

1

Introduction

This chapter introduces the terminology related to microfluidics and its practical applications. The historical perspective of this emerging discipline is introduced first. Subsequently, different natural systems with microscale structure and transport phenomena are discussed and correlated to the microfluidic systems. Various practical examples of microfluidic devices are presented to illustrate the importance of studying transport processes in microscale. Scaling laws are used to demonstrate different flow physics of small-scale devices.

1.1 History

The year 1959 is considered as the beginning of microtechnologies and nanotechnologies. In December 1959, R.P. Feynman gave a visionary speech during the American Physical Society meeting at Caltech entitled “*There is plenty of room at the bottom*”.

The beginning of the speech was as follows:

“I would like to describe a field, in which little has been done, but in which an enormous can be done in principle. This field is not quite the same as the others in that it will not tell us much of fundamental physics (in sense of “what are the strange particles?”) but it is more like solid-state physics in the sense that it might tell us much of great interest about the strange phenomena that occur in complex situations. Furthermore, a point that is most important is that it would have an enormous number of technical applications.”

Some other excerpt of his speech is:

“How many times when you are working on something frustratingly tiny like your wife’s wrist watch, have you said to yourself, ‘If I could only train an ant to do this!’ What I would like to suggest is the possibility of training an ant to train a mite to do this. What are the possibilities of small but movable machines? They may or may not be useful, but they surely would be fun to make.”

Feynman’s suggestion didn’t remain in fantasy world. The first microbeam was fabricated in 1982 and the first microspring was fabricated in 1988. Microfluidics emerged in the beginning of the 1980s and has been used in the development of ink-jet printheads, DNA

chips, lab-on-a-chip technology, micropropulsion, and microthermal technologies. In 1995, the word IBM was spelled out using only few atoms. *Microfluidics* is a field associated with flows that are constrained to small geometries, where the characteristic dimensions are of the order of few hundred microns. It deals with the behavior, precise control, and manipulation of flows at submillimeter scale. It is a multidisciplinary field intersecting engineering, physics, chemistry, microtechnology, and biotechnology, with practical applications to the design of systems in which small volumes of fluids are used.

1.2 Definition

A fundamental question initially arises about the definition of microfluidics. The basic meaning of this terminology is the flow at small scales. The primary advantage is the utilization of breakdown phenomena in scaling laws for new effects and better performance. Hence, the importance is not the size of surrounding instrumentation and the material of the device but the *space where the fluid is processed*. The minimization of the entire system may be beneficial but is not a *requirement* of a microfluidic system. The key issue of microfluidics is the microscopic quantity of fluid in which small-scale causes change in fluid behavior.

There are different points of view regarding device size and fluid quantity for the definition of microfluidic device. The microelectromechanical systems (MEMS) terminology indicates that the device size *must be smaller than 1 mm*. Electrical and mechanical engineers are interested to work on microfluidics because of their fabrication capabilities using microtechnology. Their idea is to shrink the device size and thus define microfluidics in terms of size to take advantage of the new effects and better performance. The objective is to shrink down the pathway of the chemicals. Another preferred way to define microfluidics is based on *fluid quantities*. Figure 1.1(a,b) shows the size and volume characteristics of different microsystems.

Nanodevices are of size less than 1 μm . Human hair is between 1 μm and 1 mm, and has similar size as microsystem. Microneedle, micropumps, microanalysis system, and microreactor are best defined based on the volume of fluid handled. Microanalysis system handles fluid volume more than 1 μl . Microneedle handles fluid volume between 1 pl and 1 μl . Microreactors handle fluid volume between 1 pl and 1 ml.

1.3 Analogy of Microfluidics with Computing Technology

Many days/hours of computing are required to perform numerical simulation for weather forecasting and various computational fluid dynamics applications. The development of *parallel architecture* in modern computers has contributed significantly to speed up the computational speed for these applications. Similar to parallel computer, microfluidics can revolutionize chemical screening power. Compared to *manual and bench-top experiments*, microfluidics can allow pharmaceutical industry to screen combinatorial libraries at high throughput. A microfluidic assay can have several hundreds to *several thousands* parallel processes in comparison to *few hundreds* parallel processor of parallel computer. This high-performance capability is important for DNA-based diagnostics in pharmaceutical and healthcare applications.

