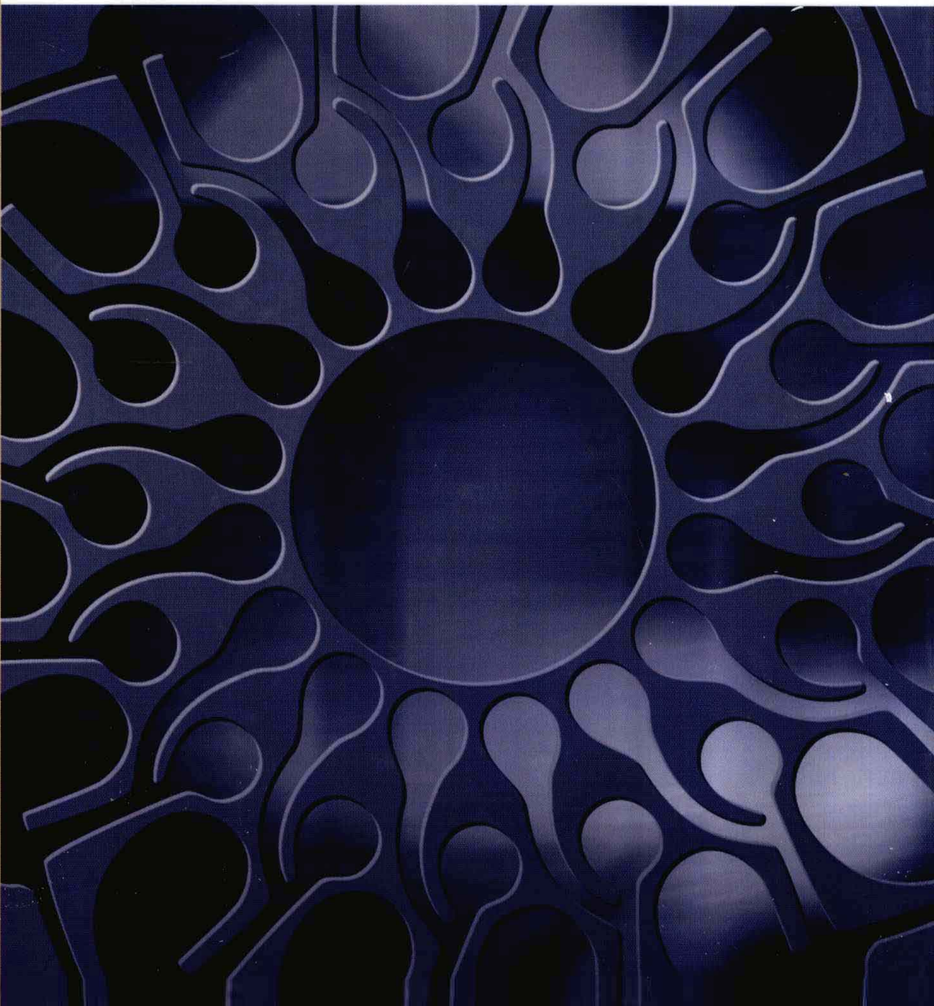
INTEGRATED MICROSYSTEMS SERIES

PRESSURE-DRIVEN MICROFLUIDICS

Václav Tesař



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Preface

The subject of this book is handling and managing fluid flows. To an outsider, this may sound like a dull subject, but it is actually exciting and also very important from a practical standpoint. Fluids (a term covering both liquids and gases) are encountered almost everywhere, in the atmosphere, in rivers and seas, and indeed in our own bodies. In particular, they are almost omnipresent in technology. There are very few technological processes that can claim avoiding working with fluids. Even in what is seemingly a purely electric system, such as a computer microprocessor, it may be found that the limiting factor in further development is circuit cooling by the surrounding atmospheric air. If the passive and not very effective cooling by natural convection is replaced by controlled coolant flows, the subject of fluidics becomes a part of the project. Admittedly, the cooling and similar effects are areas where fluidics is not the star of the show and plays only a supporting role, but even there progress in the fluidic side of the development may bring a substantial overall step forward. There are other applications, like implanted devices for control of body fluids in medicine, where fluidics is the key factor.

