11 Multiscale Modeling in Inactive and Active Materials

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Overview

This chapter approaches the question of the nature of levels in biology from the point of view of materials science. I first examine multiscale investigations of materials such as steel beams (inactive materials). I compare these methods with recent work on the modeling of active materials—specifically, the behaviors and structures of the mitotic spindle. From this materials science perspective, scale separation allows for a conception of levels that does not necessarily track part–whole relations. Perhaps surprisingly, there are interesting and fruitful connections between multiscale modeling in physics and biology.

11.1   Introduction

Materials such as steel beams, fluids such as water, and schools of fish all exist at distinct "levels" or scales. By this I mean, at least in part, that they display distinct, dominant behaviors at different spatial and temporal scales. Water, for example, displays fluid properties at rather long (everyday) time scales. Thus, it is much easier to wade into a pool of water than it is to wade into a pool of hardened concrete. However, as anyone who has ever flubbed a dive into a swimming pool can attest, at short time scales, water can display solid-like behavior.

The fluid behavior of water is well described by the equations of hydrodynamics—the Navier–Stokes equations. These same equations describe the behavior of a host of other fluids that differ in their microscopic makeup. In other words, the equations describe upper-scale behavior that is largely autonomous from the theoretical characterization of the actual molecular and atomic constituents of the different fluids. This autonomy can be understood in terms of a claim of stability that can explain how the Navier–Stokes equations can be completely wrong about the actual molecular details of a fluid (these equations treat fluids as continua—as having no component structure whatsoever at any length scale), yet be extremely accurate in characterizing the behaviors at everyday length scales. The continuum behavior of a fluid is stable under perturbations of lower-scale molecular details.

One would like to understand the relationships between behaviors of a single system at different scales. It is the same system, but its distinct behaviors seem to require theories

and models that are scale relative and applicable only at widely separated scales. For instance, the hydrodynamic equations are perfectly good for modeling the behaviors of fluid flow in a pipe, but they do not do as good a job in modeling the behavior of ink in an inkjet printer. For the latter, molecular dynamics is much more appropriate.[1]

The problem of modeling at different scales and the nature of the relationship between such models is actually at the heart of the age-old problem of the relationship between thermodynamics (a continuum theory) and statistical mechanics (a theory of collections of discrete particles). In this chapter, I will not be addressing this broad relationship between theories. Rather, I intend to discuss analogies and disanalogies that appear when attempting multiscale modeling of different kinds of systems.

In section 11.2, I consider how composite materials are modeled in materials science. Parameters that appear in continuum equations for the bending of metal bars differ in their values depending upon the type of metal—steel versus aluminum, for example. Those parameter values surely must reflect some lower-scale properties of the different materials. But in practice, the values are usually determined experimentally. This section considers the extent to which one can determine the values of those parameters theoretically. It provides a relatively detailed discussion of the modeling of materials at separate scales and the extent to which models at one scale can inform models at other scales. An important aspect to note here is that such modeling in materials science is fundamentally continuum modeling. Typically, details of the atomic or molecular level are not considered in any explicit fashion.

The next section addresses a similar problem in certain (primarily) biological systems that can be considered to be "active." Active systems differ from the materials discussed in the first section because they are inherently out of equilibrium and because the components of the systems independently burn their own energy.[2] Large-scale active systems include bird flocks and swarming bacteria. Inside cells, there are materials that are active in this sense as well. This section looks at the materials science of active matter and discusses differences and similarities with the materials science modeling of inactive materials. Can continuum models really be employed to understand the out-of-equilibrium, self-organizing structures that are characteristic of biological systems? One might be skeptical of such a possibility given the extreme complexity and nonequilibrium nature of such systems. It is, in fact, possible to study the material properties of such structures (the example discussed concerns the behaviors in the mitotic spindle) in a way quite analogous to the study of material properties in the cases of inactive matter like metal bars. I discuss briefly some of the commonalities between active and inactive material modeling and some of the differences.

The discussion suggests that a kind of "level" talk in the context of multiscale modeling yields a fruitful way of understanding the behaviors of various kinds of systems. Note that this conception of levels is *not* fundamentally based on a relation between parts and wholes. (Such a conception is common in various contexts, including biology.) Here the operative notion is that of scale separation. For the inactive materials studied in materials science, this way of thinking about levels has been very fruitful. Perhaps somewhat surprisingly, the same is true for active (typically biological) materials as well.

