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Joseph Wang

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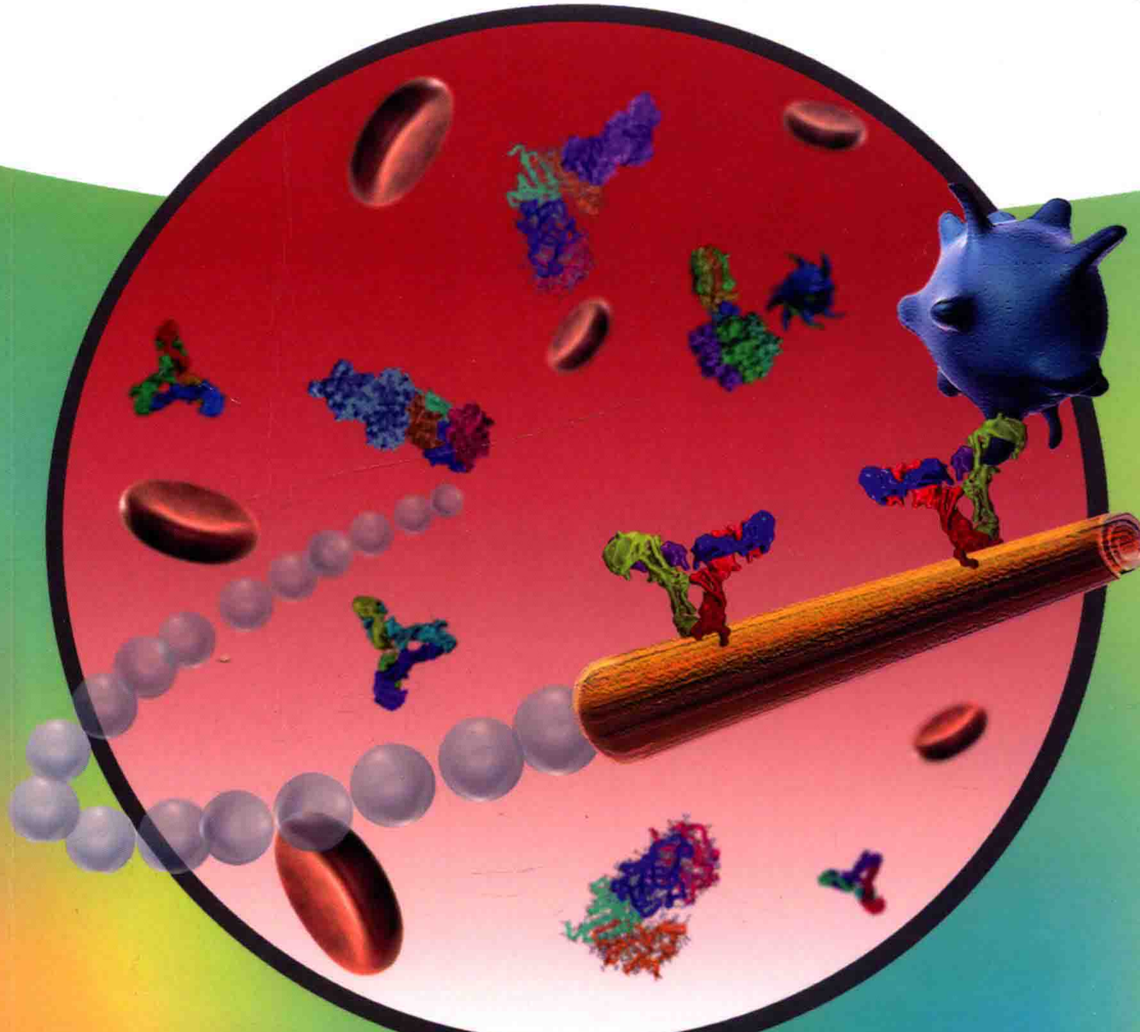
Fundamentals and Applications



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Preface

The development of synthetic nanoscale motors, capable of converting energy into movement and forces, represents one of the most fascinating topics of nanotechnology. Such motion of nanoscale objects through fluid environments is of considerable interest both fundamentally and practically, and has thus stimulated substantial research efforts. Research groups around the world are actively pursuing the dream of designing synthetic nanomachines that mimic biological motors and perform demanding tasks such as transporting therapeutic cargo and assembling nanostructures and devices.

