based well valve and Y-valve designs in closed and open configurations by Hartshorne *et al* [127, 128].

3.3.2. Ferrofluids. Ferrofluids are magnetic liquids created by suspending ferromagnetic particles of 10 nm in a carrier fluid. Carrier fluids can be water, diesters, hydrocarbons or fluorocarbons and favor many different applications. Ferrofluids conform to the channel shape, potentially providing very good seals, and respond to external localized magnetic forces, providing easy actuation. The use of ferrofluids as micropumps [125–127] and microvalves [127, 128] was suggested. The devices by Hartshorne *et al* [127, 128] contained ferrofluid plugs of 10 mm in length that were actuated by external magnets as shown in figure 9. The ferrofluid used in the devices was a colloidal suspension of ferromagnetic particles in a hydrophobic fluorocarbon carrier and was immiscible in water. With air in the channels, the well valve withstood pressures of up to 12 kPa and was opened and closed against pressures of 8.5 and 5.0 kPa, respectively, under a magnetic field of 2.8 kG. In untreated glass channels, leakage of water around ferrofluid seals was significant. However, when the channel wall was coated with a hydrophobic organosilane, leakage flows were not detectable. The typical transition time for valve opening or closing was 15–30 s.

4. Active microvalves—external

In this section, previous work on active microvalves using external systems will be discussed. The selected examples include modular built-in valves [130–133] and rotational valves [134–136]. Thin membrane [137–152] or in-line [153–159] microvalves actuated by external pneumatic air pressure or vacuum will also be described (table 4). Using external systems is one of the most practical approaches

Table 4. Pneumatic microvalves.

Reference	Type	Material	Mode	Applications	Thickness (μm)	Dead volume (nl)	Pneumatic pressure (kPa)	Vacuum pressure (kPa)	Resistible pressure (kPa)
Takao *et al* [139]	Membrane	Si	NC or NO	Pressure amplification	10		–80 to + 80		
Mathies' group [142–144]	Membrane	Latex	NO	PCR	150	50	69–83	4	
Mathies' group [145, 146]	Membrane	PDMS	NC or NO	PCR	254	8	40	80	
Go and Shoji [148]	Membrane	PDMS	NO	On/off switching		0 (zero)	10		
Kanai *et al* [149]	Membrane	PDMS	NO	On/off switching	30	0.05	20		
Lee *et al* [150]	Membrane	PDMS	NO	On/off switching	200				
Baek *et al* [151]	Membrane	PDMS	NO	On/off switching	200				
Hosokawa and Maeda [152]	Membrane	PDMS	NC	On/off switching	25	6.3		60	10
Taylor *et al* [153]	Membrane	Silicone	NO	On/off switching			138		
Yuen *et al* [154]	Membrane	3M tape	NC or NO	On/off switching		160		By manual screwing	690
Quake's group [155, 156]	In-line	PDMS	NO	On/off switching	10		60		
Studer *et al* [158]	In-line	PDMS	NO	On/off switching			100		
Wheeler *et al* [159]	In-line	PDMS	NO	On/off switching			140		
Wang *et al* [161]	In-line	PDMS	NO	On/off switching		0.1	200–550		
Rolland *et al* [167]	In-line	PFPEs	NO	On/off switching			170		

NC, normally closed; NO, normally open.

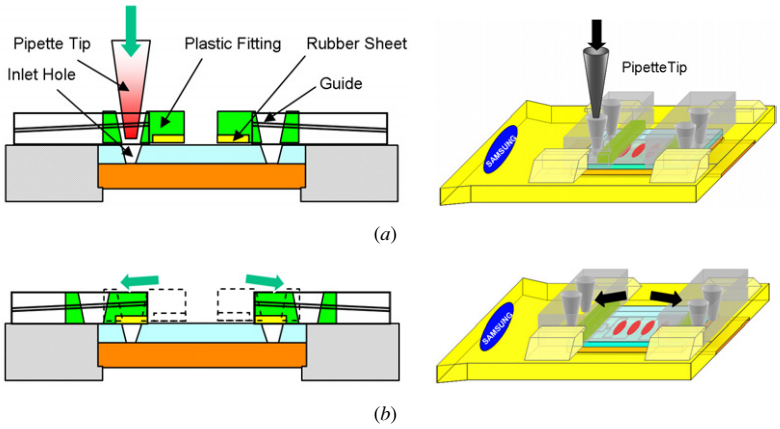

Figure 10. The world-to-chip microfluidic interfacing method with modular built-in valves by Oh *et al* [130, 131]: schematic views of (*a*) the sample loading mode and (*b*) the valving mode.

in designing microvalves. This actuation is advantageous with no leakage flows at high input pressures, even though miniaturization may be difficult due to the requirement of additional external systems.

4.1. Modular

4.1.1. Built-in microvalves. Oh *et al* [130, 131] designed a world-to-chip microfluidic interfacing method with modular built-in valves, which provided no dead volume, no leakage flow and biochemical compatibility as shown in figure 10. This world-to-chip microfluidic valving system performed excellently in both sample loading and reagent sealing, as evidenced in successfully performing real-time multiple PCR assays. Valving of the inlet, outlet or vent ports is a critical function to successfully carry out PCR. The valves underwent an internal pressure of 47 kPa generated all through thermal cycling and were reopened easily after PCR. Another modular built-in valve for microfluidic interconnections was developed by Yang and Maeda [132, 133]. The module was designed specifically for electrophoresis, so both electronic and microfluidic interconnects were incorporated. Up to ten parallel silicone tubes were used to connect the inlets and outlets of a microfluidic chip. A screw over each silicone tube worked as a valve, where a ball was inserted to prevent the screw from damaging the silicone tube. These modular built-in valves made it possible to control the fluidic flows in each channel independently up to 200 kPa.