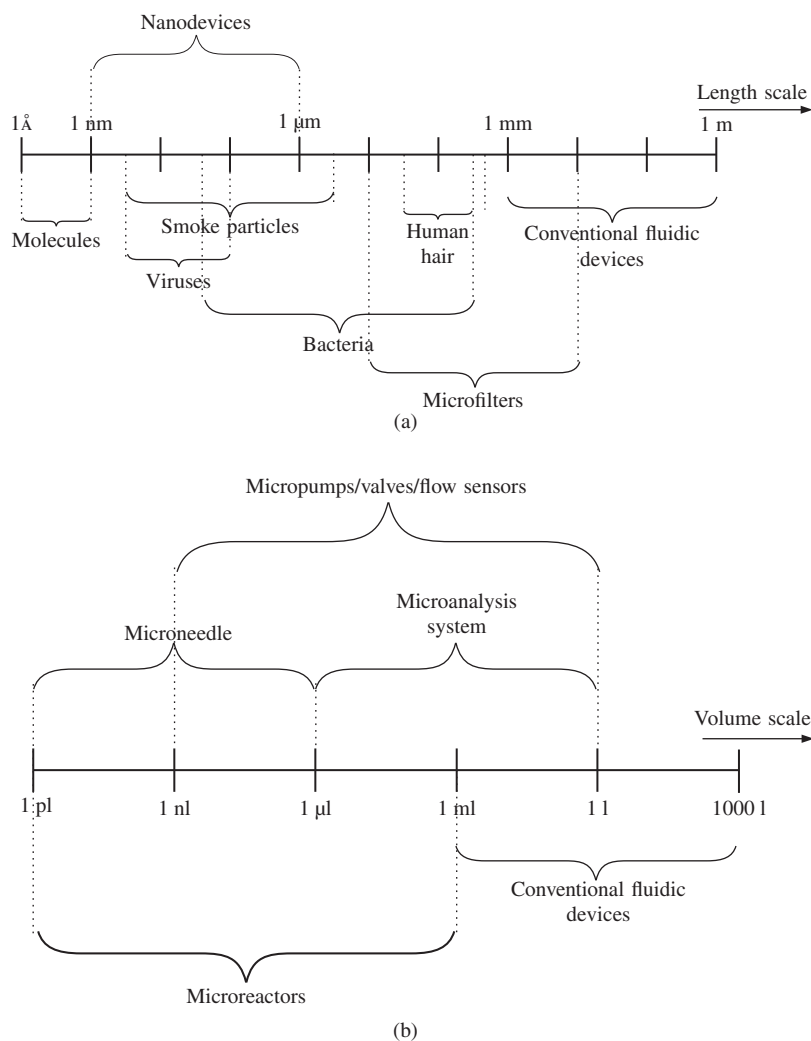


Figure 1.1 (a) Size characteristics and (b) volume characteristics of different microsystems

1.4 Interdisciplinary Aspects of Microfluidics

Owing to the rapid development of microfabrication technologies, it is now possible to miniaturize mechanical, fluidic, electromechanical, and thermal systems to micrometer sizes for various applications. This new development led to the creation of a new discipline known as microfluidics. *Microfluidics* is defined as the study of flows, which can be simple or complex, mono- or multiphase circulating in artificial microsystems, that is, systems fabricated using new technologies, namely, etching, photolithography, and microimpression.

Research on microfluidics has become a truly multidisciplinary field representing almost all traditional engineering and scientific disciplines. Initially, microfluidics developed as a part of MEMS technology using the available infrastructure and technology of *microelectronics*. Electrical and mechanical engineers are interested in contributing to the fabrication technology related to microfluidics. Fluid mechanics researchers are interested to study the *new phenomena* in fluid flows. The flow physics in microfluidic devices is governed by a transitional regime between the continuum and molecular dominated regimes. There are a new class of fluid measurement tools for microscale flows using in situ microinstruments in addition to new analytical and computational models. Microfluidic tools allow the *life scientists* and *chemists* to explore new effects that are not possible in traditional devices.

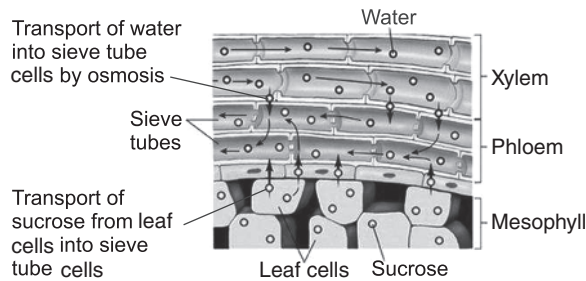
1.4.1 Microfluidics in Nature

Microfluidics is not limited to “systems made by man.” Nature also produces micrometric systems with impressive characteristics having controlled circulation of fluids.

One example is tree. The question is: how can a tree bring water and nutrients to the leaves? Nature used a complex network of capillaries to achieve this (see Figure 1.2). The trunk of the



(a)



(b)

Figure 1.2 (a) A banyan tree and (b) schematic of transport process inside the capillary network

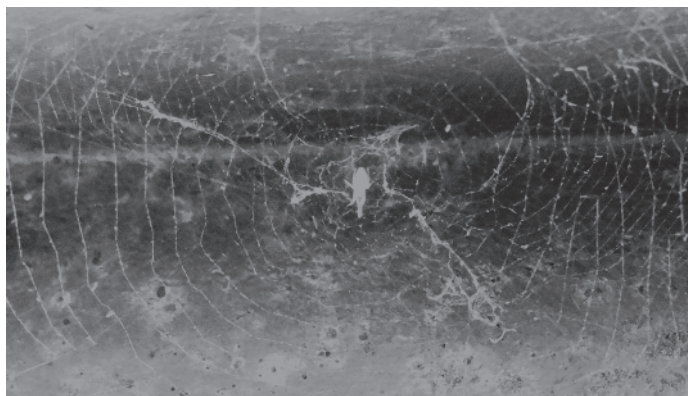


Figure 1.3 A picture of spider web having more strength than that of steel

tree has microcapillaries of a hundred *micrometers* size and leaves have *microchannels* of size equal to *several tens* of *nanometers*. Air on leaf surfaces causes water to evaporate creating a pull in the water column. There is transport of water into the cells of the root by osmosis. There is simultaneous active transport of sucrose from leaf cells into the cells of the root or stem. The supply of food carrying liquids, that is, sap, is *homogeneous* despite the complexity of the network. The pressure drop in the complex network is significant, that is, several tens of bars, implying that the sap is subjected to *negative pressure*. The hydrodynamic of this system involves consideration of deformability of the channels under the effect of pressure.

Spider web is another example of micrometric flows appearing in nature (Figure 1.3). Spider produces a long silken thread by synthesis of protein in a gland mixed with a solution. The silken thread has *exceptional mechanical properties*. Individual threads of spider web look fragile. However, they are extremely strong, that is, more than that of steel. The spider silks may be useful for human applications such as making medical sutures and high-performance ropes or used as filling in bulletproof vests. There are many examples of microfluidic systems existing in nature. Man-made systems are far from being able to compete with the natural systems.

1.4.2 Unit Systems in Small Scales

The development of various microsystems also requires new definition of unit system to describe these devices. Volume is associated with exponent equal to 3 of the length scale of a system that is, $V \sim l^3$. If length scale reduces from centimeters to micrometers, the volume decreases by 12 orders of magnitude. Therefore, micro world requires appropriate units for describing small quantities. Table 1.1 shows different units for description of microsystems.

A microfluidic system commonly contains volume of about 10 to few hundred nanoliters. A *biological cell* having a typical size of 10 μm diameter encloses a volume of 4 pl. Recently, it has been shown that miniaturized electrochemical method can detect the presence of about *zeptomole* of DNA.