Making a nanoscale motors has been a dream of many researchers in the field since the late 1950s and 1960s. Richard Feynman, Nobel Laureate in Physics, first suggested molecular-scale mechanical nanomachines in a famous lecture at the 1959 Meeting of the American Society of Physics entitled "There is plenty of room at the bottom." The idea of tiny machines that can perform such complex operations has been a major part of science fiction since the 1966 movie the *Fantastic Voyage*. In this movie, medical personnel boarded a submarine that was shrunk to microscopic size and entered the bloodstream of a wounded diplomat to save his life.

The *Fantastic Voyage* vision and challenge are currently being addressed in an interdisciplinary research activity across the globe involving the design of new functionalized nano/microscale motors that rely on different propulsion mechanisms and advanced schemes for navigating them toward their destination.

Movement is essential for life in the nanoscopic and macroscopic scales. For example, animals run away fast from dangers while protein nanomotors shuttle cargo along intracellular microtubule tracks. Such tiny biomotors display remarkable motion capabilities, with an advanced directional movement and speed regulations. The sophisticated operation of biological nanomotors has inspired scientists and engineers to design artificial nano/microscale machines, with enhanced functionalities and capabilities, and address the challenge of converting nature-inspired swimming mechanisms into man-made nanoswimmers. Researchers have turned to nature, especially to microorganisms, for inspiration, resulting in artificial nano/microscale swimmers that emulate these natural swimmers and molecular biomotors. Understanding the remarkable underlying principles of nature's remarkable biomotors has thus provided researchers with new insights into how to impart greater sophistication onto the design and operation of new artificial nanomachines. Although the research in the area is at its infancy, major scientific and technological advances have already led to substantial progress over the past decade toward addressing the major challenges of scaling of conventional machine designs to nano/microscale dimensions and providing these tiny machines with power.

Synthetic nanomachines hold great promise for major advances in diverse applications, meeting a wide range of future technological and biomedical needs and providing unlimited possibilities based on one's imagination. Artificial nanoscale and microscale machines could thus perform different functions, similar to nature nanomotors found in living cells, including transporting molecules or facilitating chemical reactions by pumping protons through membranes. Recent progress in the field of self-propelled man-made nano/microscale machines has led to major advances in the power, efficiency, directionality, motion control, functionality, and versatility of such synthetic nanomotors. Nano/microscale machines hold great promise for performing diverse operations and important tasks that include directed drug delivery, biosensing of nucleic acids or proteins, cell sorting, micropatterning, nanosurgery, exploring hazardous situations, and micromanipulation. This exciting area of research is thus expected to make important contributions to diverse fields with the new powerful machines, leading to new capabilities that are currently beyond our reach and bringing major benefits to our quality of life.

My goal is to convey a realistic picture of the latest advances in the design and operation of nano/microscale machines, and to promote activity across the field of small-scale motors toward the development of advanced machines, capable of performing different important tasks that are beyond our current reach. The book is suitable for a graduate-level course in nanomachines or as a supplement to high-level undergraduate courses in nanoengineering, nanoscience, or nanotechnology. It should also be extremely useful to those considering the use of nanomotors in their laboratories and to researchers in the areas of nanobiotechnology, nanomedicine, and nanoengineering, in general. Given the interdisciplinary nature of this exciting topic, I have tried to make the book a self-contained starting point for the interested student, scientist, or engineer.

The material is presented in seven roughly equal chapters. Chapter 1 is devoted to fundamental aspects and challenges of nanoscale motion. Chapter 2 discusses natural (biological) nanoswimmers, while Chapter 3 gives an overview of molecular and DNA machines. Chapter 4 is devoted to chemically powered catalytic nanomotors. Chapter 5 discusses fuel-free externally actuated (magnetically, electrically, ultrasound driven) nanomotors. Chapter 6 focuses on diverse potential applications of nano/microscale machines, ranging from drug delivery to target isolation, while the final Chapter 7 discusses future prospects, opportunities, and challenges.