11.2 Inactive Materials

Steel is a composite material. At the level of atoms, it is primarily a lattice of carbon and iron atoms arranged in a certain order. At the level of railroad tracks, it appears as a homogeneous structure exhibiting no lower-scale structure at all. At this continuum scale, we can take the tracks to be roughly in (thermal) equilibrium yet subject to stresses when a train glides over them. When stressed, the track bends—it is perturbed from its equilibrium state—but (we hope) returns reasonably quickly to a quasi-equilibrium state after the train passes by. The way it returns to its equilibrium state depends on certain material parameters that characterize its bending and stretching behavior. From this continuum perspective, the equations that govern the behavior of the track under loading are called the Navier–Cauchy equations:

$$(\lambda + \mu)\nabla(\nabla \cdot \mathbf{u}) + \rho\nabla^2\mathbf{u} + \mathbf{f} = 0, \tag{1}$$

where $\mathbf{u}$ is the displacement vector, ρ is the material density, and $\mathbf{f}$ are the body forces (e.g., gravity) acting on the material. The material parameters, λ and μ, are the "Lamé" parameters. They codify the bending and stretching behaviors of the material. In order to model a system using these equations, values for such material parameters (along with a value for the material density ρ) need to be specified. Different values for these determine how steel differs in its loading behavior from, say, aluminum or wood. Typically, the values for the Lamé parameters are determined by *empirical experiments* on a workbench.

When the Navier–Cauchy equations were first written down, there was no consensus about whether materials like steel or iron had (atomic or molecular) structure at any scale below that of the continuum. In other words, the hypothesis that there are atoms and molecules was not remotely settled.[3] From our contemporary perspective, we know that materials do indeed have lower-scale structure. Steel, at atomic scales, is a lattice of iron and carbon atoms. And, at (meso) scales in between the atomic and the continuum, there are a host of other features. Surely, the material parameters, λ, μ, and ρ, must reflect some aspects of the lower-scale structures present in the material. In recent years, there has been considerable mathematical work on establishing appropriate connections between material structures at lower scales and *ranges* of allowed values for the material parameters. This work allows one, to a certain extent, to *upscale*—to determine values for the material parameters—in terms of structures at lower scales.

It turns out that the actual details at the level of the atomic lattice are largely irrelevant to the continuum scale behavior of the steel. This is important and reflects the *relative autonomy* of the continuum equations (the Navier–Cauchy equations and, for that matter, the equations of thermodynamics) from the detailed atomic and molecular configurations of the various systems. If we are interested in why the Navier–Cauchy equations work so well for designing safe bridges and buildings, we would need to demonstrate the stability of such structures under perturbation of lower-scale details. The functional form of the Navier–Cauchy equations gets things right at continuum scales. An important explanatory question is why? The answer, as noted, is in part that the important features in the modeling of material behavior are the structures that exist at mesoscales. We need to see how to talk about them.

11.2.1   Upscaling and RVEs

At everyday continuum scales, a steel bar looks reasonably homogeneous. If we look at it with our naked eyes or with a magnifying glass, we don't see much structure: it appears to be uniform. However if we zoom in, using high-powered microscopes or X-ray diffraction techniques, we will begin to see structures that are hidden at everyday lengths. In order to describe the main/dominant/important features of the steel at these shorter length scales, we employ the very important concept of a *representative volume element* (RVE). Consider the steel bar. A representative volume element is a material volume that is statistically representative of features of the steel at some particular spatial scale. In figure 11.1, the left side displays a material point, and it is surrounded by an infinitesimal material element. Structures in the material element—the voids, cracks, grain boundaries, and so on—are to be treated as the microstructure of that (macro) material element.

  As is evident from the figure, the conception of the RVE involves the introduction of two length scales. There is the continuum or macroscale (D) by which the neighborhood of the material point is characterized, and there is a microscale (d) that represents the smallest microstructures whose properties (typically shapes are most important) are believed to directly influence the overall response to stresses and strains imposed upon the neighborhood surrounding the material point. These length scales must typically differ by orders of magnitude so that ($d/D \ll 1$). The requirement of this scale separation is independent of the nature of the distribution of the microstructures in the RVE. For example, they may be periodically or randomly distributed throughout the RVE. Of course, that difference can be important and may very well affect the properties displayed by the RVE under stresses and strains.
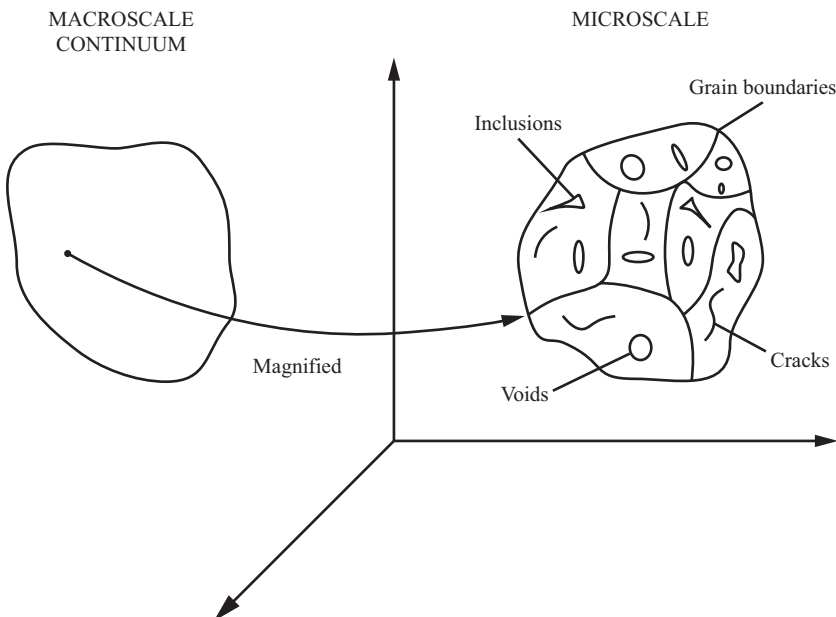
Figure 11.1
RVE.