Table 1.1 Unit system used to describe microsystems

Unit name	Power	Unit name	Power
milli	10^{-3}	atto	10^{-18}
micro	10^{-6}	zepto	10^{-21}
nano	10^{-9}	yocto	10^{-24}
pico	10^{-12}		
femto	10^{-15}		

1.5 Overall Benefits of Microdevices

Micron-sized devices are becoming more prevalent in both commercial and research applications. The growing number of publications and patents in the area of microfluidics is constantly showing the versatility of this technology. The introduction of commercially successful devices is bringing microfluidics out of research and development into a variety of applications. Unlike microelectronics, where the current emphasis is on reducing the size of transistors, microfluidics is focusing on making more complex systems of channels with more sophisticated fluid-handling capabilities, rather than reducing the size of the channels. The following are the various benefits of microfluidic devices.

- Ability to manipulate and detect small volumes
- Low consumption of reagents
- Less human error
- Higher repeatability
- Quick system response
- Reduction of power consumption
- Parallel devices and faster processes leading to high throughput
- High rate of heat transfer in heat exchanger applications
- Safety, reliability, portability, and user-friendly devices.

One important advantage of the microfluidic devices is that miniaturized components and processes use smaller volumes of fluid, thus leading to reduced reagent consumption. This decreases costs and permits small quantities of precious samples to be stretched further (e.g., divided up into a much larger number of screening assays). Quantities of waste products are also reduced. The low thermal mass and large surface-to-volume ratio of small components facilitate rapid heat transfer, enabling quick temperature changes and precise temperature control. In exothermic reactions, this feature can help to eliminate the buildup of heat or “hot spots” that could otherwise lead to undesired side reactions. The large surface-to-volume ratio is also an advantage in processes involving support-bound catalysts or enzymes, and in solid-phase synthesis. Microfluidic devices sometimes enable tasks to be accomplished in entirely new ways. For example, fluid temperature can be rapidly cycled by moving the fluid among chip regions with different temperatures rather than heating and cooling the fluid in place. The laminar nature of fluid flow in microchannels permits new methods for performing solvent exchange, filtering, and two-phase reactions.

Many microfluidic technologies permit the construction of devices containing multiple components with different functionalities. An integrated chip could perform significant biological or chemical processing from beginning to end, for example, the sampling, preprocessing, and measurement involved in an assay. This is the kind of vision that led to the terms “lab-on-a-chip” (LOC) and “micrototal analysis system (μ -TAS)”. Performing all fluid-handling operations within a single chip saves time, reduces risk of sample loss or contamination, and can eliminate the need for bulky, expensive laboratory robots. Furthermore, operation of microfluidic devices can be fully automated, thus increasing throughput, improving ease of use, improving repeatability, and reducing the element of human error. Automation is also useful in applications requiring remote operation, such as devices performing continuous monitoring of chemical or environmental processes in inaccessible locations.

1.5.1 Importance of Flow through Microchannels

Nominally, microchannels can be defined as channels whose dimensions are less than 1 mm and greater than 1 μm . For channels of size greater than 1 mm, the flow exhibits behavior similar to that of macroscopic flows. For channels of size lesser than 1 μm , the flow is better characterized as nanoscopic. Most microchannels used today in various microdevices fall into the range of 30–300 μm . Microchannels are fabricated from glass, polymers, silicon, and metals by using various processes, that is, surface micromachining, bulk micromachining, molding, embossing, and conventional machining with microcutters. The advantages of microchannels are due to their high surface-to-volume ratio and their small volumes. The large surface-to-volume ratio leads to higher heat and mass transfer rates, making microdevices as excellent tools for compact heat exchangers. Microchannels are also used to transport biological materials such as (in order of size) proteins, DNA, cells, and embryos or to transport chemical samples and analytes. One successful example of the application of microchannels is in the area of bio-microelectromechanical systems (Bio-MEMS) for biological and chemical analyses. The primary advantages of microscale devices in these applications are good match with the scale of biological structures and potential for placing multiple functions for chemical analysis on a small area, that is, the concept of a “*chemistry laboratory on a chip*”. Flow rate in biological and chemical microdevices are usually much slower than those in heat transfer and chemical reactor microdevices.

1.5.2 Multiphase Microfluidics

In multiphase microfluidic systems, interfacial forces dominate over inertia and gravity. The first application is the generation of particles using fluid–fluid interfaces. Instabilities can occur at the interface between two fluids in motion because of the difference in shear velocities, which causes waves to propagate at the interface. This can lead to droplet breakup with correct geometric configuration. The second application is using gas–liquid interface for the enhancement of heat and mass transfer. Air bubbles inside a liquid-filled microfluidic channel elongate into plugs. These plugs are surrounded by thin liquid film, which causes the bubbles to move faster than the liquid creating a recirculating wave behind the bubble. This can be used to enhance the mixing and heat transfer inside the channel. The third application is using

solid–liquid interface for control of boiling. Single bubbles form and depart from the wall for nucleate pool boiling. The frequency and size of the bubbles can be influenced by the surface wet ability. By patterning surfaces with wetting and nonwetting regions, the growth of bubbles can be controlled to enhance the heat transfer.

1.5.3 *Microfluidic Applications*

In microfluidics, small volumes of solvent, sample, and reagents are moved through microchannels embedded in a chip. Current applications of microfluidics include detection and control of chemical reactions, sample preparation, various sensors (flow sensors, pressure sensors, and chemical sensors), actuators (microvalves, micropumps, and microfluidic amplifiers) for proper manipulation, control of flow in various microdevices as LOC and μ -TAS (total analysis system) for biological diagnostics, such as DNA analysis by means of PCR (polymerase chain reaction), and so on. The large surface-to-volume ratio makes microdevices as excellent tools for compact heat exchangers and fuel cells, which provide a powerful platform for thermal management of high power density microprocessors and cellular phones. The printing of text is achieved by a well-synchronized cooperation between a precisely manufactured set of micronozzles and a myriad of microelectronic circuits of an ink-jet printer.