4.1.2. Rotary microvalves. A rotary ten-way switching microvalve with auto positioning of outlets was developed by Hasegawa *et al* [134]. To prevent the leakage flows between a rotor and a manifold housing, a silicone rubber ring was integrated into the manifold. The modular structures were fabricated by a 3D micro stereo lithography process. The microvalve successfully switched ten outlets from one inlet without dead volume at pressures up to 700 kPa. In addition, Cepheid's GeneXpert® system, a real-time PCR instrument with a sample preparation process, included a microfluidic modular cartridge with a random access rotational valve. The cartridge with the modular rotational valve was designed to enable fluid transfer from chamber to chamber as shown in figure 11 [135, 136]. Furthermore, the cartridge contained up to 11 separate reagent chambers, a waste chamber, a syringe drive and a PCR reaction tube.

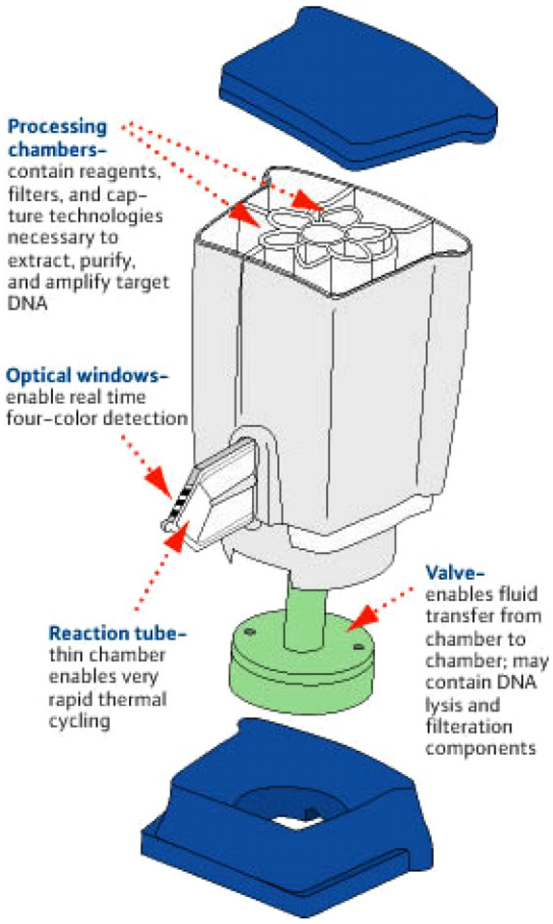

Figure 11. The GeneXpert® cartridge with a rotary valve for sample preparation and real-time PCR by Cepheid [135, 136].

4.2. Pneumatic

4.2.1. Membrane microvalve. Membrane-type microvalves were made of micromachined silicon membranes [137–141],

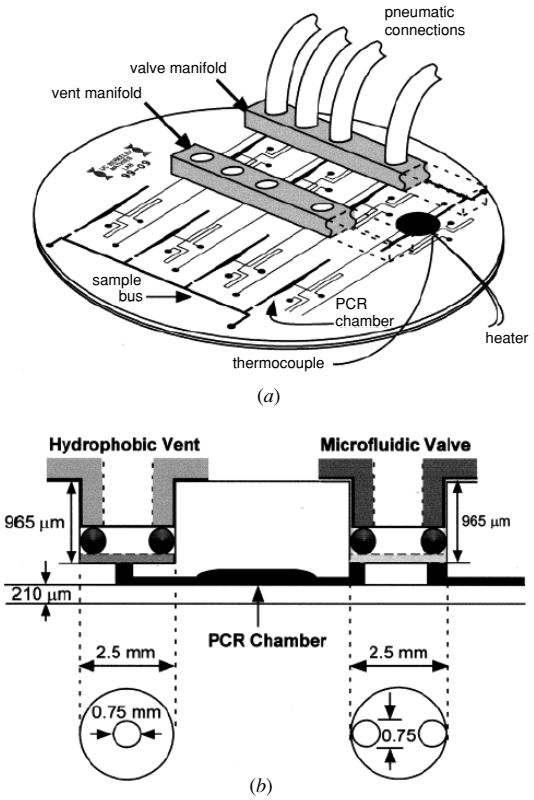

Figure 12. The microfluidic PCR-CE device (*a*) with pneumatically actuated membrane microvalves (*b*) by Lagally *et al* [143].

thin latex sheets [142–144], spin-coated PDMS layers [145–152], thin silicone rubber sheets [153] or thin 3M tape sheets [154]. A pneumatically actuated silicon microvalve applicable to functional microfluidic integrated circuits was presented by Takao *et al* [137–139]. The microvalve worked as a transistor-like device by means of external pneumatic air pressures. A silicon membrane worked as the gate controlled by pneumatic pressure, while an inlet served as the source and an outlet as the drain. A pressure amplifier was also fabricated as an example of the microfluidic-integrated circuits using an analogous relationship with MOSFET and the pneumatic microvalve. A maximum pressure gain of 40 (32.0 dB) was obtained in the pressure amplifier.

Mathies' group focused on practical pneumatic microvalves with latex membranes [142–144] or PDMS membranes [145, 146] for fully integrated PCR-CE microsystems as shown in figure 12. Two aluminum manifolds for hydrophobic vents and latex membrane valves were placed onto ports and clamped in place using vacuum. The manifolds were connected to external solenoid valves for pneumatic air pressure and vacuum actuation. Samples were loaded from an inlet port by opening the valve using vacuum (4 kPa) and pressing the samples underneath the 150 μm thick latex membrane using pressure (69–83 kPa). Vacuum was simultaneously applied to a hydrophobic vent to evacuate the air from the chamber. The sample stopped at the vent, and the valve was pressure-sealed to enclose the sample. While the latex membrane microvalve had large 50 nl dead volume per 280 nl microchamber, the PDMS membrane microvalves had as small as 8 nl dead volume, and three valves in series formed versatile membrane pumps [145, 146].