Microfluidics is the outgrowth of fluidics—the technical field of working with fluids, mainly controlling their flows in a system of channels. Microfluidics is characterized by the small size of the channels. It emerged together with the more general area of microelectromechanical systems (MEMS), which became possible by applying the microfabrication techniques originally developed for microelectronics. Typical for MEMS are microfabricated moving mechanical components and among them there are also components acting on fluid flows. There are many existing applications, and even more proposed ones, taking a distinct advantage from the small size of microfluidic devices. The trauma of invasive implanting is lessened if the implanted device is very small. There are, however, still other applications where the small scale is not the decisive factor. There the devices may take over the operating principles of the earlier larger-scale fluidic (or perhaps mesofluidics). As the complexity of the actions performed by fluidics tends to increase, so does the complexity of the fluidic circuits and with this comes the general requirement to make the systems physically smaller. If not at present, fluidics is likely in the foreseeable future to move gradually toward microfluidics.

At the microscale, there is a general trend of the surface forces acting on the fluid becoming more important than the other, more conventional force types. Much interest in present-day development of microfluidics is devoted to the technique of driving the fluid by the surface-type electro-osmotic effects. While such aspects are not avoided and there is an ample discussion of such driving phenomena (often limited to special types of the fluids), this book tends to concentrate on the classical manner of driving the fluid flows, mainly by the action of a pressure difference. Not only does this driving mechanism have a much more general applicability, but it has also made it possible to include here among the treated subjects some interesting and little known principles used in the classical larger-scale fluidics.

However new is the subject of microfluidics, there are already in existence other books on this subject. Many of them naturally concentrate on the novel ideas associated with the microfabrication technology, producing the tiny devices, and with the mechanical actions made possible by the development in the field of MEMS. A typical book of this type is *Fundamentals and Applications of Microfluidics* by Nam-Trung Nguyen and Steven T. Wereley, Second Edition. The present book was carefully planned taking into consideration the existence of such literature. It aims at avoiding direct competition, and concentrates on those aspects of microfluidics that are outside the main interest in this and similar books, discussing the complementary aspects and issues.

Microfluidics can lead to profound changes in the world as we know it. It may have a large influence on transportation and even producing food and similar very essential aspects of human existence. In particular, its interest focuses discernibly toward collaboration with and influencing living organisms at the cellular level. This may bring many benefits in improvement of health care and various therapies, but may be also abused. One conclusion, however, seems to be clear. Fluidics—and its outgrowth microfluidics—is here and is going to stay with us. Engineers must learn its weaknesses and the advantages it offers.

Contents

Chapter 1

Introduction and Basic Concepts

The subject of this book, microfluidics, is the technology of handling small fluid flows in small devices. It is a new technology, existing roughly for two decades—a time too short for full recognition of its potential. According to the rather arbitrary definition in [1], microfluidic devices are characterized by dominant (smallest) channel width (or analogous transverse dimension of fluid flow paths) smaller than 1 mm. The general development trend is to make microfluidic devices gradually smaller, sometimes even so tiny that they are hardly visible with the naked eye (which can discern features larger than ~10 μm). Present-day microfluidics originated by using the manufacturing technology developed in microelectronic engineering for making fluid flow channels. It is possible—and advantageous—to make both electric and fluidic circuits on the same silicon chip (Figure 1.1) so that they can mutually collaborate. The task of fluidics is to handle fluid flows through the channels while a typical task of electronic sensors is to generate signals carrying information about the fluid presence and/or its properties so that the other parts of the electronic circuitry can process this information, perhaps influencing the fluid flows in a feedback action.