It is important to note at least three features of RVEs:

First, the RVE concept is *scale relative*. The actual characteristic lengths of the structures in a RVE can vary considerably. As Nemat-Nasser and Hori (1999) note, the overall properties of a mass of compacted fine powder in powder-metallurgy can have grains of micron size, so that a neighborhood of 100 microns can very well serve as a RVE: "Whereas in characterizing an earth dam as a continuum, with aggregates [stones, sticks, clay etc.] of many centimeters in size, the absolute dimension of an RVE would be of the order of tens of meters" (p. 15).

Second, the RVE and the structures within it are all considered continua. That is to say, we are operating at scales much higher than that of the spacings in an atomic lattice but much lower than that of the scale where the material appears as a homogeneous continuum. So, there are at least *three* widely separated scales. Call the scale of the atomic lattice or the scale of intermolecular interactions between fluid molecules δ_a. Then, strictly speaking, we have the following relation:

$$\delta_a \ll d \ll D.$$

One typically eschews the very hard problem of upscaling from scales of order δ_a to D in favor of starting with those structures at the relevant RVE, namely, at scales of order d. This procedure, or this class of procedures, is known as "homogenization." In the next section, I provide a brief introduction to some of the mathematics.

Third, in employing RVEs to gain information about a material, one is implicitly ignoring boundaries or edges. In other words, one is essentially treating the material in bulk. We do not pay attention to what happens on the surface of the steel bar. This is, in effect, to treat the material as infinite in extent and is a natural and useful idealization.[4]

11.2.2 Upscaling

Our hypothesis is that the material parameters depend upon largely unknown aspects of the actual atomic or molecular makeup of the materials. Introducing material parameters such as the Láme parameters that code for lower-scale details actually introduces a level or scale intermediate between that of the continuum and the atomic.[5] The idea is that the nature of the important structures in the relevant RVE (which are at an intermediate scale d, $\delta_a \ll d \ll D$) largely determines the stable material parameters that characterize the material at the continuum scale. The appeal to an RVE, therefore, introduces a middle level or scale between the atomic and continuum. It is difficult to determine the nature of the inclusions, cracks, grain boundaries, and so on that are present in an RVE. Recall figure 11.1. One can employ various imaging techniques to determine such structure. In addition, in analogy with work on so-called hydrodynamic descriptions of fluids (Kadanoff & Martin, 1963), one can attempt to employ correlation functions to try to map out structures. See also Torquato (2002) for a discussion of N-point correlation functions. More on this below in section 11.3.2.

We can see how this works by considering a composite material 50% of which is a good thermal conductor while the remaining 50% is an insulator. Suppose that the two distinct materials are well mixed. They might be periodic or randomly distributed, but suppose for illustrative purposes that for any reasonable RVE, the volume fractions of each are basically 1/2. If we tried to infer the conductivity of the material simply by averaging over
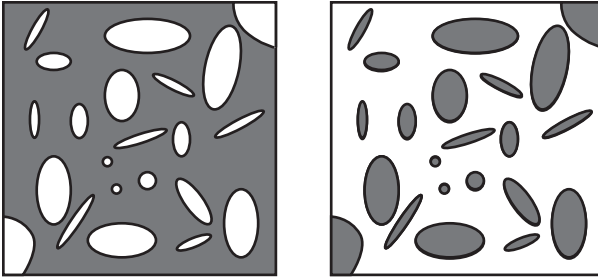
Figure 11.2
50–50 volume RVEs.

the volumes, we most likely will be grossly in error. If the dark material in figure 11.2 is the conductor and the configuration is as in the left RVE, then the material will be a very good conductor. But if the material is as in the right configuration, the material will be a terrible conductor.