In early days of microcomputing, computers were accessible to a limited part of the population. However, they are today commonly encountered in almost every sphere of life. It is expected that products based on microfluidics will be an integral part of our lives in the near future. The current trend in microfluidics is toward the development of integrated devices, which may transform our world in a manner similar to that of microelectronics.

A number of microfluidic applications in biology, analytical biochemistry, and chemistry have grown as a range of new components and techniques have been developed and implemented for delivering, mixing, pumping, and storing fluids in microfluidic channels. Many companies have ventured into developing microscale devices for chemical and biological analyses. Some of the applications of microfluidics are discussed in the following sections.

1.5.3.1 **Lab-on-a-Chip**

Lab-on-a-chip (LOC) is a term for devices that integrate (multiple) laboratory functions on a single chip of only millimeters to a few square centimeters in size. These devices are capable of handling extremely small fluid volumes down to less than picoliters. LOC devices are a subset of MEMS devices and often indicated as μ -TAS. Microfluidics is a broader term that also describes mechanical flow control devices such as pumps and valves or sensors such as flow meters and viscometers. In other words, “lab-on-a-chip” indicates generally the scaling of single or multiple lab processes down to chip format, whereas “ μ -TAS” is dedicated to the integration of the total sequence of lab processes to perform chemical analysis. The following processes can be performed with LOC:

- Real-time PCR; detect bacteria, viruses, and cancers.
- Biochemical assays.

- Immunoassay; detect bacteria, viruses, and cancers based on antigen–antibody reactions.
- Dielectrophoresis-based detection of cancer cells and bacteria.
- Blood sample preparation; can crack cells to extract DNA.
- Cellular lab-on-a-chip for single-cell analysis.
- Ion channel screening.

1.5.3.2 Microreactors

Microreactors are used to synthesize material more effectively than batch technologies. Microreactors are devices in which chemical reactions take place in a confinement with typical lateral dimensions less than 1 mm. The main feature of microstructured reactors is the high surface area-to-volume ratio in comparison to the conventional chemical reactors. Heat transfer coefficient in microchannel reactor is significantly higher than that of traditional heat exchangers. The high heat-exchanging efficiency allows to carry out reactions under isothermal conditions. In addition to heat transport, mass transport is also improved considerably in microstructured reactors. Process parameters such as pressure, temperature, residence time, and flow rate are more easily controlled in this reactor. Owing to enhanced mass transfer capability and controlled thermodynamics, microreactors can be effectively used to synthesize material.

1.5.3.3 Microdiluters

Microfluidic diluters (‘Microdiluters’) are systems in which solutions or liquid reagents are carried through a series of controlled dilutions and then used in assays. These diluters perform some of the functions of multiple well plate assays, but use smaller quantities of reagents, and are less labor-intensive. Microdiluters that perform multiple cycles of dilution are the microfluidic version of a multiwell plate. Two fluids are repeatedly split at a series of nodes, combined with neighboring streams, and mixed in a microdiluter system (Dertinger *et al.*, 2001).

1.5.3.4 Microarrays

Microfluidic systems consisting of crossed sets of microchannels provide a way of studying the interaction of a large number of molecules with proteins or cells in a combinatorial layout. A microfluidic chemostat with an intricate system of plumbing is used for growing and studying bacteria (Balagadde *et al.*, 2005). Ismagilov *et al.* (2001) described a combinatorial tool based on two layers of polydimethylsiloxane (PDMS) microfluidic channels bonded together at right angles to each other and separated by a thin membrane. The membrane permits chemical contact between the two layers of channels, while keeping small particles from crossing the two streams.

1.5.3.5 Biomedical Industry

Disposable blood pressure transducers have become an integral part of various biomedical devices, that is, respirators, lung capacity meters, medical process monitoring, kidney dialysis

equipments, and so on. Microchannels provide a convenient mechanism for treatment of cells – or portions of cells – with soluble reagents. Takayama *et al.* (2001) exposed selected regions of mammalian cells to fluids containing fluorescent dyes by positioning cells at the interface of two different streams of fluids flowing at low Reynolds number.

1.5.3.6 Micro Heat Exchangers

Micro heat exchanger technology exploits enhanced heat transfer resulting from structurally constraining streams to flow in microchannels, which reduces resistance to transferring heat. Fluid flowing through the channels on a plate may evaporate or condense, and heat is transferred. Micro heat exchangers have been demonstrated with high convective heat transfer coefficients (10,000–35,000 W/m²·°C, or about one order of magnitude higher than that typically seen in conventional heat exchanger) with low-pressure drops. This technology has high potential for mass production and can be used in a variety of applications, such as automobiles, commercial and residential heating/cooling, manufacturing, and electronics cooling.

1.5.4 Consumer Products

Various microdevices, that is, MEMS products, have also found applications in various consumer products, that is, sport shoes with automatic cushioning control, digital tire pressure gauges, smart toys, washers with water-level controls, and so on.

1.6 Microscopic Scales for Liquids and Gases

One of the basic scales of gas and liquid systems is the *size of the molecules*. The size of simple molecule is of the order of few angstroms. A second important scale is the *average distance between* molecules. Let us consider the intermolecular distance of air. The volume occupied by a single air molecule can be written as

$$l^3 = \mathcal{V}/N \quad (1.1)$$

where $\mathcal{V}$ is the volume of air containing N molecules. The length scale l can be represented as average intermolecular distance. The ideal gas law from kinetic theory of gases is

$$P\mathcal{V} = nRT = NK_B T \quad (1.2)$$

where n is the number of moles; R , the universal gas constant = 8.314 J/mol·K; K_B , the Boltzmann constant = 1.38066×10^{-23} J/K = R/N_A ; and N_A , the Avogadro's number = 6.0221×10^{23} /mol. Using the gas law, we have

$$l = \left(\frac{\mathcal{V}}{N}\right)^{\frac{1}{3}} = \left(\frac{K_B T}{P}\right)^{\frac{1}{3}} \quad (1.3)$$

For $P = 10^5$ Pa, $T = 300$ K, $K_B = 1.3807 \times 10^{-23}$ J/K, $l = 3.5$ nm.