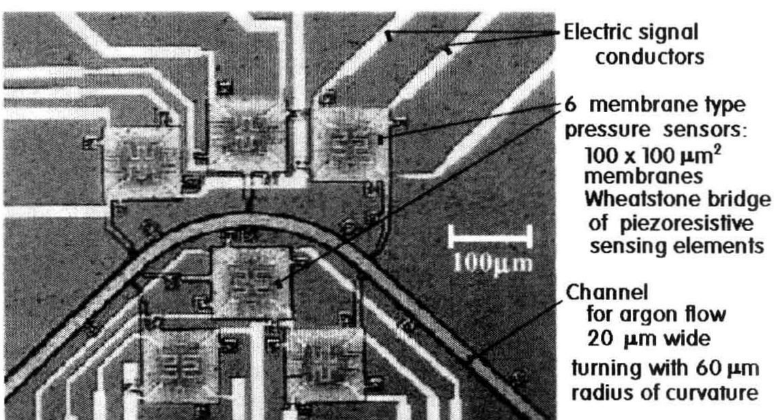
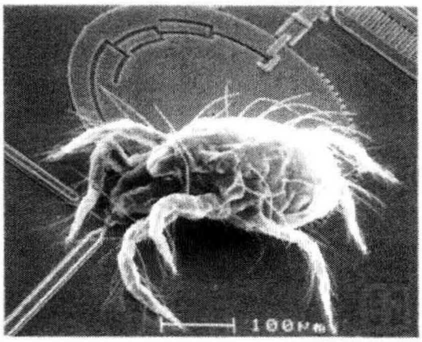
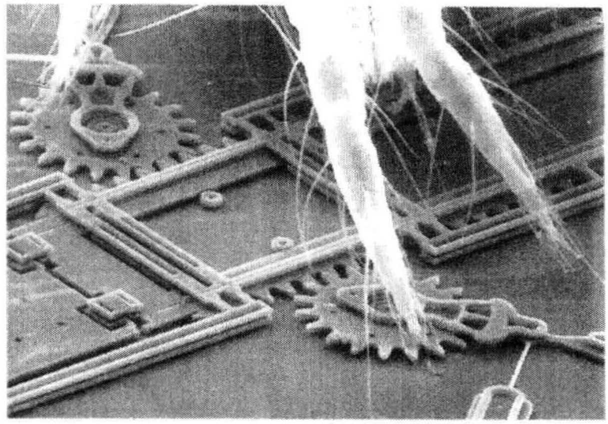


Figure 1.1 Detail of a silicon chip with typical coexistence and collaboration of microfluidics and microelectronics. The microfluidic part is extremely simple here – just a 90° bend of a constant width channel. Microelectronics converts the pressure readings at 6 locations along the channel into the electronic output. (*From* [2]. © 2001 Institute of Physics. Reprinted with permission.)

1.1 MEANING AND USE OF MICROFLUIDICS

Often, though not always, microfluidics is a part of MEMS technology [3, 4]: micro-electromechanical systems, characterized by electronics cooperating at the small scale with miniature mechanical devices implied by the name (Figures 1.2 and 1.3), but also with devices of other characteristics, such as fluidic [5], optical, thermal, acoustic, or chemical.

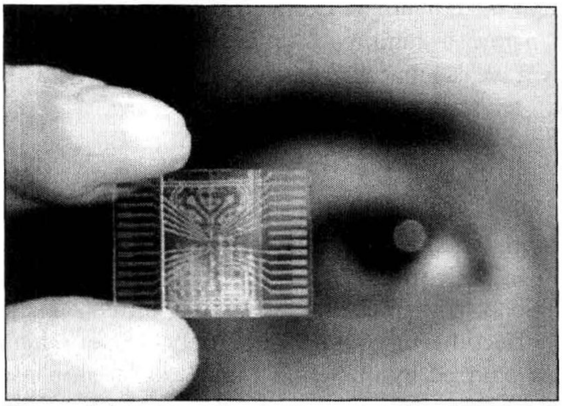



Figures 1.2 (Left) and 1.3 (Right) MEMS mechanism made by etching in silicon, compared with a mite, a creature normally hardly recognizable with the naked eye. (Courtesy of Sandia National Laboratories SUMMiTTM Technologies.)