A consequence of this simple example is that the sort of volume averaging typically assumed in statistical mechanics is not a good means for upscaling to determine continuum properties of systems. For instance, consider how, in typical statistical mechanical discussions, one might reasonably try to determine the density of an ideal gas. One would choose an RVE containing a large but finite number (N) of molecules and divide that number by the volume (V) of the RVE; then, taking limits ($N \to \infty$ and $V \to \infty$), one would arrive at a reasonable value for the density of the gas. Likewise, the identification of thermodynamic temperature with mean molecular kinetic energy also involves such simple averaging. But, these averages, as a rule, will only work for *homogeneous* systems as the example in figure 11.2 clearly shows. Therefore, making direct connections from the atomic/molecular level to the continuum scale is not as straightforward as many reductionist programs assume.

11.2.3   Homogenization

In fact, most upscaling starts at the mesoscale level and proceeds using sophisticated mathematics called "homogenization" to determine ranges of values or *bounds* for the various material parameters appearing in the continuum equations like equation (1). The simple example of figure 11.2 leads directly to the need for homogenization as opposed to averaging. Let's call the RVE in, say, the left figure Ω. Let's say light region is Ω_1, and the dark region is Ω_2. Let the thermal conductivity of the entire heterogeneous material in Ω be designated by γ. The conductivity of the material in Ω_1 is γ_1. Likewise, γ_2 is the conductivity for the material in Ω_2.[6] In other words,

$$\gamma(x) = \begin{cases} \gamma_1, & \text{if } x \in \Omega_1 \\ \gamma_2, & \text{if } x \in \Omega_2. \end{cases}$$

Denote the temperature at a point $x \in \Omega$, $u(x)$.[7] Since the conductivities differ in the two regions, we have

$$u(x) = \begin{cases} u_1(x), & \text{if } x \in \Omega_1 \\ u_2(x), & \text{if } x \in \Omega_2. \end{cases}$$

The flux of the temperature is given by

$$q = \begin{cases} q_1 = \gamma_1 \text{ grad } u_1 & \text{in } \Omega_1 \\ q_2 = \gamma_2 \text{ grad } u_2 & \text{in } \Omega_2. \end{cases}$$

We assume the continuity of the temperature and of the flux at the interfaces between the two materials:

$$\begin{cases} u_1 = u_2, & \text{on } \partial\Omega_1 \cap \partial\Omega_2 \\ q_1 \cdot n_1 = q_2 \cdot n_2, & \text{on } \partial\Omega_1 \cap \partial\Omega_2 \end{cases} \tag{2}$$

where the n_i are outward normal unit vectors on the boundaries $\partial\Omega_i$, $(i = 1, 2)$ and $n_1 = -n_2$ on the boundary $\partial\Omega_1 \cap \partial\Omega_2$.

If we take $f(x)$ to be a heat source, then the heat conduction problem (to find the temperature $u(x)$ given the heat source and the above boundary conditions) can be written as follows:

$$\begin{cases} -\text{div}(\gamma(x)\text{grad } u(x)) = f(x) & \text{in } \Omega_1 \cup \Omega_2 \\ u = 0, & \text{on } \partial\Omega \\ u_1 = u_2, & \text{on } \partial\Omega_1 \cap \partial\Omega_2 \\ q_1 \cdot n_1 = q_2 \cdot n_2, & \text{on } \partial\Omega_1 \cap \partial\Omega_2. \end{cases} \tag{3}$$

Had the region Ω contained an isotropic single material with constant conductivity, this problem is an easily solvable elliptical partial differential equation. However, because we are considering a composite that satisfies the conditions (2), this means both that the gradient of the temperature u is *discontinuous* and that the flux q is *not differentiable*. Thus, to solve the problem (3) for the composite presents considerable difficulties. In fact, the problem requires the mathematics of weak solutions, with a weak notion of derivative that involves a formulation on a particular of space of functions known as a Sobolev space, H. Without going into detail, the heat conduction problem expressed in (3) is given a *variational* formulation:

Find $u \in H$ such that[8]

$$\sum_{i=1}^{N} \int_\Omega \gamma(x) \frac{\partial u}{\partial x_i} \frac{\partial v}{\partial x_i} \, dx = \int_\Omega f \, v \, dx, \quad \forall v \in H. \tag{4}$$

In many cases of physical interest, it is reasonable to assume (contrary to our 50–50 example) that one of the materials has a much smaller volume than the other. So let us suppose that Ω_1 is much smaller in volume than Ω_2, and then we can proceed as follows. Further simplifying (again as is often reasonable), suppose that the heterogeneities of material in Ω_1 with conductivity γ_1 are periodically distributed throughout the RVE. See figure 11.3 for an idea of what this means.