In-plane PDMS membrane microvalves have been reported from several groups [145–153]. A three-way microvalve for whole blood handling was developed by Ohori *et al* [147]. The microvalve had the advantages of easy assembly, large on/off flow ratio (about 10^4), no bubble problem and low cost due to the partly disposable structure. A 3D hemisphere PDMS microvalve without dead volume and leakage flow was presented by Go and Shoji [148]. A closing time of 0.1 s and an opening time of 0.5 s were obtained by applying a pneumatic pressure of 10 kPa to the PDMS membrane. Even though a faster response for closing was possible, it took a longer time to release the membrane for opening. Kanai *et al* [149] realized a microchamber with a PDMS membrane for biological cell culture of rat mast cells. The device had negligible sample dead volume of less than 0.05 nl. The 30 μm thick PDMS membrane was closed by applying a pneumatic actuation pressure of 20 kPa. Pneumatically actuated microvalves using thick centered PDMS membranes (200 μm) were reported [150, 151]. Lee *et al*'s microinjection device was fabricated by fusing a glass microneedle and the PDMS-based microvalve [150]. Baek *et al*'s device employed pneumatic or magnetic actuation for general valving structures [151]. In addition to the normally open microvalves, a normally closed three-way microvalve composed of three independent one-way valve units was presented by Hosokawa and Maeda [152]. Each valve unit had a 25 μm thick PDMS membrane actuated by negative pressure. No detectable leakage flows were observed up to 10 kPa in the normally closed state. To open the membrane valve a negative pressure of 60 kPa was applied by an external vacuum pump.

Taylor *et al* [153] assembled microfluidic cassettes performing integrated biological sample preparation and DNA analysis from whole blood. Pneumatically actuated membrane pumps and valves were employed to achieve precise microfluidic manipulation and enabled the execution of several sample processing steps within a single cassette. The membrane was a commercially available thin 40 durometer silicone rubber film operated by an air pressure of 138 kPa. A CNC machined Plexiglas microvalve system with flexible 3M tape membranes was shown by Yuen *et al* [154]. The valve, designed for human cell isolation and DNA amplification systems, could process human whole blood with minimal dead volume of less than 0.16 μl and maximum sealing pressure up to 690 kPa.

4.2.2. In-line microvalves. Quake's group reported a series of microfluidic systems using a multilayer soft lithography process [155–157, 162–165]. A building block in the microfluidic systems was a pneumatically actuated in-line microvalve as shown in figure 13. It consisted of a pneumatic channel that could be deformed under pressure to pinch off the flow of fluids in an in-line microchannel. Two layers formed by the PDMS rapid prototyping method were bonded together in a crossed architecture [155, 156]. The bonded structure was sealed onto the top of a glass substrate. When pressurized gas was applied to the upper pneumatic channels, the rubber deflected at the intersection of the in-line microchannels at the

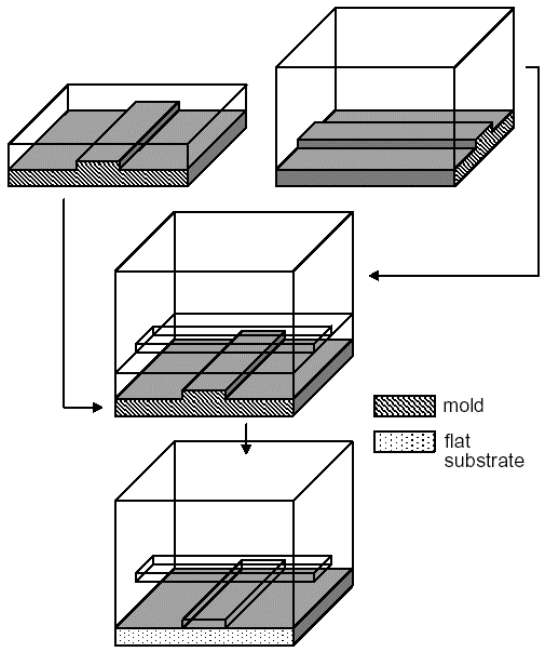

Figure 13. The pneumatically actuated in-line microvalve using PDMS rapid prototyping by Quake's group [155].

bottom layer. Typical channels were 100 μm wide and 10 μm high, giving the valve an active area of 100 μm $\times$ 100 μm. The valve was closed with a pneumatic pressure of 60 kPa within several milliseconds, and back to its initial opening position by its own restoring spring force (40 kPa) [155].

The concept of these pneumatically actuated in-line microvalves was utilized for various biochemical micro total analysis systems, such as single cell sorting [157–159], enzymatic assays [160, 161] and polymerase chain reactions [162–164], due to easy manipulation of nanoliter volumes in the in-line microchannels. Large-scale integration (LSI) in microfluidic systems analogous to LSI in electronic integrated circuits was realized by building up each in-line microvalve [165]. As an example of the microfluidic LSI, a 20 $\times$ 20 microfluidic channel matrix to perform 400 PCR reactions was demonstrated [164]. A single input of 2 nl aliquot of polymerase was connected to 400 independent reactors (3 nl). In total, 2860 in-line microvalves were controlled by only two independent pneumatic pressure supplies. Furthermore, the large valves or the small valves were selectively actuated because they had different thresholds of hydraulic pressure necessary for actuation. The microfluidic LSI provided a general method to perform chemical and biological experiments with precious reagents in a highly automated fashion.

Despite the advantages of PDMS rapid prototyping for microfluidics technology, this material suffers from a serious drawback in that it swells in most organic solvents [166]. The swelling of PDMS-based devices makes it impossible for organic solvents to flow inside the microchannels. To overcome this problem, Rolland *et al* [167] replaced PDMS materials with photocurable perfluoropolyethers (PFPEs), which are liquid at room temperature and chemically resistant like Teflon. An in-line microvalve based on photocurable PFPEs was formed by the similar rapid prototyping method in the crossed architecture. The microvalve was actuated pneumatically by introducing pressurized air at 170 kPa.