Typical current applications of microfluidics are in biomedical sciences. An application that may serve as a characteristic example is an implanted device for diabetes sufferers, delivering insulin into the blood flow. It is easy to visualize—though at present not yet so easy to develop—a device for continuous glucose monitoring in a patient's blood, using this information for feedback-controlled insulin delivery (Figure 6.151). Both blood samples as well as the pumped insulin solution are liquids so that the need for fluidics is obvious. The small scale of microfluidics minimizes the problems associated with implanting the devices.

Another example where much current effort is directed is DNA "fingerprinting" [6], the exact identification of organisms. This has a vast potential not only for forensic purposes but also for objective diagnosis of illnesses by identification of the bacterial DNA and tailoring the medical treatment to the genetic makeup of the patient (see Section 6.7.2). This involves the polymerase chain reaction and analysis of the reaction product, again processes requiring precisely controlled handling of liquids. The small scale makes it possible to perform simultaneously a huge number of such analyses, perhaps in a portable "lab-on-chip." Typically, the background of biomedical research leads to the preference for microfluidic devices and circuits built on glass substrate (Figure 1.4) rather than silicon. Mass-produced final versions, still mostly under development, plan to use yet another material: plastics. So cheap as to be discarded after use, they eliminate any cross-contamination between the samples.

An emerging area of vast application potential for microfluidics is also microchemistry (e.g., [7]). All handling of the reactants (e.g., dosage and mixing) as well as of the reaction products (perhaps involving separation from product mixture) involves fluid motion. Performing chemical reactions in tiny microreactors has several distinct advantages; the obvious one is the possibility to perform simultaneously a huge number of slightly differing reactions in a drug or catalyst discovery activity. This saves the time needed for finding the best-performing drug.



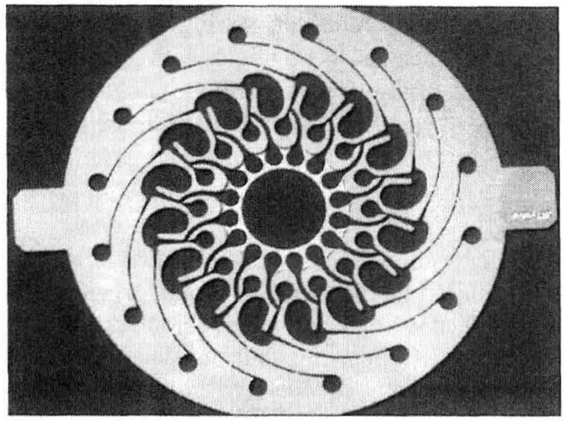


Figure 1.4 (Left) Microfluidics and electronic sensors on a glass chip for biological application: counting and classification of living cells (*From*: [4]. © 2004 Elsevier. Reprinted with permission.)

Figure 1.5 (Right) A typical high-temperature microfluidics: an array of 16 valves taking reactant samples from micro-chemical reactors that perform the Fischer-Tropfsch reaction, the synthesization of liquid hydrocarbon fuels.

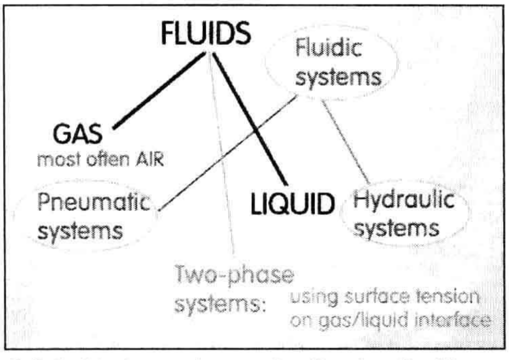
Instead of silicon, the background and experience of chemical engineers has led to the common trend of using stainless steel (Figure 1.5) as their preferred material for microfluidic devices in this application. Especially in the case of exothermic reactions, the microchemistry is an example of non-MEMS microfluidics: the electronic circuitry is placed outside the chip, at a safe distance from the high temperature.