Table 1.2 Typical values of mean free path of different gases at normal conditions

Gas name	λ (nm)
Helium	177
Argon	64
Nitrogen	60
Air	61

The typical intermolecular distance of liquids is 0.3 nm, which is 10 times smaller than that of air. For liquids, the intermolecular distance is *comparable* to the size of the molecule. For gases, the intermolecular distance is much larger than the *size of the molecule*.

The *mean free path*, λ is another fundamental scale necessary for describing the dynamical properties of gases. Mean free path is defined as the average distance traveled by the molecule between two successive collisions. Kinetic theory of gases establishes the following two expressions for the mean free path of gases.

$$\lambda = \frac{1}{\sqrt{2}\pi\rho a^2} = \frac{K_B T}{\sqrt{2}\pi P a^2} \quad (1.4)$$

where ρ is the density, that is, the number of molecules per unit volume, T is the temperature, K_B is the Boltzmann constant, P is the pressure, and a is the size of the molecule. At normal condition, the typical values of mean free path for different gases are given in Table 1.2. The above equation indicates that mean free path increases with an increase in temperature and decreases with an increase in pressure.

1.7 Physics at Micrometric Scale

One question arises while dealing with microscale systems, that is, is there anything extraordinary happening at this scale?

In a simple liquid, molecular sizes and intermolecular distances are of the order of nanometers, which is much smaller than the dimensions of any ordinary microsystem. In a *cubic micrometer* space, there are about 10^{12} atoms of tetradecane, which is sufficiently large to disregard the identity of atoms. The *thermodynamic fluctuations* can be neglected justifying the application of macrometer approach. In an *interface*, the ranges of intermolecular forces are no larger than 30 nm, which is smaller than the size of the micrometric systems. The above facts do not support any requirement of special attention to microscale systems. However, there are several microsystems, where the microscopic description must be amended. For *gas flows in microchannels*, the boundary condition need to be modified with an expression for the mean free path of the gas, which is not traditionally present in regular hydrodynamics problems. Boundary conditions for liquid flows in microsystems are not same as that in macrosystems because of various reasons, which are described in the next chapter. Similarly, surface tension forces, electrical forces, and magnetic forces are predominant in some

microsystems, necessitating special treatment compared to conventional macrosystems. Other examples are large molecules, that is, DNA or high-molecular-weight proteins that must be *individually treated* in a microsystem.

1.7.1 Macromolecules

Macromolecules are molecules containing a large number (few thousands or millions) of atoms, that is, proteins, DNA, polymers, and so on. Figure 1.4 represents three biological molecules of different sizes showing the difference in size between molecules and large macromolecules. The macromolecules *adopt different* shapes, that is, sheets, helices, and so on, depending on the *solvent type* and *temperature* in which they are immersed. Three geometric measurements are used to characterize the macromolecules.

Contour length (R_c) is the length of the macromolecules measured along its backbone. For example, a polymer having N monomers with separation distance between each of them equal to l , the contour length, R_c is given by

$$R_c = Nl \quad (1.5)$$

Contour length of a DNA molecule is the arc length of the backbone contour, that is, the distance we would travel if we move along the curved backbone from one end of the molecule to the other. *Radius of gyration* (R_g) is the average distance between the extremities of a frame around the macromolecules in a folded form. The radius of gyration of a DNA molecule is the statistical measure of the linear distances between different points on the DNA backbone. The following relationship represents the radius of gyration of a macromolecule as a function of number of atom, N making the molecule.

$$R_g \sim N^{\frac{1}{2}} \quad (1.6)$$


 Sugar, amino acids – 0.5–1 nm


 Globular proteins – 2–10 nm

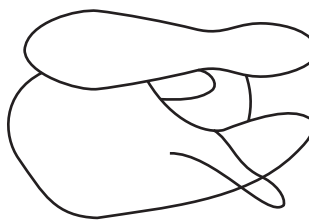

 Ribosome ~ 30 nm

Figure 1.4 Three molecules of different sizes

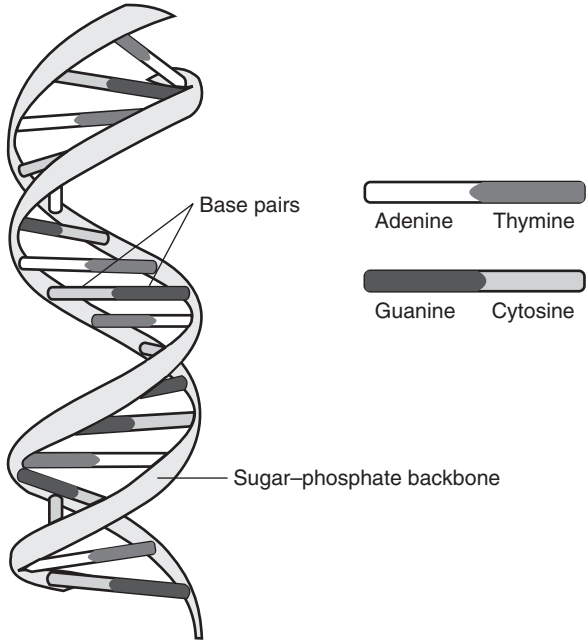


Figure 1.5 A sketch showing the double helical structure of DNA

Table 1.3 Comparison of contour length and radius of gyration for two different molecules (see Figure 1.5)

Molecules type	Contour length	Radius of gyration
DNA of a human chromosome	5 cm	1 μm
DNA of the bacteria <i>Escherichia coli</i>	1.5 mm	100 nm

Table 1.3 compares the size measure of two macromolecules. It shows the order of magnitude difference between the contour length and radius of gyration of a molecule.