5. Passive microvalves—mechanical

In this section, selected examples of passive microvalves with mechanical moving parts will be briefly reviewed. Most passive microvalves, or check valves, are incorporated in inlets and outlets of reciprocal displacement micropumps as mechanical moving parts, such as flaps [168–180], membranes [181–192], spherical balls [194–197] or mobile structures [198–200] (table 5). Passive valves only open to forward pressure, showing diode-like characteristics. The one-way behavior of these check valves significantly affects the pumping performance of a reciprocal displacement micropump. Leakage in the check valves reduces backpressure and pumping rate in the micropump.

5.1. Flap

Cantilever-type flaps were made of thin layers of silicon [168–177], metals [178–180] or polymers [181]. Zengerle *et al* [168, 169] developed a bidirectional electrostatic silicon micropump by actuating higher frequencies (2–6 kHz) than the resonance frequency (1–2 kHz) of a 5 μm thick silicon flap. Xu *et al* [170] reported 12 μm thick silicon flaps for an SMA micropump. Yang *et al* [171] fabricated a pair of bivalvular silicon microvalves by using the p+ etch-stop method. Each valve had two 2 μm thick flexible p+ silicon wings with a slit width of 25 μm. Water flow rates of 1600 μl min^{-1} at 4 kPa of forward pressure and 50 μl min^{-1} at 4 kPa of backward pressure were obtained. Various static and dynamic simulations have been performed for cantilever-type silicon flaps [172–176]. Oosterbroek *et al* [177] reported a new method to fabricate duckbill-like flap microvalves with thin {1 1 1} crystallographic planes on a ⟨1 0 0⟩ silicon wafer by an anisotropic wet etching techniques. The duckbill check valves with dimensions of 1 mm long, 5 μm thick and 300 μm high showed a forward-to-backward flow ratio of about 4.6 at 30 kPa.

A pair of 2 μm thick cantilever-type aluminum flaps for a phase-change type micropump demonstrated a forward flow rate of 470 μl min^{-1} at 1 kPa [178]. In contrast, the backward flow rate was 39 μl min^{-1} at 1 kPa. The backward leakage flow rate of the flap valves was less than one-tenth of the forward flow rate, which was too small to affect the magnitude of the net pumping flow rate. An electroplated 2.2/0.3 μm thick Cu/Ni flap was used in a surface tension driven micropump [179]. The static leakage flow rate of the valve in reverse pressures was observed to be about 4 μl min^{-1} at the lower pressures. However, the valve closed completely when the reverse pressure was above 0.3 kPa. Paul and Terhaar [180] fabricated two laminated metal flaps, a hinged flap valve and a bridged floating disk valve each with a thickness of 125 μm and a diameter of 2.2 mm inside 3 mm holes. Average diodicity defined as the ratio of forward to backward flow rates was 1.7 for the flap valve and 12.8 for the float valve between 20 Pa and 11 kPa. Feng and Kim [181] fabricated a cantilever-type

Table 5. Passive check microvalves with mechanical moving parts, such as flaps, membranes or balls.

Reference	Type	Actuator	Material	Fluid	No. of beams	Valve size (μm)	Orifice size (μm)	Forward flow		Reverse flow	
								Flow rate (μl min^{-1})	Applied pressure (kPa)	Flow rate (μl min^{-1})	Applied pressure (kPa)
Zengerle *et al* [168, 169]	Flap (cantilever)	ES	Si		1	1700 × 1000 × 5	400 × 400				
Xu *et al* [170]	Flap (cantilever)	SMA	Si		1	3300 × 1200 × 12	700 × 2500				
Yang *et al* [171]	Flap (bivalvular)	None	Si	DI	1	780 × 1580 × 2	25 × 1580	1600	4	50	4
Oosterbroek *et al* [177]	Flap (duckbill-like)	None	Si	L		1000 × 300 × 5		192	30	42	30
Sim *et al* [178]	Flap (cantilever)	TP	Al	DI	1	1300 × 1000 × 2	350 × 350	470	1	39	1
Yun *et al* [179]	Flap (cantilever)	C	Cu/Ni	DI	1	660 × 310 × 2.2/0.3	180 × 180	800	0.7	4	0.3
Paul and Terhaar [180]	Flap (hinged)	None	Laminated metal	G	1	⌀2200 × 150	⌀1500		Diodicity: 1.7		
Paul and Terhaar [180]	Flap (bridged floating)	None	Laminated metal	G	2	⌀2200 × 150	⌀1500		Diodicity: 12.8		
Feng and Kim [181]	Flap (cantilever)	PE	Parylene		1	3					
Li *et al* [182]	Membrane (bridge)	PE	Ni	DI	4	300 × 300 × 10	⌀200	1080 000	345		
Bien *et al* [183]	Membrane (bridge)	None	P-Si	M	4	400 × 400 × 2.5	100 × 100	2500	11	85	11
Hu *et al* [184]	Membrane (bridge)	PE	Si (SOI)	DI	3	960 (hexagon) × 50	900 (hexagon)	35 600	65.5	0.01	600
Feng and Kim [181]	Membrane (bridge)	PE	Parylene		4	4					
Chung *et al* [185]	Membrane (bridge)	None	Parylene		4	⌀1200 × 6					
Nguyen *et al* [186–188]	Membrane (bridge)	PE	SU-8	DI	4	⌀1000 × 100		2500	3	1200	3
Wego *et al* [189, 190]	Membrane (hole)	TP	Kapton			⌀5000 × 7.8			Forward resistance: 950 kPa min μl^{-1}		
Bohm *et al* [191]	Membrane (hole)	PE or EM	Mylar			⌀2500 × 7	⌀200	2000	2.5		
Santra *et al* [192]	Membrane (hole)	EM	Silicone			⌀4700 × 100	⌀200		Forward resistance: 0.0475 kPa min μl^{-1}		
Jensen and Gravesen [193]	Membrane (bump)	None	Si			11 000 × 11 000 × 50	1500 × 1500	200 000	70		
Carrozza *et al* [195, 196]	Ball	PE			0	⌀1200	⌀500				
Yamahata *et al* [197]	Ball	EM		G	0	⌀700		20 000	10	1000	40
Pan *et al* [198]	Ball	EM		DI	0	⌀800	⌀560			<1	5–30

EM, electromagnetic; ES, electrostatic; PE, piezoelectric; TP, thermopneumatic; SMA, shape memory alloy; C, capillary driven; G, gas; L, liquid; DI, deionized water; M, methanol; O, opening; C, closing; PI, polyimide; P-Si, poly-silicon; SOI, silicon-on-insulator; Diodicity, the ratio of forward flow to backward flow.