This book is mainly devoted to a particular area of microfluidics, characterized by the fluid flow in nonmoving part devices driven by the action of applied *pressure differences*. This is actually an approach building on past successes of large-scale pressure-driven fluidic devices. It should be said that in present-day microfluidics there is often an interest in using other driving mechanisms. A typical case would be electrokinetic or electroosmotic phenomena dominated by processes in an extremely thin near-wall layer. These are attractive due to their novelty; the small scale with resultant large surface-to-volume ratio leads to dominant effects of surface phenomena, impossible to use and mostly actually negligible at the large scale. The more traditional pressure-driven flows may be less spectacular, but they are more widely applicable. No special fluid properties are required, while electrokinetic flows are usable only with liquids; in fact, requiring a polar character of the liquid. Though quite special from a physical point of view, this generally means water and aqueous solutions, encountered very often in many applications. Nevertheless, in gas flows such as in the microchemistry of processing gaseous fuels, pressure-driven flows are the only possibility. Being applicable even at large scales, the pressure-driving in microfluidics can employ useful ideas developed earlier in large-scale fluidics, of which microfluidics is a direct descendant.

Many microfluidic devices were demonstrated to operate successfully using moving parts acting on the fluid [1]. As already mentioned, the attention here is focused on *purely fluidic* devices, operating without moving or deformed mechanical components. The absence of mechanical parts makes pure fluidics easier to manufacture, more robust, and more reliable, evading the problems caused by seizure or breakage. On the other hand, admittedly, generation and control of fluid flow is in principle easier with mechanical components. Fluid simply cannot enter a channel when its entrance is blocked by an inserted mechanical part in a mechano/fluidic valve. Similarly, a mechano/fluidic micropump is easier to design because fluid has no option other than to move when displaced by a moving piston. Pure fluidics employs more subtle phenomena. It relies on setting up special, sometimes downright exotic, flowfields inside the devices, such as a flowfield with some hydrodynamic instability. A complete change of the character of the flow is therefore triggered even by a weak input disbalancing the instability. This is more difficult to design, but also more interesting.

1.1.1 Why fluids?

The term "fluid" is a generalization, covering both liquids and gases (Figure 1.6), the latter differing from the practical point of view mainly in their much larger specific volume (lower density) and much higher compressibility. Compressibility can significantly influence the character of the flow, but in steady flows the effect becomes important only at very high velocities, rarely encountered in microfluidics. Also covered by the term "fluid" are multiphase mixtures, such as bubbly liquids (including foams), suspensions of solid particles or living cells, emulsions of mutually immiscible liquids, and so on. These cases, which may all lead to quite complicated fluid mechanics, are currently used more and more. A typical property of small scales is increasing importance of surface forces, usually negligible in large-scale flows. This is the case of surface tension on the interface between liquid and gas, which becomes the dominant factor in some microfluidic devices, sometimes even handling individual drops in gas (air) or individual air bubbles in liquids



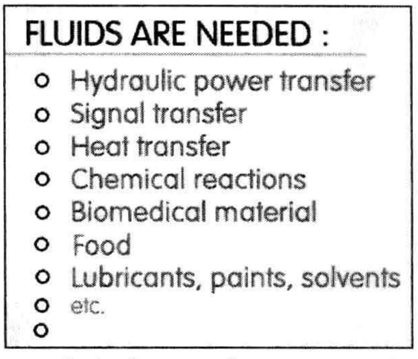
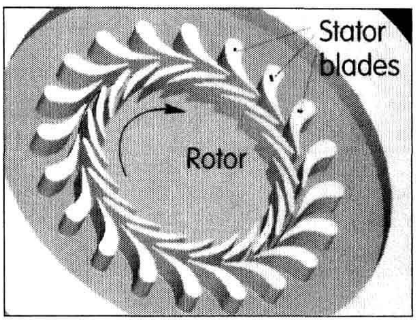