1.8 Scaling Laws

Scaling laws are simple and are generally deduced at the macroscopic level. However, they can be used to understand the behavior of the micro and nano worlds. Scaling laws illustrate the fact that shrinking a body leads to not only size reduction but also different modifications of physical effects. Scaling laws are useful to analyze the *equilibrium points* in miniaturized systems, that is, the transformation in behavior when ordinary macrometric systems are miniaturized. Different physical quantities are related to the size l of the system. For an object having similar dimensions in order of magnitude in three spatial dimensions the length scale, l represents the

order of magnitude of the object size. For *anisotropic object* (length larger than width and height) l , should be the scale controlling all the dimensions of the system, that is, change in l should lead to corresponding change in other dimensions of the system maintaining same aspect ratios. Mass (M) and volume ($\forall$) can be related as

$$M \sim \forall \sim l^3 \quad (1.7)$$

The relationship between physical quantity under consideration and the object size, l may or may not be influenced by other physical quantities depending on the situations. Let us consider an example of fluid flow circulating through a microchannel at a fixed pressure difference. For a laminar flow, inside a tube of radius a , we have the flow rate Q as

$$Q = \frac{\pi a^4 \Delta P}{8 \mu L} \quad (1.8)$$

Thus, the order of magnitude of velocity inside the capillary can be written as

$$U \sim \frac{a^2 \Delta P}{\mu L} \quad (1.9)$$

where U is the average velocity, a is the transverse dimension, L is the channel length, μ is the fluid viscosity, and ΔP is the pressure difference applied along the channel length. For a fixed ΔP , a , and μ , we can write

$$U \sim l^{-1} \quad (1.10)$$

We note that for this situation, the average velocity is inversely proportional to the length of the channel. Similarly, keeping ΔP , μ , and L constant, we observe different relationships between the average velocity and the transverse dimension of the channel.

1.8.1 Application of Scaling Law to Natural System

Let us look into the small animals in nature. Animals in general eat food *proportional to their weight*, which is the source of chemical energy. We can assume the generation of thermal energy (Q_G) to scale as

$$Q_G \sim l^3 \quad (1.11)$$

The animals transfer heat toward outside. Assuming the heat transfer to take place through a layer of thickness δ and surface area A , the heat transferred per unit time, Q_R , by the animal is

$$Q_R = \frac{KA}{\delta} \Delta T \quad (1.12)$$

where K is the thermal conductivity of the surroundings and ΔT is the temperature difference between the animal body and the exterior. For constant value of K and ΔT , we can write the scaling law for heat transfer as

$$Q_R \sim l \quad (1.13)$$

For smaller organism (l is small) from equations (1.11) and (1.13), we have $Q_R > Q_G$. Therefore, it is necessary to compensate for thermal losses by eating food and to maintain the *internal*

temperature level. An example is *pygmy shrew* (second smallest mammal), which must eat at regular intervals to maintain its internal temperature at a fixed value for survival. It is like a live *jet engine*, *consuming* fuel and converting it to energy quickly. Therefore, small animals are not warm blooded. In contrast, larger animals have difficult time to get rid of the thermal energy. The *whale*, the largest mammal in earth, uses its blood circulation to transfer heat toward exterior. The arterial wall properties of whale are considerably different from other animals for enhancing the heat transfer. When *hunters* kill the whale, the blood circulation stops leading to the cessation of the heat exchange. This causes internal tissues to get cooked and the hunter prefers to cook the meat this way.

Another application of scaling law is *insects walking* on water surface. Gravitational force is associated with l^3 , and *surface tension force* is associated with l . Thus, at small scales, the surface tension force dominates in comparison to the gravitational forces. The gravitational force that tends to immerse the foot is compensated by the capillary force.

Note: One may think that in micro world, *automobile accidents* would not take place by collisions but by drops of water abandoned in the road. One may also be surprised not to have many machines driven by surface tension till now.

1.8.2 Scaling Laws in Microsystems

The dynamics of a microsystem depend on the relevant forces, that is, volume forces (gravity and inertia) and surface forces (viscous effect). The ratio of these two forces based on the scaling law is given by

$$\frac{\text{Surface forces}}{\text{Volume forces}} \sim \frac{l^2}{l^3} = l^{-1} \quad (1.14)$$

As l becomes smaller, the ratio approaches infinity. Hence, volume forces, which are prominent in real-life system, are unimportant in microfluidic system. The surface forces become dominant, and our intuition may not be valid at all situations in case of microsystem. Some examples are provided in the following sections to clarify this point.

1.8.2.1 Parallel-Plate Capacitor

The capacitance C of a parallel-plate capacitor, with plate area equal to A , voltage difference between the two plates V , and separation distance d , is given by

$$C = \frac{\epsilon A}{d} \quad (1.15)$$

where ϵ is the permittivity of the medium. The electrostatic energy stored in the parallel-plate capacitor is

$$W_e = \frac{1}{2} CV^2 = \frac{\epsilon AV^2}{2d} \quad (1.16)$$

Force used to displace one of the plates leads to a gradient of the energy given as

$$F = -\frac{dW_e}{dZ} = \frac{\epsilon AV^2}{2d^2} \quad (1.17)$$

where Z is the axis perpendicular to the plate.

Using $V = Ed$ where E is the electric field, we have

$$F = \frac{\epsilon AE^2}{2} \sim \epsilon E^2 l^2 \quad (1.18)$$

Hence, for constant electric field E and fixed environment, we have

$$\text{Electrostatic force} \sim l^2 \quad (1.19)$$

Note: (1) Gravitational and inertia forces vary as l^3 . The above equation indicates that the electrostatic force is dominant over gravitational and inertia forces for microsystems. Therefore, electric field can be used to exert *rapid acceleration* in microsystems. The weak inertia allows detection of sudden impacts involving automobiles and the microsensor using parallel-plate capacitor, which can be used as an *excellent accelerometer* for air bag.

(2) Miniaturization also helps in *preventing electric discharge* inside the parallel plates of the sensor. The sudden imposition of electric field between two electrodes can lead to the formation of sparks because of *ionization of gas molecules* situated between the two electrodes. A large number of electrons are liberated and electric current flows between the two electrodes. There is a simultaneous luminous emission known as *electric arc*. Generally, under normal conditions, the breakdown electric strength for air is of the order of 30 kV/cm. In miniaturized systems, much higher electric field can be produced without the generation of an electric arc.