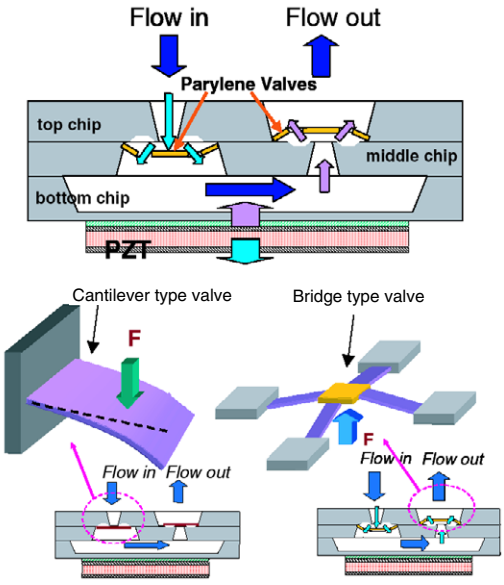

Figure 14. The parylene cantilever-type flap and bridge-type membrane valves for a piezoelectric micropump by Feng and Kim [181].

3 μm thick Parylene flap valve with a fundamental resonant frequency of around 500 Hz for a piezoelectric micropump as shown in figure 14. They used Parylene for the valve materials due to its low permeability to liquid and low Young's modulus which is 30 times less than that of silicon.

5.2. Membrane

Membrane check valves can be formed with bridges [182–188], holes [189–192] or bumps [193]. For large movable distances, bridge-type membranes are generally used. Li *et al* [182] fabricated a bridge-type membrane valve integrated with a piezoelectric micropump. The check valve with a nickel membrane held by four bridges (50 μm $\times$ 400 μm each) supported high pressures up to 10 MPa. Bien *et al* [183] developed a 2.5 μm thick polycrystalline silicon membrane valve held by three bridges. The ratio of reverse to forward flow rates of methanol was found to be less than 3% at a pressure of 11 kPa. Hu *et al* [184] built a 90 μm thick silicon membrane valve using a silicon-on-insulator (SOI) wafer. A maximum flow rate of 35.6 ml min^{-1} was obtained at a forward pressure of 65.5 kPa, and a negligible leakage flow rate of 0.01 μl min^{-1} was observed at a reverse pressure of up to 600 kPa. The resonance frequency of the valve in air was 17.7 kHz.

Membrane check valves were made of various polymer materials, such as Parylene [181, 185], SU-8 [186–188], Kapton [189, 190], Mylar [191] or silicone [192], due to large deflections which in turn lead to linear forward resistance. Feng and Kim [181] fabricated 4 μm thick bridge-type Parylene membrane valves with a fundamental resonant frequency around 1 kHz for a piezoelectric micropump. The dynamic behavior of the check valves was studied along driving frequencies in detail. Chung *et al* [185] developed cerebrospinal fluid shunt microvalves with a 6 μm thick Parylene membrane connected to an anchor by bridges. The valve should have resistance to the backflow to endure the high pressure acting on the valve generated by a finger pushing on the outer housing. A maximum displacement of 72 μm and maximum resistible pressures up to 4 kPa were observed. In a piezoelectric micropump a 100 μm thick bridge-type SU-8 thick membrane with 1 mm diameter held by four bridges, showing diodicity of about 2 at 3 kPa, was fabricated by Nguyen and Truong [186, 187]. Six different SU-8 membrane check valves with different bridge designs showed diodicity up to about 20 at 6 kPa [187, 188]. Wego *et al* [189, 190] integrated a 7.8 μm thick Kapton membrane with a thermopneumatic micropump based on printed circuit board (PCB) technology. A forward resistance of 950 kPa min μl^{-1} with a 40 fluidic resistance of reverse to forward flow directions was obtained. A 7 μm thick Mylar polyester film for a membrane check valve with holes of 200 μm was incorporated in both electromagnetic and piezoelectric micropumps [191]. A 100 μm thick silicone membrane check valve with holes of 200 μm integrated with electromagnetic micropumps showed a linear forward flow resistance of 0.0475 kPa min μl^{-1} [192]. Similar membrane check valves using a 50 μm thick micromachined silicon membrane with a bump were also demonstrated by Jensen and Gravesen [193].

5.3. Spherical ball

The popular application of ball valves is for heart valve prostheses [194]. The valve, known as the Starr–Edwards heart valve, is designed for implantation in a human body that has valvular disorders. It has a silicone rubber ball inside a Lucite cage with thick struts and a machined ring orifice. The valve is inserted between two chambers of the heart. If blood flow is regurgitated, the ball moves toward the ring orifice and stops blood flow. In a similar manner, these ball-type valves were miniaturized as passive check valves in micropump structures [195–197]. Carrozza *et al* [195, 196] used ball-type check valves for a piezoelectric micropump fabricated by stereolithography. Each ball valve consisted of a cylindrical chamber connected to a hemispherical chamber which contained a mobile ball with a diameter of 1.2 mm. When the valve was closed, the ball stayed in an inlet orifice. When negative pressures acted on the valve, the ball moved upward and the fluid flowed through the valve chamber. Yamahata *et al* [197] developed passive ball valves for an electromagnetic micropump with a PDMS membrane embedded with a permanent magnet. A ball with a diameter of 0.7 mm was encapsulated inside each conical hole shaped by a power blasting erosion process. The characteristic curve of flow rates versus static pressures in the ball valve showed similarity to the *I–V* curve of an electronic diode. In a similar manner, Pan *et al* [198] used stainless steel balls with a diameter of 0.8 mm as ball check valves, which were assembled using a tapered plastic micropipette and heat shrink tubing, in an electromagnetic micropump with a PDMS membrane. As reviewed in section 2.1.1, these ball-type valves were also used as active microvalves operated by external magnetic fields [34–36].