Figure 1.6 (Left) Just as the term *fluid* involves liquids as well as gases, *fluidics* is a general term encompassing both hydraulic systems working with liquids, and pneumatic systems working with air or another gas. Of increasing importance in contemporary microfluidics is handling two-phase flows, both gas and liquid (e.g., to generate and use air bubbles).

Figure 1.7 (Right) Some of the many reasons why handling fluids is indispensable.

The objects of interest in this book are direct descendants of classical hydraulic and pneumatic systems. Again, the term "fluidic" system (Figure 1.6) is a generalization covering both of them. Such systems usually involve generation of fluid motion, perhaps by a pump, distribution and transport of fluid into various destinations, and finally their use in the destination location. In classical large-scale hydraulics the fluid is just a working medium used to transfer power or, in lesser degree, transfer the control signals. The fluidic character of the transfer is in principle not very important; it may be thought of as replacing a mechanical transmission. The use of fluid brings some practical advantages. It may make it easier to transfer the power into a moving final destination by a flexible hose, but the properties of the fluid itself are of secondary importance. The fluid, for example a hydraulic oil, is perhaps chosen on the basis of its lubricating properties, preventing seizure of the moving parts.

On the other hand, the transport and handling of a fluid in modern fluidics is often chosen because a particular fluid is needed at the output destination. Figure 1.7 presents a list—far from exhaustive—of such typical uses that are the actual reasons why handling fluids is useful and in fact indispensable. Even in the classical application of fluids used to generate a force (piston force-generating drives have a number of advantages over electric drives for slow linear motions) and to perform energetic conversions in thermal machines, the fluid is not just a passive medium. Nevertheless, today these are rather exceptional motives for applying microfluidics – even though, for example, there were successful demonstrations of combustion microturbines (Figures 1.8, 6.19, and 6.20) made by etching in a chip.



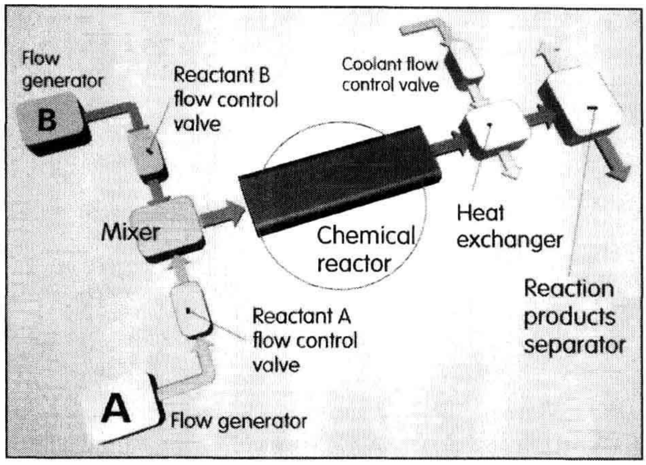


Figure 1.8 (Left) Even radial microturbines of millimeter overall size were made by etching. Such scaling down of large machines is rather exceptional in present-day microfluidics as the efficiency at Reynolds numbers is generally low.

Figure 1.9 (Right) An example of a more promising application: schematic representation of fluid transport used to perform a binary chemical reaction between two reactants A and B.

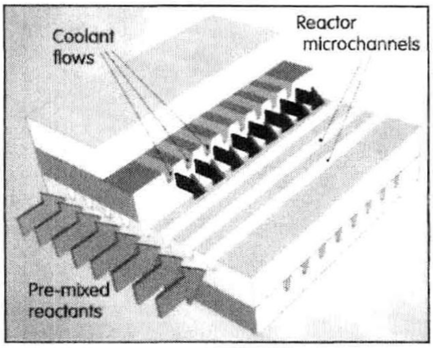
The idea is to use the extremely high density of energy storage in hydrogen as a fuel. The turbine driving an electric current generator should provide a more compact power package than energy storage in chemical batteries.