The periodicity is represented by the small parameter ε. Given this, the conductivity γ for the composite as a whole becomes a function of ε, and problem (4) now has the following formulation:

Find $u^\varepsilon \in H$ such that
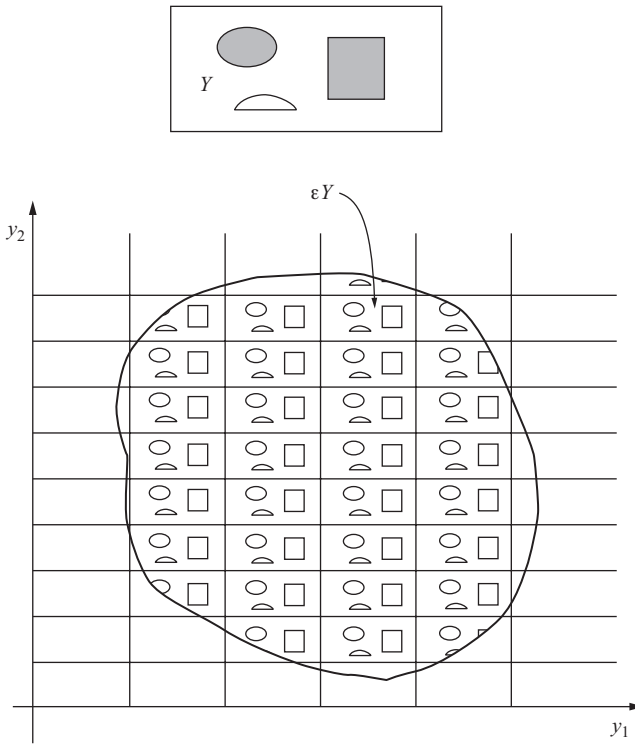
Figure 11.3
Periodic heterogeneities with period ε (Cioranescu & Donato, 1999, p. 5).

$$\sum_{i=1}^{N} \int_{\Omega} \gamma^{\varepsilon}(x) \frac{\partial u^{\varepsilon}}{\partial x_i} \frac{\partial v}{\partial x_i} \, dx = \int_{\Omega} f \, v \, dx, \quad \forall v \in H. \tag{5}$$

To represent the periodicity explicitly is reasonable to define γ^{ε} as follows:

$$\gamma^{\varepsilon} = \gamma\left(\frac{x}{\varepsilon}\right) \text{ almost everywhere on } \mathbb{R}^N. \tag{6}$$

We let γ be a periodic function with period Y; then by (6), the heterogeneities in Ω having size of order ε are periodic with period equal to εY. Now our problem (5) can be rewritten as follows:

Find $u^{\varepsilon} \; \varepsilon \; H$ such that

$$\sum_{i=1}^{N} \int_{\Omega} \gamma\left(\frac{x}{\varepsilon}\right) \frac{\partial u^{\varepsilon}}{\partial x_i} \frac{\partial v}{\partial x_i} \, dx = \int_{\Omega} f \, v \, dx, \quad \forall v \in H. \tag{7}$$

Two scales now appear in the problem. There is a macroscopic scale x and a microscopic scale $\frac{x}{\varepsilon}$. Now, speaking metaphorically (but in a way that can be made mathematically precise), we note that as $\varepsilon \rightarrow 0$, $\frac{x}{\varepsilon}$ will get larger (hence we are upscaling). Furthermore, the heterogeneities will get ever smaller, and we can hope to get a smoother, more *homo-*

geneous mixture in that limit.[9] This is a very different way to upscale than is the typical volume averaging employed in statistical mechanics. It allows one to find effective values for continuum parameters that will more accurately reflect the structures present at mesoscales in various materials.

11.2.4 Bounds

A desideratum for upscaling would be to demonstrate that there are determinate ranges of values for the continuum scale Lamé parameters or for the thermal conductivity, γ, given some minimal facts about the nature of composite materials. If all we know is the volume fraction of the various components (of, e.g., the materials with conductivities γ_1 and γ_2) but we lack information about the geometry or distribution of the materials in the RVE, can we still delimit bounds within which the values of the effective parameters will be guaranteed to reside?

In fact, some rigorous mathematical results allow us to do exactly that. These results are particularly useful for determining the range of responses to composite materials under stresses.[10]

11.2.5 Summary Remarks

The main upshot of this discussion is that for heterogeneous materials and for nonhomogeneous (nonideal) gases, the volume averaging techniques typically assumed in philosophical assertions of a direct/reductionist connection between statistical mechanics and thermodynamics will almost surely fail. Intermediate, mesoscale structures characterized by appropriate RVEs are crucial to upscaling. In fact, such mesoscale structures are typically the best places to start to bridge between models of materials at different scales.