5.4. In-line mobile structure

Hasselbrink *et al* [199] developed an in-line microvalve using a mobile polymer structure, created by an *in situ*

photopolymerization method inside microchannels. The mobile structures were created by completely filling the microchannels of a glass microfluidic chip with the monomer/solvent/initiator components of a non-stick photopolymer and then selectively exposing the chip to UV light in order to define mobile pistons inside the microchannels. Sealing pressures up to 30 MPa and actuation time less than 33 ms were measured. Similar mobile structures in an on-chip high pressure picoliter injector were photopolymerized for HPLC applications by Reichmuth *et al* [200]. The valve element in the injector performed injection approximately two orders of magnitude smaller than that in [199] (from 10 to 0.18 nl) and demonstrated leakage flows reduced by three orders of magnitude at similar pressure differentials (from 9.6 to below 0.012 nl min^{-1}). In addition, Seidemann *et al* [201] fabricated an in-line check valve using a mobile SU-8 structure in a 360 μm thick and 200 μm wide microchannel. With higher inlet pressures, the triangular shaped in-line valve suspended by an anchored S-shaped spring resulted in the closure of the microchannel. The compliant spring produced the restoring force for opening when the inlet pressures were reduced.

6. Passive microvalves—non-mechanical

In this section, selected examples of passive microvalves without mechanical moving parts will be briefly reviewed. 'Valveless' micropumps using some sort of nozzle [202–207], diffuser [208–212] or Tesla [213, 214] elements have been widely used in inlets and outlets of reciprocal displacement micropumps. These diffuser-type microvalves, together with the mechanical passive microvalve discussed in section 5, are often categorized with the check valve as shown in table 1. Another approach to controlling liquid flow, where advantage of the large surface-to-volume ratio in microfluidic systems is taken, is the passive capillary microvalves utilizing the geometries or the surface properties in the microchannels [215–225].

6.1. Diffuser

When passive check valves are replaced by diffuser elements as flow rectifying elements, the risk of valve clogging will be eliminated. However, valving efficiency in a reverse flow direction is relatively poor, since these diffusers are always open, resulting in leakage flows. Passive valves using diffusers or nozzles are based on the direction-dependent behavior of tapered flow channels. The fluid dynamic resistance with the flow direction changes at higher flux velocities with higher Reynolds numbers. Converging wall direction is the positive flow direction and they are therefore denoted as *nozzles*, with a sharp entrance and a large tapered angle of around 70° [202, 204]. Fluid flow rectifying nozzles with large tapered angles were fabricated by using traditional silicon bulk micromachining technology [204–207]. In these cases, a tapered angle of 70.5° was chosen due to the geometry formed by a silicon wet etching process.

In contrast to the nozzles with large tapered angles, converging wall direction can be the negative flow direction and they are therefore denoted as *diffusers*, with a round inlet, a sharp outlet and a small tapered angle of around 10° [202, 203, 208, 209]. Tsai and Lin [210] generated a net flow from an inlet to an outlet by a thermally actuated bubble micropump. A pair of flat-walled diffusers with 30 μm in a narrow neck, 274 μm in an open mouth and a tapered angle of 14° was fabricated by a silicon deep reactive ion etching (DRIE) process. Similar silicon diffusers with a neck cross-sectional area of 30 μm × 30 μm were fabricated using the DRIE process by Andersson *et al* [211]. Jang *et al* [212] developed a thermally driven micropump with 10° tapered diffusers fabricated by surface micromachining technology. Another type of passive valve without mechanical moving parts using Tesla elements was proposed by Morris and Forster [213] and Feldt and Chew [214].

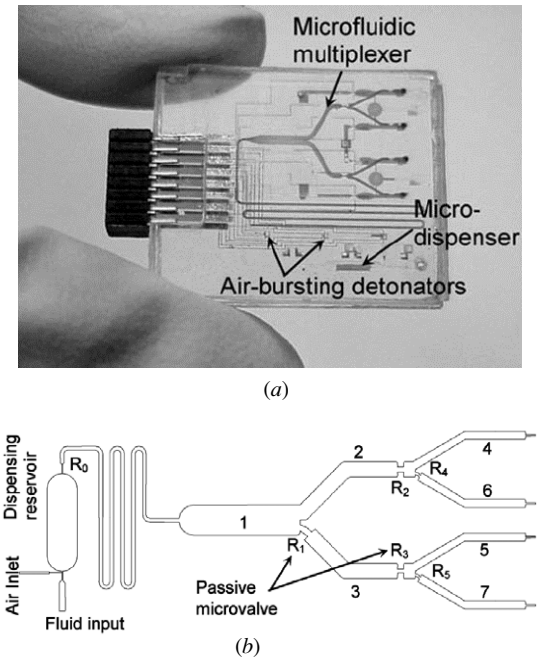

Figure 15. (*a*) The microfluidic multiplexer with an integrated dispenser that can be used to demonstrate the concept of structurally programmable microfluidic system (sPROMs) and (*b*) a series of microchannels with passive valves located at programmed positions by Ahn's group [215].