Fluid flows are also used to carry *signals* and even to process the information they carry. Again, despite several successful demonstrations (for example fluidic arithmetic units were demonstrated to perform mathematical operations even when heated to glowing red and hit by a hammer) this is not an important application in present-day fluidics. Electronic signal transfer and processing is generally more effective, mainly because fluid flows are slow and an almost universal requirement in information processing is fast operation. The limit to propagation speed in electronics is the speed of light, while with fluids the limit is the much lower velocity of sound.

Returning to Figure 1.7, it should be said that an increasingly often encountered reason for bringing a fluid into microsystems is *cooling*, carrying away generated heat. This is currently an area of intensive development activity. One of the main limits in further development of computer microprocessors is the increasing dissipated heat per surface unit. According to Moore's exponential law governing the progress in microelectronics, the thermal power density in the next generation of microprocessors will be comparable with the values existing in nuclear reactor cores. Increasing cooling effectiveness is indispensable for further miniaturization. As well, exothermic reactions in microchemistry (Figure 1.10) may require quite sophisticated cooling techniques.

Quite often, the reason for handling fluids in a mechanical MEMS device is *lubrication*: to prevent a friction contact between moving components (example: Figure 6.22). This need not be the traditional oiling of bearings; perhaps more important nowadays is data storage on a moving medium (such as a floppy disk) with creation of the supporting air layer between the medium and the read/write head past which it moves.

Fluids may be also simply consumed at the end of their flow path through the system: evaporated, discarded after use as tested sample, or used as food for captive biological organisms. In fact, the human food processing field has found many successful ways to use microfluidics, in particular, for producing an oil-water suspension, the basis for mayonnaise or salad dressings.



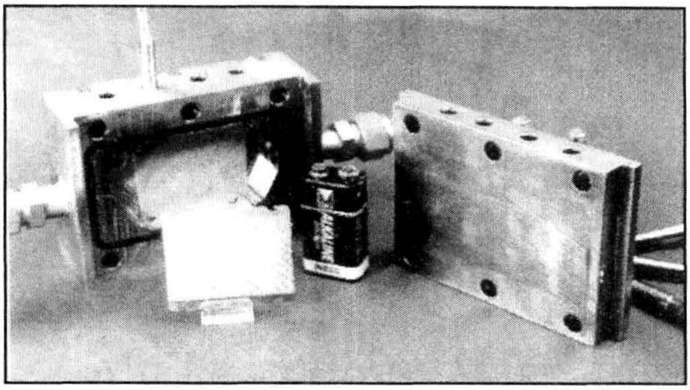


Figure 1.10 (Left) Chemical microreactors are basically just more or less simple channels - unless complicated by a requirement of large exposed surfaces coated by solid catalyst – so that they are usually arranged in large numbers in parallel. In the case of exothermic reactions, the reactor body may require intensive cooling.

Figure 1.11 (Right) An example of a typical contemporary microchemistry: a reformer for converting liquid fuels into hydrogen, needed for fuel cells. Devices developed from laboratory models like this are expected to cause a revolution in cars (© 2002 IMM - Institute for Microtechnology, Mainz, Germany, Printed with permission.)

