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INTRODUCTION

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Multiscale physical problems, with important features across multiple length and time scales, are becoming increasingly prevalent in the computational sciences. The term *multiphysics* is used to describe problems in which different physical mechanisms are dominant at different length scales. For example, as one moves to the nanoscale, the roles of surface forces and thermal fluctuations become increasingly important. Multiscale problems encompass diverse fields such as mathematics, chemistry, physics, engineering, computer science, and materials science. Monoscale approaches to complex physical problems often prove to be inadequate, even with the increasing availability of high-performance supercomputers. With potentially many scales and many variables associated with problems of interest, there is a need for systematic approaches to modeling multiscale systems.

Examples of multiscale problems can be found in the field of fluid mechanics, for instance. One example is gas flow through micro- and nanochannels, where the mean free path of the gas molecules can be compared to the length scale of the flow volume via the dimensionless Knudsen number (Kn). For large-Kn problems, in which the mean free path (typical distance that a gas molecule travels between collisions) is larger than the dimensions of the channel conduit, the continuum approximation breaks down and flow must be calculated using discrete approaches such as direct

simulation Monte Carlo or lattice Boltzmann [1]. For $\text{Kn} \ll 1$, the fluid behaves as a continuum, and the well-known Navier–Stokes equations with no-slip boundary conditions can be used to calculate the flow. For $\text{Kn} = O(1)$, gas flows behave in a transitional regime where modified continuum-level equations such as the quasi-gas dynamics or Burnett equations can be used with phenomenological wall slip boundary conditions. Another multiscale example from fluid mechanics is turbulent flow, where energy transfer occurs between self-similar vortices of varying dimension that form coherent structures in the fluid [2]. In boundary layer theory, as exemplified by the classic problem of flow past a plate, there is a thin region close to the wall in which viscosity effects are important, and this local solution must be matched to an outer solution governed by ideal flow [3]. A fourth example of a multiscale problem that arises naturally in fluid mechanics is the flow of complex fluids such as polymer melts or suspensions (see Chapters 11 and 12), in which the microstructure of polymer chains or suspended particles has a profound influence on the macroscopic rheological properties of the fluid. Some of these problems have previously been considered quite successfully using classical analytical methods or phenomenological models derived from experimental observations, whereas other problems lend themselves more readily to multiscale computational approaches.

Particle interactions and, in particular, the collective phenomena that arise from nearby discrete units, represent a hallmark of multiscale problems. In biology, for example, one finds a natural hierarchy of discrete length scales: from electrons to atoms, molecules, macromolecular assemblies, organelles, cells, multicellular aggregates, tissues, organs, organisms, and populations of organisms. The interactions between proteins and between cellular “particles” receive the most attention in Part II of the book, although a broader range, from molecular- to organ-scale phenomena important in angiogenesis, is discussed in Chapter 10. As we have written elsewhere, to gain a mechanistic rather than “black box” understanding of complex systems, it is necessary to concern oneself with the phenomena that occur at least one length scale below the scale you care most about. This is certainly true in biomedical systems, where the ultimate motivation must be the overall health of the organism.

In Part I, on nanoparticle applications, we have adopted broader definitions of interacting particles. Pozrikidis (Chapter 4) examines the mechanics of an atomic sheet, treating this as a particulate sheet connected by elastic springs. Sinno (Chapter 2) considers atomic defects in crystalline silicon as “particles” that perturb the lattice strongly up to a finite distance from the edge of the feature and only weakly or not at all farther away. Both Kopelevich (Chapter 3) and Stern (Chapter 8) are focused on the self-assembly of amphiphilic molecules into micelles and bilayers, where surfactant molecules or clusters of atoms are represented as interacting particles. Ventikos and co-workers (Chapter 6) study, among other phenomena, the rupture and coalescence of nanodroplets comprised of many interacting liquid molecules. The authors of other chapters in Part I examine the interaction between deformable capsules (Chapter 7) or water molecules (Chapter 5). A lattice of spatial nodes can be used to reduce dramatically the dimensionality of such computational problems (see Chapters 2 through 4, and 7).

Granularity refers to the extent to which a system is broken down into small parts. An important theme in multiscale modeling is coarse graining, where some of the fine detail of low-level models has been smoothed over or averaged out. Stern (Chapter 8) provides an excellent review of coarse graining in molecular dynamics (MD) simulations. Atomistic MD simulations provide the finest level of detail and, in principle, should be the most accurate. However, the time step required for numerical integration must not exceed the period of the highest-frequency motion of the system: in most cases, covalent hydrogen bond vibrations of order about 1 fs. Thus, on inexpensive computers, simulations of about 1 ns in duration can be executed: far shorter than biologically relevant molecular events such as lipid self-assembly or protein–ligand docking. In coarse-grained MD, one “particle” represents three or four atoms, effectively averaging over vibrational dynamics and resulting in an order-of-magnitude improvement in computational speed. Bagchi (Chapter 11) discusses some coarse-grained models specific to fluid dynamics. Sinno (Chapter 2) points out that with coarse-grained models it is often difficult to identify whether lack of agreement with experimental data is due to a poor choice of parameter values or to a fundamental shortcoming of the physical model and its associated assumptions, and presents strategies to address this.

Another important concept in multiscale modeling is linking between scales; that is, how one reconciles coupled fine-scale and coarser-grained models in an accurate, predictive, and unambiguous way. Sinno (Chapter 2) provides an excellent strategy for accomplishing this by first categorizing multiscale simulations into either sequential or concurrent frameworks. Sequential simulations, where parameters are passed from one scale to another, are the focus here. Atomistic simulations can be used as *in silico* experiments, and coarser-grained models tested against data generated by the atomistic simulation. This proves to be an effective approach, as mechanistic elements of the coarse-grained model are isolated and tested independent of the model parameters. Balazs (Chapter 7) describes a hybrid model that involves sequential linking between a lattice Boltzmann fluid dynamical model and a lattice spring model to simulate the elastic shell of a compliant microcapsule, although these lattices are of comparable spatial scales. In Chapter 10, Popel categorizes multiscale models of transport in biological systems as either continuous or discrete models. The continuous models, usually arising from differential balance equations, have been used at the molecular, cellular, tissue, and organ scales. Discrete models treat cells as discrete objects, and are also discussed in Chapters 11 and 12 in the context of blood cell transport and adhesion.

In this book we present a variety of approaches and methodologies for the use of multiscale computational models to study and predict the behavior of complex systems. The chapters are organized around applications in nanoscience (Part I) and biology (Part II), although other connections can be made, such as molecular dynamics (Chapters 3, 5, 6, and 8) and stochastic receptor–ligand binding (Chapters 9 and 12). Slide-show presentations to support the content in each chapter are available at the book Website at (www.Wiley.com) for instructors who wish to use this book for graduate teaching. It is our hope that the common themes and breadth of current examples will enable and inspire researchers seeking to understand multiscale physical systems and the particle interactions that lead to collective phenomena.

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