I hope that you will find the content of the book highly useful, and I look forward to new exciting developments that the work described in this book is likely to inspire.

Finally, I wish to thank my wonderful wife, Ruth, for her great patience, love, and support; to Wei Gao, On Shun Pak, Allen Pei and other members of the UCSD nanomotor team for their help; the editorial and production staff of Wiley-VCH for their support and help; and to numerous scientists and engineers across the globe who led to the remarkable advances and to the *Fantastic Voyage* reported in this book. Thank you all!

San Diego, USA
January 2013

Joseph Wang

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1.1
Introduction

The motion of natural and synthetic nanoscale and microscale objects has been of considerable fundamental and practical interest and has thus stimulated substantial research activity. Using nanoscale and microscale machines to perform mechanical operations represents an exciting research area. Nature has provided tremendous inspiration for designing artificial nanoscale motors and has developed powerful nanoscale biomotors through millions of years of evolution. Yet, the development of synthetic nanomotors that mimic the function of nature's amazing biomotors is only in its infancy. Scientists and engineers have been pursuing aggressively the development of advanced artificial nanomachines for only about a decade. Such development represents a major challenge when trying to mimic the essential functions of natural motors while keeping the complexity low. Synthetic nano- and microscale motors, capable of converting energy into movement and forces, represent one of the most exciting challenges facing nanotechnology (Ebbens and Howse, 2010; Fischer and Ghosh, 2011; Mallouk and Sen, 2009; Mei *et al.*, 2011; Mirkovic *et al.*, 2010; Ozin *et al.*, 2005; Paxton *et al.*, 2006; Peyer *et al.*, 2013; Pumera, 2010; Sengupta, Ibele, and Sen,, 2012; Wang, 2009; Wang and Gao, 2012). Recent activity in microtechnology and nanotechnology has allowed researchers to explore the microfabrication of devices capable of propulsion at the micro- and nanoscale. Powerful self-propelled and externally powered artificial nanomotors have thus been developed. Such synthetic nanomachines already offer an advanced performance, functionality, and capabilities along with a precise (spatial and temporal) remote motion control, and hold considerable promise for numerous transformative practical applications (Manesh and Wang, 2010; Nelson, Kaliakatsos, and Abbott, 2010; Peyer, Zhang, and Nelson, 2013; Sengupta, Ibele, and Sen, 2012; Wang and Gao, 2012).

As their name implies, nanomachines are extremely small devices. Their size is measured in nanometers (a nanometer is one-billionth of a meter), and can reach hundreds of nanometers. Larger microscale machines have size ranging from 1 to 100 μm (a micrometer is one-millionth of a meter). Such microscale machines are also covered extensively in this book, particularly in Chapters 4–6.

Nanomachines: Fundamentals and Applications, First Edition. Joseph Wang.

Central to any molecular machine or micromachine is the motor component responsible for generating the mechanical energy. At the heart of every machine is its motor. *The Oxford Dictionary of English* defines a motor as "a thing that imparts motion"; work as "the operation of a force in producing movement or other physical change"; and motion as "the condition of a body, when at each successive point in time it occupies a different position or orientation in space." A motor is the most important part of the machine as it generates the necessary power and movement by cyclically converting various energy forms (e.g., chemical, electrical, or thermal energy) into mechanical work.

This monograph will cover the generation and control of motion at the nano- and micrometer scales, including single- and multimolecule synthetic and natural motors, and particularly chemically powered and externally triggered synthetic microscale devices. The design, propulsion, and guidance of these tiny motors will be discussed along with diverse motor applications in solution and in engineered systems, and motor-driven transport systems.

Designing a self-propelling micro/nanoscale object is not a simple task because as the size decreases, the influence of Brownian collisions, viscous drag, and various surface phenomena becomes dominant. Novel strategies of supplying power (or fuel) to micro/nanoscale devices are thus required to promote their propulsion. Traditional on-board power supplies, for example, batteries, cannot be scaled to these tiny dimensions. Accordingly, two main approaches have been proposed to address this challenge, including the use of external energy fields and harvesting energy from the surrounding environment. Two classes of nano/microscale motors have thus been demonstrated to date; the first – driven primarily by deformations – requires actuation by external fields; the second is fully autonomous and powered by the asymmetric surface catalytic decomposition of solution-borne fuel molecules. These micro/nanomotors can thus be classified into two broad categories: externally powered propellers and chemically powered motors.