One particular case belonging to this category, and of large and increasing importance, is the fluid consumed in a chemical conversion—burned as a fuel or undergoing more complex chemical reactions. Most industrial chemical reactions actually take place in the fluid phase. This is because the molecules of the reactants must be mobile so that they can meet and interact. The schematic block-diagram example in Figure 1.9 shows that performing even a simple binary chemical reaction may require a number of fluidic peripheral devices handling the flow of the reactants as well as of the reaction products. Analytical chemistry and biochemistry, where the small size makes it possible to perform a large number of simultaneous analyses, is a field where the advantages of microfluidics are particularly obvious. The microreactors are often made on a silicon chip together with electronic sensors, needed for example to monitor the reaction. The tiny amounts of samples needed for the analysis are an advantage in themselves, especially when samples are taken from a living organism. On the other hand, it is also advantageous in synthetic chemistry to perform the processes in microreactors, "numbered up" rather than "scaled up" to meet the requirement of a large production rate (Figure 1.11). The large surface-to-volume ratio makes possible much closer control of the reaction, the short residence time makes possible fast changes of the product composition, and there is less danger if the reaction or its product should explode. Obviously, fluidic no-moving-part technology has advantages in the supporting devices, such as sensors for sensing the reaction conditions, flow control valves, mixers, and separators.

Processing fluid samples is essential for one very important application of microfluidics: anti-terrorist warfare. Mass-produced—and therefore cheap—detectors taking molecular amounts of samples, for example, from the air and processing them to detect trace amounts of explosives, drugs, and other illicit substances may deprive terrorists of their present huge economic advantage: the crude bombs they use are cheap while current methods of detecting them are expensive.

1.1.2 Why devices without moving parts?

The devices mentioned above may be also made with moving components acting on the fluid. This is the standard way that fluid flow manipulating devices are designed at large scales. In a typical mixer, the pair of mixed fluids is contained in a vessel and agitated by a rotating impeller. There are pure fluidic mixer versions, accomplishing the mixing task by generating a flowfield in which the two fluids perform large-scale relative motions deforming the contact interface between them. Typically the two flowing fluids impinge on inclined or curved fixed plates protruding into the flowpath. The final mixing step takes place by diffusion across the interface. Obviously, such pure fluidic version is more suitable for scaling down and manufacturing at the microscale. To make, typically by etching, a free-moving component that can rotate inside an etched cavity and be driven from outside by a micromotor is possible (similar devices were actually demonstrated), but the process is far from simple and the resultant device is likely to be rather delicate. Making a small-scale version of the pure fluidic counterpart without the moving components is certainly much easier. The device is likely to be more robust, withstanding adverse operating conditions, and its operation life and reliability are generally much better. It may be discovered, however, that scaling down may lead to a different flow regime in which the mixing is far less effective.

Experience with other devices, such as the valves shown in Figures 1.12 and 1.14, is similar. The pure fluidic solutions are more suitable for being made at a small scale and offer operating advantages evident from comparing Figures 1.13 and 1.14 – provided the scaling down does not result in a very low Re flow regime with degraded efficiency. The term *fluidics* was actually originally coined just to describe the devices operating without moving components. It was introduced in the 1960s in an analogy to *electronics* and was initially meant to be applied to signal processing systems, where the fluid carried the signals just like electrons do in electronics. At about the same time, the progress in semiconductors in electrical engineering led to replacement of relays with mechanically moved contacts in industrial automation by no-moving-part switching and amplification of electric currents. The analogous switching of fluid flows by the no-moving-part devices seemed at that time to be similarly promising. The key element then was the no-moving-part fluidic signal amplifier, invented in 1959 by Bowles, Warren, and Horton at Ordnance Fuze Laboratories in Washington, D.C. The absence of mechanical components and their inertia made accessible unprecendently high operating frequencies, approaching the frequency band of early transistors. Serious attempts were undertaken to compete with electronics in information processing by building fluidic binary logical and computation circuits (binary fluidic flip-flop device, based on the Coanda jet-attachment effect, was described by Warren in 1962). They were demonstrated to withstand extreme conditions at a time when electronic devices were delicate and sensitive to variations in temperature.

In signal and information processing, however, fluidics lost and electronics won the competition. One of the principal reasons was the relative slowness of signal transfer by fluid flows by several orders of magnitude, which leads to inevitable slowness of the information processing. Another disadvantage was the size, larger than the size of comparable microelectronic