Why was this section titled "Inactive Materials?" The answer is because by and large, the composite materials considered here are assumed to be (essentially) in thermal equilibrium. Among other things, this assumption allows one to focus on bulk continuum behaviors of the systems, effectively ignoring any boundaries that might exist. But not all materials are like this. In fact, living systems are definitely not like this. There is a relatively new field at the intersection of biology and physics that has come to be known as the study of "active matter." These systems include swarms of bacteria, schools of fish, flocking birds, and processes in living cells. Understanding the behaviors of such systems requires some interesting twists to multiscale modeling. In the next section, I consider the nature of upscaling for active systems.

11.3 Active Materials

A crucial assumption of the discussion of upscaling in the last section (upscaling for what I call "inactive" materials) is that the system is a composite that is essentially in a state of equilibrium or quasi-equilibrium. However, the world is not static, and sometimes one needs to consider the upper-scale behavior of systems that are not in equilibrium. Relatively standard physics can be brought to bear on studying out-of-equilibrium behavior in *steady states*. A paradigm example is Rayleigh–Bénard convection. In this phenomenon, a fluid is contained between two plates with the distance between the plates considerably less than that of the extent of the plates. Initially, the temperatures of the two plates are the same, and the
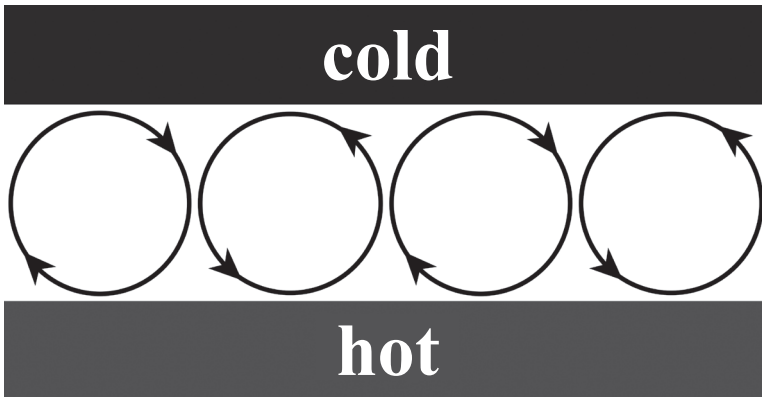
Figure 11.4
Cartoon of Rayleigh–Bénard convection (Research Group Felix Otto, n.d.).

fluid is at thermal equilibrium with the plates. Upon increasing, slightly, the temperature of the lower plate, the system will no longer be in thermal equilibrium and a temperature gradient between the plates will be established. As a result of this gradient, there will appear alternating clockwise/counterclockwise motions, as displayed in figure 11.4.

This behavior is stable under reasonably small perturbations and will continue as long as the temperature differential between the top and bottom plates is maintained. Note, though, that this out-of-equilibrium steady-state flow *requires* that thermal energy be introduced to the fluid-plate system exogenously. This is very interesting behavior, but it does not present any real modeling challenges.

On the other hand, the swarms, flocks, schools, and so on mentioned above are behaviors that do present new challenges. The difference is that the energy involved is not exogenous. Each component of the swarm, flock, school—each bacterium, bird, or fish—has its own energy source. Considered as microscopic degrees of freedom, they burn their own internal energy. This can lead to (emergent/collective) behaviors quite distinct from collections of passive or inactive components. Needleman and Dogic (2017, p. 136) say that active particles can "self-organize," whereas passive particles "self-assemble."[11] The collective behavior of the fluid molecules in the Rayleigh–Bénard cells is an example, in their terminology, of self-assembly.

As a rough guide, we can say that active matter has the following unifying features:

They are composed of self-driven units … each capable of converting stored or ambient free energy into systematic movement. The interaction of the active particles with each other, and with the medium they live in, give rise to highly correlated collective motion and mechanical stress. Active particles are generally elongated and their direction of self-propulsion is set by their own anisotropy, rather than fixed by an external field. (Marchetti et al., 2013, p. 1144)