New nanomotors with diverse capabilities and functionalities are currently being developed by multiple research teams around the globe. This exciting research area is expected to grow rapidly as additional technological breakthroughs emerge and as nanomachines demonstrate increased capabilities and functionalities. These developments and capabilities will lead to a wide range of practical real-world applications, such as targeted drug delivery, microsurgery, nanoscale assembly or patterning, environmental remediation, biosensing, or cell sorting (Mallouk and Sen, 2009; Mei *et al.*, 2011; Mirkovic *et al.*, 2010; Nelson, Kaliakatsos, and Abbott, 2010; Peyer, Zhang, and Nelson, 2013; Sengupta, Ibele, and Sen, 2012; Wang, 2009; Wang and Gao, 2012). Similar to the dramatic evolution in electronics, from the pocket calculator of the 1960s to the latest iPhone 5, we expect to see a very fast evolution of present nano/microscale machines into sophisticated multifunctional nanovehicles that can perform advanced and demanding operations and multiple complex tasks. Yet, in terms of miniaturization, propulsion mechanisms have not followed the remarkably fast scaling-down in size of electronics over the past 50 years – described by Moore law – owing to major challenges to nanoscale locomotion (described in Section 1.3). Nevertheless, nanomachines are expected to lead to new and exciting capabilities that are currently beyond our reach, and will provide unlimited opportunities based on one's imagination.

1.2 Nanomachines History

The implications of inertia-less to the realization of self-propulsion were recognized already in 1930 (Ludwig, 1930). The invention of dark field microscopy around the same time allowed observations of flagella and cilia. Back in 1951 Taylor wrote a historic paper on the swimming of microorganisms, discussing how force-free swimming is possible in a viscous medium and proposing a two-dimensional sheet as a model for flagellated cells passing traveling waves as a means of locomotion (Taylor, 1951). In 1973, Berg proved that *Escherichia coli* bacteria use molecular motors to rotate their helical flagella, following which helical propulsion has become an active area of research. The challenges facing microorganisms attempting to propel themselves in low Reynolds numbers regime were summarized later by Purcell in his landmark 1977 paper (Purcell, 1977).

Scientists (and science-fiction writers) have contemplated nanomachines at least since the late 1950s, when physicist Richard P. Feynman considered the scale limits for machines during his famous lecture "*There is plenty of room at the bottom*" at the 1959 Meeting of the American Society of Physics (Feynman, 1960). In the 1966 movie *Fantastic Voyage* by Harry Kleiner and a book by Issac Asimov, a team of scientists board a submarine that shrinks to a micrometer size and enters the bloodstream of a wounded diplomat to destroy a life-threatening blood clot and save his life. Despite the waves of blood that rocked the sub with every heartbeat, and antibodies that attacked it as an infection, the scientists were able to navigate their submarine through the blood stream and succeed in saving the man's life. Feynman's idea and the vision of *Fantastic Voyage* remained largely undiscussed until the mid-1980s when Eric Drexler published the book *Engines of Creation*, which introduced the term nanotechnology and promoted the potential of molecular nanotechnology and nanomachines (Drexler, 1986). According to Drexler, the ultimate goal of nanomachine technology is the production of the "assembler," which is a nanomachine designed to manipulate matter at the atomic level.

Pioneering contributions by Fraser Stoddart, Ben Feringa, Vincenzo Balzani, and others during the late 1990s led to a rapid progress in the development of autonomous molecular systems and shuttles that can execute complex actions (Balzani *et al.*, 2000; Koumura *et al.*, 1999). Active research toward understanding the operation of natural biomotors has been followed by the use of protein motors for nanoscale transport in engineering microchip systems (Hess and Vogel, 2001; Soong *et al.*, 2000). Autonomous and stimuli-induced DNA nanomachine systems (tweezers, walkers, gears) were introduced in the early 21st century (Chen, Wang, and Mao, 2004; Yan *et al.*, 2002; Yurke *et al.*, 2000).