6.2. Capillary

Capillary forces can be controlled actively or passively using different effects: electrocapillary, thermocapillary or passive capillary. The electrocapillary effect, also known as electrowetting, is caused by the localized potential difference on the surface [229–235]. The thermocapillary effect is caused by the temperature gradient on the surface. The passive capillary effect utilizes dependence on the geometries [215–223] or the surface properties (hydrophobic or hydrophilic surfaces) [224, 225]. This section details selected examples of passive microvalves using the passive capillary effect: abrupt [215–219], burst [220–223] or hydrophobic patch microvalves [224, 225].

Ahn *et al* [215] integrated abrupt passive microvalves with a disposable smart lab-on-a-chip for point-of-care clinical diagnostics. Figure 15 shows a microfluidic multiplexer with an integrated dispenser that can be used to demonstrate the

concept of structurally programmable microfluidic system (sPROMs). The sPROMs basically consisted of a series of microchannels with passive valves located at programmed positions. Abrupt cross-sectional area changes in hydrophobic microchannels would generate pressure drops across the passive valves, resulting in fluidic flow valving. The passive microvalves, based on cyclic olefin copolymers (COC) with a contact angle of 92°, had a round geometry rather than an abrupt geometry with right-angled corners, so as to avoid any residue trapped in the dead corners. Inlet pressures of 4–6 kPa were measured for water to overcome the round junction passive microvalve.

Yamada and Seki [216] developed a microdispenser array made of PDMS, in which a pressure barrier allowed liquids to enter a narrow and hydrophobic microchannel. Man *et al* [217] reported abrupt passive capillary valves with surface micromachined Parylene microchannels on a silicon substrate. Yokoyama *et al* [218] employed bubble barrier valves with a thermal micropump for a loop-type microchannel, in which thermally generated bubbles flowed in one direction due to the difference in the capillary diameter between inlet and outlet valves. Melin *et al* [219] suggested a new concept of capillary microvalves by the effect of liquid triggering to avoid trapping of air bubbles when two liquids meet at the junction. Two geometrical capillary microvalves were joined at the junction. Thus, liquid from one inlet port reaching the junction waited for liquid from the other inlet port to reach the junction before moving through the outlet. The movement of the first liquid is triggered by the presence of the second liquid at the junction. The pressure required to overcome the stop valve function for water at a single inlet of the Y-junction was 7.3 kPa.

Similar capillary microvalves were used in rotational compact disk (CD) platforms [220–223], which are already commercialized under GyroLab (from Gyros AB, Sweden) and LabCD (from Tecan Group Ltd, Switzerland). The capillary microvalves actuated by centrifugal pressure were used to valve the flow of liquids. At a 'burst' rotational frequency, the liquids gathered at the discontinuity of inner microchannels would start to burst into outer microchannels. Capillary burst microvalves using PDMS [220], PMMA [221, 222] or PC [223] polymers were fabricated by rapid prototyping [220], CNC machining [221, 222] or a hot embossing process [223].

A different approach for capillary microvalves, a hydrophobic patch microvalve involving hydrophobic regions in otherwise hydrophilic microchannels, was taken by Andersson *et al* [224, 225]. They used the plasma polymerization process of fluorocarbons (C_4F_8) by inductively coupled plasma (ICP) in a silicon microchannel to form the hydrophobic patch regions with a contact angle of 105°. An inlet pressure of 0.76 kPa was suggested for water to run over the hydrophobic patch microvalve.

7. Discussion

Throughout this review, the development of microvalves has been surveyed with respect to various operation mechanisms and their applications. The applications of the microvalves include flow regulation, on/off switching, or sealing of biomolecules, micro or nano particles, chemical reagents, oils, water, bubbles, gases, vacuum and many others. The desired characteristics of the microvalves include no leakage flow, reduced dead volume, reduced power consumption, large pressure resistance, normally closed or open mode, insensitivity to particulate contamination, rapid response time, potential for linear operation, ability to operate with both liquids and gases and disposability [29]. To meet these requirements, various approaches have been explored in the development of microvalves. Apparently there is no such microvalve that favors all applications ranging from life sciences to vacuum. Therefore in practice, only a subset of the selected characteristics of a specific microvalve is important in a given application.

Most active microvalves actuate mechanical moving parts using magnetic [3, 30–42], electric [43–55], piezoelectric [56–65], thermal [66–84] or other actuation methods [85–93]. Conventional valves for pressure or flow control normally employ magnetic actuation in the form of solenoids to drive membranes or pistons, since they can generate large forces and deflections rapidly. For miniaturized structures, electrostatic actuation becomes more attractive. However, it is difficult to achieve high forces and large deflections because of the extremely high voltages required. Piezoelectric actuation can yield very high forces, but very small deflections even with very large voltages. Thermal actuation can provide large forces via large strokes, but is relatively slow and may not be suitable for many fluids due to heat dissipation. Bistable actuation is preferred in terms of power consumption, since it requires power only during the transition between two stable modes .

Active microvalves without mechanical moving parts could be built based on electrochemical [94–98], phase change [99–123] and rheological [123–129] actuations. Electrochemical actuation by electrolysis can provide large forces and deflections with relatively low voltages. The phase change actuation mechanism is available using phase changeable materials such as hydrogel [99–112], sol–gel [113, 114], paraffin [115–122] and ice [123]. Phase change actuation consumes energy resources, such as temperature, pH, electric fields or lights, and is very useful in disposable biochip applications due to its relatively low cost. Electro or magneto-rheological materials can be used as movable plugs remotely controlled by electric or magnetic fields. These actuations cannot provide large forces due to indirect polarization or magnetization by the external fields.