11.3.1   Materials Science of the Mitotic Spindle

One area of rather intense research on the (bio)physics of active particles concerns the behavior of the mitotic spindle within the cytoskeleton of eukaryotic cells. The spindle (figures 11.5 and 11.7) is a mechanism that segregates chromosomes in cell division and is an ensemble of filament structures called microtubules, molecular motors, and other proteins.
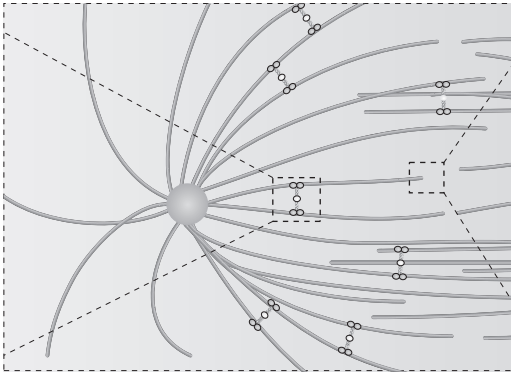
Recent research approaches the behavior of the spindle from the point of view of materials science.[12] The molecular motors "walk" along the filament structures that are often polarized—oriented with plus and minus ends. In fact, these molecular motors often crosslink the microtubules and in the process cause the filaments to slide past one another. See figure 11.6. The motors are fueled by ATP (Adenosine Triphosphate) and so are out-of-equilibrium components. Their motions and their effects on the microtubules allow the spindle to segregate chromosomes into daughter cells during mitosis. See figure 11.6. These sliding motions allow for the mesoscale formation of different structures within the cytoskeleton.[13] In fact, the nonequilibrium nature of the spindle allows for it to do some really quite remarkable things.
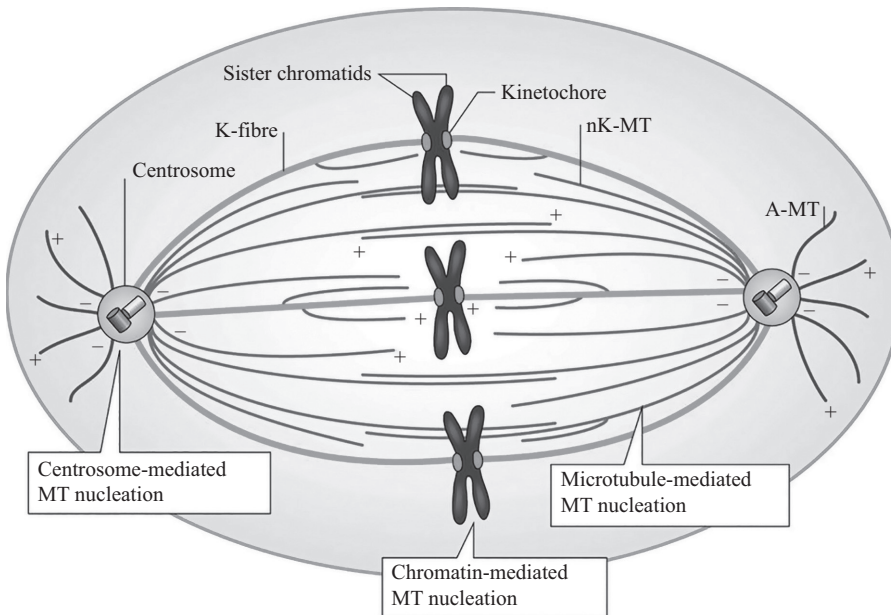
Figure 11.5
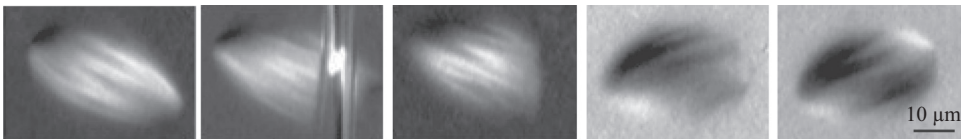Mitotic spindle (Prosser & Pelletier, 2017, p. 188).
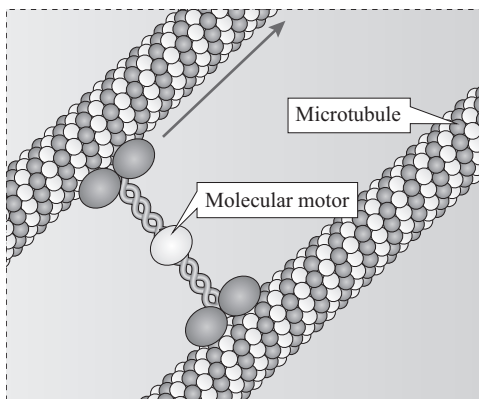
Figure 11.6
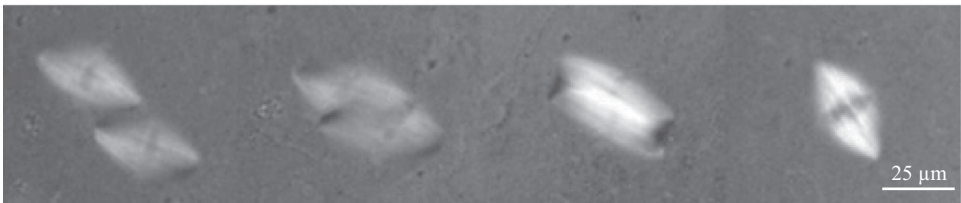Microtubules and molecular motors (Needleman & Dogic, 2017).
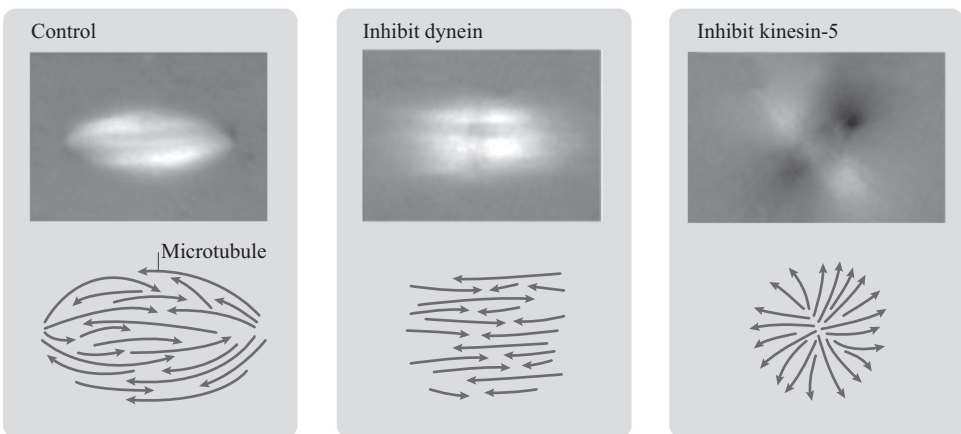
Figure 11.7
Spindle (Needleman & Dogic, 2017).