Figure 1.6 shows the electric field breakdown voltage of air as a function of the pressure–separation distance product. It shows that at large values of pressure–distance product, the breakdown electric field strength is approximately equal to 30 kV/cm. At small values of this product, the breakdown electric field strength increases significantly. This phenomenon is due to the *rarefaction effect*. When the mean free path becomes comparable to

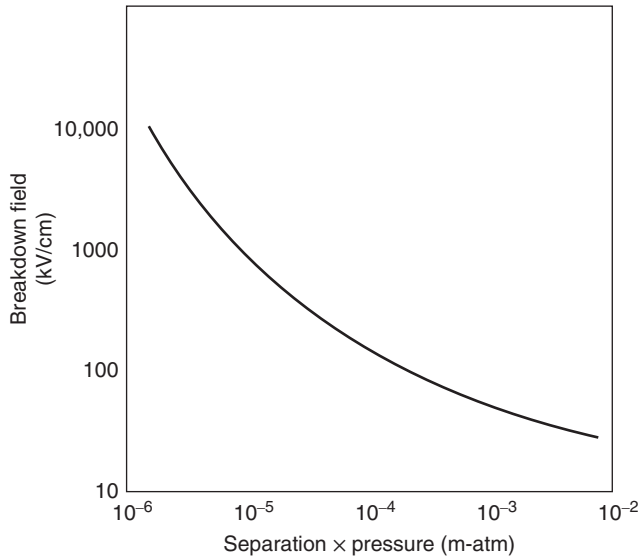


Figure 1.6 Electric field strength for dielectric breakdown of a parallel-plate capacitor in air

the distance between the electrodes, the majority of collision takes place between the gas and the electrode surface and not within the gas. This inhibits the formation of electric discharge in the gas.

1.8.2.2 Thermal Inertia of Chemical Reactor

The temporal heat flux ($q(t)$) associated with a variation of temperature dT during time period dt is given as

$$q(t) = \rho C_p \frac{dT}{dt} \quad (1.20)$$

where ρ is the density and C_p is the specific heat at constant pressure. Suppose that the heat flux is attained by an external heat source of higher temperature by conduction. The heat flux will have a corresponding heat transfer given as

$$q(t) = -K\nabla^2 T \quad (1.21)$$

Thus, combining these two equations, the time constant for this process can be written as

$$\tau \sim \frac{\rho C_p l^2}{K} \sim \frac{l^2}{\alpha} \quad (1.22)$$

where α is the thermal diffusivity of the material. This expression shows that *miniaturization lead to lower time constant*. Hence, miniaturized system subjected to a sharp temperature change can reach thermal equilibrium faster when compared to the macrosystems. This characteristic is very useful for *chemical sciences and engineering* applications. Many reactions of chemical processes are dependent on precise control of thermal conditions. Improper thermal control leads to development of *unwanted parasite reactions*. Miniaturization improves the *selectivity* of the process output.

1.8.2.3 Microscale Heat Exchanger

The heat produced by chemical reaction in a microcombustor (Q_V) can be expressed as

$$Q_V \sim l^3 \quad (1.23)$$

The heat transfer from the combustor (Q_R) can be estimated based on the Fourier law as

$$Q_R = \frac{KA\Delta T}{l} \quad (1.24)$$

where A is the area, ΔT is the temperature difference, and K is the thermal conductivity. We can write the following scaling law for conductive heat loss.

$$Q_R \sim Kl\Delta T \sim l \quad (1.25)$$

The above scaling law shows that the exponent for volumetric heat generation is higher than the heat evacuated by conduction indicating that $Q_R > Q_V$. Thus, *micro heat exchangers* are very effective in miniaturized systems for transport of combustion energy. One can correlate this to a microscale power plant where the role of boiler for transferring heat from combustion becomes very efficient due to its small scale.

1.8.2.4 Microdroplets

Droplets are present in many engineering systems, that is, fuel injection system, LOC system, and so on. The evaporation of a drop of diameter d at time t is governed by D^2 law, that is,

$$d^2 = d_0^2 - \beta t \quad (1.26)$$

where d_0 is the initial diameter and β is a constant independent of the drop size.

The time τ for the drop to disappear, that is, $d = 0$, is given by

$$\tau = \frac{d_0^2}{\beta} \sim l^2 \quad (1.27)$$

The above-mentioned scaling law indicates rapid evaporation of droplets in microsystems because of smaller time constants in comparison to the larger droplets. This can be a disadvantage for LOC applications involving the transport of a small amount of liquids because of the loss of liquid by evaporation during transport. However, it can be an advantage in microcombustor applications, where the evaporation of droplets takes place rapidly.

1.8.2.5 Miniaturized Resonator

Micromechanical resonator has emerged as a promising component for rapidly developing *telecommunication systems*. These resonators also have a wide range of *sensing applications*. High-frequency resonators can use *capacitive or piezoelectric transduction*. To understand the importance of miniaturization, let us consider a cantilever beam. The natural frequency of the beam is given by the relation:

$$f \approx \frac{hC}{2\pi L^2} \quad (1.28)$$

where h is the thickness of the beam, L is its length, and C is the speed of sound in the beam. Thus, the scaling law can be expressed as

$$f \simeq l^{-1} \quad (1.29)$$

This expression indicates that resonance frequency of the system increases as its size reduces. A silicon beam of 1 μm thick and 3 μm long where $C \simeq 7470$ m/s has a resonant frequency equal to $f \simeq 132$ MHz. This value is well suited for radiofrequency applications. However, a larger silicon beam of 1 mm thick and 3 mm long will have resonant frequency equal to 132 kHz.

1.8.3 Scaling Laws Limitation

Scaling laws are simple. However, the conclusion based on scaling is not always directly applicable to microsystem. Let us consider an example of mixing in microsystems. The question is whether mixing time can be reduced in microfluidic system by agitating the fluids. This can be answered using the mixing timescale by convection and diffusion mechanisms. We can write the *hydrodynamic transport time* as

$$\tau_a \sim \frac{l}{U} \sim l^0 \quad (1.30)$$

where l is the length scale and U is the speed.