One of the most promising applications of the microvalves would be in life sciences and chemistry applications. On/off switching or sealing of biomolecules and chemical reagents without leakage flows even at high input pressures is a critical feature in ensuring successful biochemical assays. If there exist leakage flows through the microvalves, leaking reagents contaminate each other and eventually influence the assays. Also, it is imperative that the microvalves should tightly seal reaction chambers, in order to prevent evaporation of reagents and air bubble generation at an elevated reaction temperature. In practice, microvalves using external systems, such as modular and pneumatic microvalves, are very useful due to their excellent performance in on/off switching or sealing [130–167]. To date, pinch-type microvalves with external

actuation forces by indirect contact with any flexible polymer-based membranes [137–154], in-line channels [132, 133, 155–167] or tubes [38] integrated on the disposable LOC have been favored often because they can provide zero leakage flow and large resistible pressure, eliminating the risk of contamination. But it is strongly recommended that the external systems, such as air/vacuum pumps and solenoid valves, that provide the external forces to the pinch-type microvalves should be further miniaturized for hand-held biochemical applications.

While active valves control flow rate by pressure differences and have complex structures due to their various actuation principles, passive valves only open to forward pressure and have simple structures, showing diode-like characteristics. In the reverse flow direction the valving efficiency of passive valves is relatively poor, since the performance of these check valves depends on input pressure. This lack of efficiency results in leakage flows at low pressure. Despite this drawback, most passive microvalves are incorporated as check valves in inlets and outlets of reciprocal displacement micropumps: flaps [168–180], membranes [181–193], spherical balls [194–198], mobile structures [199–201], nozzles [202–207], diffusers [208–212] or Tesla elements [213, 214]. For example, commercially available micropumps have successfully employed these passive check valves for their piezoelectrically actuated micropumps (from thinXXS Microtechnology, Zweibrücken, Germany and Star Micronics, Shizuoka, Japan). In addition, passive microvalves using capillary effects are sometimes useful for microfluidic applications since autonomous and spontaneous valving can be realized due to the geometry [215–223] and surface properties [224, 225] of the microchannels. These passive capillary valves are recommended to block and pass fluidic flows without sealing at elevated temperatures.

Mechanical active microvalves (or passive check valves integrated with micropumps) have several disadvantages: unavoidable leakage flow and relatively high cost due to their complicated structures. Though leakage flow becomes a critical feature for on/off switching applications, it is not critical for flow regulation applications. Therefore, many micromachined active microvalves were used for gas or selected liquid regulation [30–33, 35, 36, 41, 43, 44, 46–50, 56, 57, 59, 60, 62–66, 71, 72, 80]. In these applications, an important issue is the linear operation over wide ranges of pressures or flow rates with applied powers. Considering the cost, mechanical active microvalves are mainly reusable and they can be assembled into the reusable instruments' side rather than the disposable LOC devices' side as stand-alone components [226–228]. For life sciences applications, non-mechanical active or capillary passive microvalves are preferred due to the possibilities of low cost and easy integration into the LOC devices, as well as miniaturization of instruments. If the size of the instruments does not matter, microvalves using external systems are recommended [130–167]. For example, on/off switching and sealing in PCR systems have been successful using these non-mechanical active microvalves [120–122], modular microvalves [130, 131] and pneumatic microvalves [142–146, 162–164].

Besides the microfluidic platforms embedded with microvalves, valveless platforms are of course promising due to reduced problems in valving the fluids. One

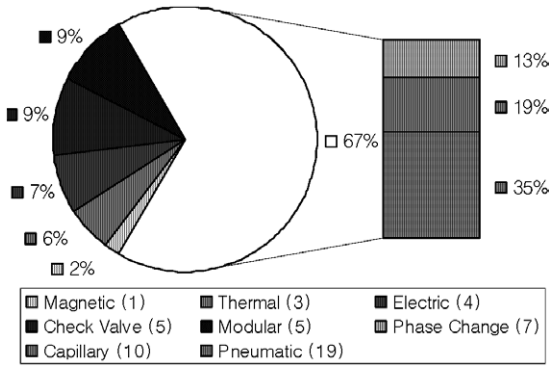

Figure 16. A research trend toward developing non-traditional microvalves in the recent proceedings of the μTAS 2005 conference [243].

of the valveless microfluidic platforms is a droplet-based digital microfluidic platform [229–235]. The platforms are based on an electrowetting effect, electrically controllable surface wettability of aqueous liquids. The droplets can be created from the reservoir, driven, divided or mixed, by the electrowetting actuation. Another group of valveless microfluidic platforms are electrohydrodynamic- or electro-osmotic-based microfluidic systems [236–241]. Of course, 96-well based high throughput platforms are valveless and successfully used in real-life systems, which have enabled the completion of the human genome projects [8]. In addition, Linder *et al* [242] developed reagent-loaded cartridges for valveless and automated fluid delivery in microfluidic devices.

8. Conclusions

As outlined before, the pioneering work started in the late 1970s and had shifted toward the MEMS-based microvalves in the 1990s. The first explorative microvalve research phase soon revealed the advantages and drawbacks of the various MEMS-based microvalve concepts. A second phase started around 2000 with the study of non-traditional technologies, such as phase change, external pneumatic or passive capillary microvalves. For example, a recent proceeding of the μTAS 2005 conference reflected further expansion of efforts in developing non-traditional microvalves, as shown in figure 16 [243].

The development of microvalves has been progressing rapidly in recent years. As a result the performance of microvalves has been constantly improved and features such as leakage flow, resistible pressure, power consumption, dead volume, response time, biochemical compatibility and disposability have been partially addressed and solved. However, there is an abundance of room for improving the performance of the microvalves and making them cost effective for further commercialization. Breakthrough ideas will make it possible to realize a fully integrated disposable microfluidic lab-on-a-chip for personal diagnostics or wellness applications. In addition to the LOC applications, the microvalves will become building blocks in high throughput microfluidic platforms for stem cell study or drug discovery. Furthermore, the microvalves will be embedded in various microfluidic systems, including space exploration, fuel cell,

etc. There is no doubt that in the near future microfluidic platforms embedded with microvalves will be as prevalent as microprocessors are today.

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