Extensive efforts over the past decade have resulted in synthetic nano/microscale motors that achieve their movement and directionality in different ways. Chemically powered propulsion was demonstrated first by Whiteside's team in 2002 (Ismagilov *et al.*, 2002), whereas the self-propulsion of catalytic nanowire motors was demonstrated in 2004 and 2005 (Fournier-Bidoz *et al.*, 2005; Paxton *et al.*, 2004). Since these pioneering studies, the number of publications in this field has grown rapidly and substantially. Magnetically and electrically propelled artificial nano/microscale objects were described in 2009 (Zhang *et al.*, 2009a, 2009b; Chang *et al.*, 2007; Calvo-Marzal *et al.*, 2009). Catalytically active Janus particles and bubble-propelled tubular microenegines were introduced in 2007 and 2008, respectively (Howse *et al.*, 2007; Mei *et al.*, 2008). The first demonstrations of micromotors transporting therapeutic payloads or sensing their surroundings were reported in 2010 (Kagan *et al.*, 2010a; Kagan *et al.*, 2010b). The use of ultrasound to drive the movement of nano/microscale objects was demonstrated in 2012 (Kagan *et al.*, 2012; Wang and Gao, 2012; Wang *et al.*, 2012). Given the continuous flow of innovative ideas, this exciting area of research is expected to make important contributions to diverse fields, and continue to be one of the most fascinating topics in nanotechnology in the foreseeable future.

1.3 Challenges to Nanoscale Propulsion

Motion of nanoscale objects through fluid environments represents a major challenge confronting nanotechnology. Specifically, achieving micro/nanoscale propulsion in fluid is challenging due to the absence of inertial forces, which we all exploit for swimming at the macroscopic scale. Considering the fluid behavior on these small length scales, it is apparent that scaling of conventional machine designs to nano/microscale dimensions, and providing these tiny machines with power, face a number of major challenges. These challenges are responsible for the slow scaling down of artificial swimmers during the 20th century. In particular, due to the absence of inertial effects, miniature devices cannot propel using conventional swimming mechanisms involving gliding between time-reversible movements. This was famously visualized by a single-hinged miniature "scallop" achieving no net progress by symmetrically flapping its arms (Purcell, 1977). The difficulties have been summarized by Purcell's famous "scallop theorem" (Purcell, 1977) (discussed later in this section), which states that a reciprocal motion – based on time-reversal symmetry (i.e., a periodic back and forward displacement) – cannot lead to any net displacement and hence directed movement of tiny objects.

Another key factor and challenge to nanoscale motion through liquid environments is the dominance of Brownian motion, named after the English botanist Robert Brown. Brownian motion involves the random (irregular) movement of microscopic particles suspended in a liquid, caused by thermally driven collisions with molecules of the surrounding solvent. These collisions can alter the trajectory of moving nano/microscale motor particles and hence represent a challenge for imparting directionality on such objects. Such motion is independent of the chemical makeup and physical density of the particle. Brownian motion cannot be avoided and it depends on the temperature. Such motion is related to the macroscopic measurement of diffusion characterized by the diffusion coefficient D. The diffusion of a purely Brownian particle in one dimension (x) over time (t) is given by

$$\langle x^2 \rangle = 2Dt \tag{1.1}$$

Displacement of an object can thus be estimated. Unlike the movement of macroscopic motor particles, achieving directed propulsion of nanoscale objects through liquid environments requires overcoming the major difficulties posed by both the relatively strong Brownian noise and negligible inertia.

A better understanding of the role of inertia in nanoscale movement can be obtained by using the Reynolds number (Re). The Reynolds number is a dimensionless parameter that refers to the relative scales of the object, its inertial forces, and the viscous forces. This number is named after the British engineer Osborne Reynolds who proposed it in 1883. The Reynolds number represents the ratio of momentum to viscosity:

$$Re = \rho UL/\mu = UL/\nu = \text{Inertial forces/Viscous forces} \tag{1.2}$$

where ρ is the density of the fluid (kg/m^3), μ the dynamic viscosity of the fluid, whereas U refers to the velocity of the object relative to the flow, L is the characteristic dimension of the object, and ν is the kinematic viscosity. The Reynolds number thus measures the significance of inertial forces relative to the viscous forces. If the Reynolds number is large, then inertia dominates. When the Reynolds number is very low, which could be due to small size and/or high viscosity, then hydrodynamics is governed by viscous forces.