The *molecular diffusion time* is

$$\tau_D \sim \frac{l^2}{D} \quad (1.31)$$

where D is the diffusion coefficient. For constant diffusivity coefficient D , we can write

$$\tau_D \sim l^2 \quad (1.32)$$

Comparing the equations (1.30) and (1.32) for a microsystem, we have

$$\tau_a \gg \tau_D \quad (1.33)$$

This expression indicates that it is *useless to agitate* the fluid in order to enhance the mixing process.

We can also use the complete expression instead of scaling laws as

$$\frac{\tau_D}{\tau_a} = \frac{Ul}{D} = \text{Pe} \quad (\text{Peclet number}) \quad (1.34)$$

Let us take an example of mixing fluorescein with water ($D = 3 \times 10^{-6} \text{ cm}^2/\text{s}$). For a microsystem with $l \sim 100 \text{ }\mu\text{m}$ and $U \sim 30 \text{ }\mu\text{m/s}$, the Peclet number is equal to 10. Thus, $\tau_D > \tau_a$, which is contrary to equation 1.33. This indicates that *diffusion phenomenon is much slower* than hydrodynamic transport phenomenon, which is contrary to what was suggested based on the scaling analysis. Hence, the scaling laws cannot be used blindly. It provides an estimate of the process, which need to be verified from the exact analysis.

1.9 Shrinking of Human Beings

A famous movie named “The Fantastic Voyage” by Richard Fleischer in 1966 used the concept of shrinking human beings. In this movie, a submarine and its human occupants are shrunk to the size of a few hundred micrometers. They are then injected into the body of a Czech scientist for repairing some brain problem. Based on the movie, the question is what would be our shape to survive under such conditions? Are we going to have the same concept of *good-looking* boys and girls?

Let us consider shrinking the body size by a factor of 10^3 . The weight of the body will decrease by a factor of 10^9 . In order to support this weight, the diameter of the bone has to be reduced to a comparable factor. The weight of the body should be balanced by the maximum stress limit (σ) of the bone as

$$\sigma \sim \frac{mg}{A} \quad \text{or} \quad \sigma A \sim mg \quad (1.35)$$

For a given material, σ is constant. Therefore, the diameter d of the supporting material, that is, bone, can be estimated based on the above-mentioned equation as

$$d^2 \sim L^3 \quad \text{or} \quad d \sim L^{3/2} \quad (1.36)$$

Therefore, the diameter of the bone has to decrease by a factor upto $10^{9/2} \simeq 3.16 \times 10^4$. Thus, the diameter of the legs should be comparatively much smaller than the size. For such a

small size of the foot, the adhesion force of the feet on the ground would be more important than the gravitational force. Human beings will adhere to the ceiling *similar to insects*. Therefore, the dimensions of the feet would have to be similar to small points in order to move on the ground. This will lead to stability problem. Human beings will require at least *four legs* instead of walking on two legs.

The other critical issue is the vision. The minimum diameter of the irradiated zone is given by $L = 2\lambda/\pi\text{NA}$ where NA is the numerical aperture. Numerical aperture (NA) is a dimensionless number, which is used to characterize the range of angles over which an optical system can accept or emit light. It is defined as $\text{NA} = n \sin \theta$, where n is the index of refraction of the working medium and θ is the half angle of the maximum cone of light that can enter or exit the lens. In case of monochromatic light such as laser beam, θ is considered as the divergence of the beam and $\text{NA} \simeq \frac{\lambda}{\pi w_0}$, where $2w_0$ is the diameter of the beam at its narrowest spot. Hence, the wavelength of illumination $\lambda \sim L$, that is, the same order of magnitude as the diameter of the lens. Hence, the eye would have to look at the wavelength of emitted light of 10^{-3} times that of visible light, that is, X-rays. We know that the absorption length of X-rays in living matter is of the order of few centimeters compared to few micrometers for visible light. Thus, the thickness of the eye should be larger than the length of the body.

Problems

- 1.1 Based on the scale analysis, estimate the ratio of surface force to volume force for a reservoir of $1\text{ }\mu\text{m}^3$ volume with that of 1 mm^3 volume.
- 1.2 Compare the ratio of electrostatic force to inertia force of an automobile air bag using an accelerometer based on parallel-plate capacitor with separation distance of 1 mm between the two plates with that of separation distance of 10 μm .
- 1.3 A 1-mm-diameter methanol droplet takes 1 min for complete evaporation at atmospheric condition. What will be the time taken for a 1- μm -diameter methanol droplet for complete evaporation at same conditions based on the scaling analysis?
- 1.4 If the mean free path of air at $P = 10^5\text{ Pa}$, $T = 300\text{ K}$ is equal to 61 nm, what will be the mean free path if the temperature of air is raised to 600 K?
- 1.5 What is the natural frequency of a microcantilever (thickness: 10 μm and length: 30 μm) used in a piezoelectric transducer? The speed of sound in the beam is equal to 8000 m/s.

References

- Balagadde FK, You LC, Hansen CL, and Arnold FH 2005 Quake SR: long-term monitoring of bacteria undergoing programmed population control in a microchemostat. *Science*, **309**, pp. 137–140.
- Dertinger SKW, Chiu DT, Jeon NL, and Whitesides GM 2001 Generation of gradients having complex shapes using microfluidic networks. *Anal. Chem.*, **73**, pp. 1240–1246.

Ismagilov RF, Ng JMK, Kenis PJA, and Whitesides GM 2001 Microfluidic arrays of fluid-fluid diffusional contacts as detection elements and combinatorial tools. *Anal. Chem.*, **73**, pp. 5207–5213.
Takayama S, Ostuni E, LeDuc P, Naruse K, Ingber DE, and Whitesides GM 2001 Subcellular positioning of small molecules. *Nature*, **411**, pp. 1016.

Supplemental Reading

Gad-el-Hak M 2000 *Flow Control, Passive, Active and Reactive Flow Management*. Cambridge University Press.
Nguyen NT and Wereley ST 2006 *Fundamentals and Applications of Microfluidics*. Artech House, Inc.
Tabeling P 2005 *Introduction to Microfluidics*. Oxford University Press.