As expected from Eq. (1.1), the extremely small dimension (L) of nanoscale objects leads to very small Reynolds numbers (Figure 1.1). Size affects the modes of motion long before reaching the nanoscale. Viscous forces dominate even at the mesoscopic dimensions of bacteria. For example, for the *E. coli* bacterium swimming in water (L ~1–10 μm; U ~10 μm/s; ρ ~10^3 kg/m^3), the Reynolds number is 10^{-5} to 10^{-4} (Figure 1.1b). In contrast to large-scale swimmers, the world of micro- and nanoscale swimmers is thus dominated by viscosity while inertial forces are negligible. The absence of inertial effects at the low Reynolds number regime rules out propulsion by a conventional swimming mechanism that cannot lead to any net displacement and hence to actual movement. Since the physics that governs mechanical dynamic processes in the two size regimes is completely different, macroscopic and nanoscale motors require fundamentally different mechanisms for controlled transport or propulsion. Movement of nano/microscale objects at this inertia-less limit (low Re number) regime thus requires the use of swimming strategies that are largely different from the flapping-like (time-reversible) symmetric strategies used by larger macro-scale swimmers (Purcell, 1977; Vandenberghe, Zhang, and Childress, 2004; Lauga and Powers, 2009).

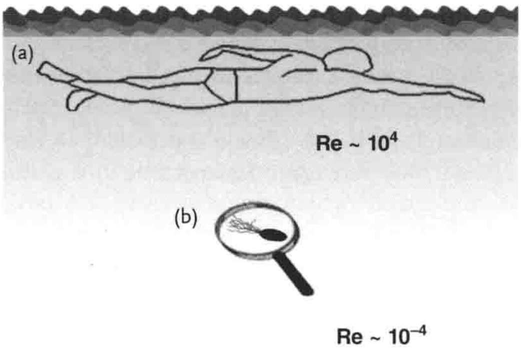

Figure 1.1 The extremely small dimension of micro/nanoscale swimmers leads to very small Reynolds numbers and requires the use of different swimming strategies that are largely different from those used in the macroscale world. When the Reynolds number is very low due to tiny dimensions, hydrodynamics is governed by viscous forces (even in water which is not viscous fluid).

In his famous lecture and the subsequent 1977 paper *Life at Low Reynolds Number*, Purcell described how a nonreciprocating motion is required for a net displacement, and proposed his "scallop theorem" (Purcell, 1977) delimiting the types of swimmer designs that are not effective on small scales. The Purcell's scallop theorem can be stated as follows: if the sequence of shapes displayed by the swimmer is identical to the sequence of shapes displayed when seen in reverse – the so-called reciprocal motion – then the average position of the body cannot change over one period. No net translation is expected from a reciprocal motion, such as opening and closing of the "scallop" when swimming at low Reynolds numbers. This implies that swimming motions that are symmetric with respect to time reversal (i.e., a reciprocal motion) cannot lead to net displacement and cannot be used for locomotion of small-scale swimmers. As illustrated in Section 1.4, the inertia-less equations governing the surrounding fluid are linear and independent of time on very small scales (Stokes equation). Hence, any actuation on the fluid remaining identical under time reversal (reciprocal actuation) cannot generate any net motion.

The main message of Purcell's paper is that tiny swimmers should deform their shapes with time in a nonreciprocal fashion in order to generate net motion (Lauga, 2011). A unique feature of propulsion of these microscale objects, compared with their macroscopic counterparts, is that a body striving to move must change its shape with time in a nonreciprocal fashion. The requirement of nonreciprocal body deformations adds significant complication to the design of tiny machines. Small swimmers thus require a different class of shape changes compared with their larger counterparts (Figure 1.1). To overcome the viscous drag forces at the low Reynolds number regime, nano/microscale swimmers must execute nonreciprocal motion, that is, require breaking of time-reversibility and