A Self-healing

10 μm

B Fusion

25 μm

C Shape transitions

Control

Inhibit dynein

Inhibit kinesin-5

Microtubule

Figure 11.8
Mesoscale properties of spindles (Needleman & Dogic, 2017).

In vitro studies provide evidence for this. In figure 11.8, a spindle is cut and heals itself. In other instances, two spindles can fuse into one. Furthermore, by inhibiting certain molecular motors, one can change the shape of the spindle structure. All of this provides evidence of how larger-scale material structures can result from self-organizing active matter.

11.3.2 Mesoscale Descriptions of Active Materials

In section 11.2, we saw that material parameters reflect crucial features of composite (or noncomposite) inactive materials at scales of the relevant RVE. As noted, they introduce a third level or scale between the atomic and the macroscopic. Similarly, in condensed matter physics, another type of parameter, an *order* parameter, plays a crucial role in describing the continuum behaviors of fluids, magnets, and superconductors.[14]

In the mitotic spindle, as noted, some of the filaments are polar. One can study these structures at a mesoscale noting that different structures can be classified by different symmetries. If there is no relative orientation of the tubules with respect to one another, one will have isotropic structure at large length scales. If the tubules are polar yet oriented along an axis but pointing in different directions, one has essentially a nematic liquid crystal. If they are polar, axially oriented, and pointing in the same direction, one has a polar liquid crystal. See figure 11.9. These structures are well understood in (soft) equilibrium condensed matter physics. Their responses to external pressures and stresses are also well understood.

In active materials, things become more complicated but nevertheless allow for the mesoscopic study of stresses and strains in the relevant RVEs. In fact, adding active stresses resulting from the actions of molecular motors genuinely leads to new behaviors and different material properties. Dipolar active stresses preserve volume and therefore can initiate

A Structure

Isotropic   Nematic   Polar
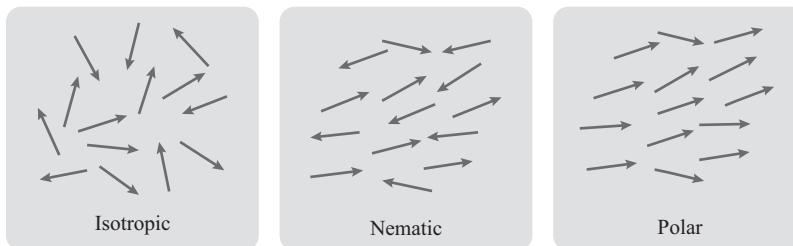
B Topological defects

+1/2   −1/2   +1
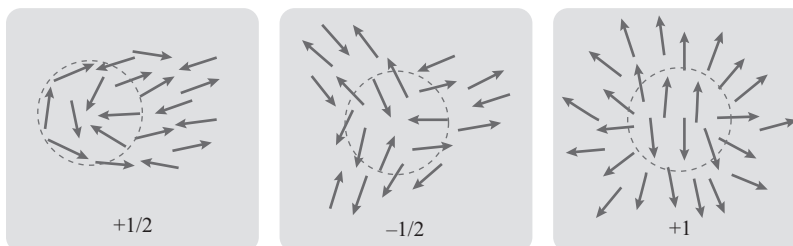
Figure 11.9
Symmetries of polar objects (Needleman & Dogic, 2017).

flowing behavior in different directions, thereby helping to explain some of the larger-scale shape shifting one sees during mitosis. Figure 11.10 provides an idea of how isotropic and dipolar stresses can effect shape changes and induce motion or flow in the relevant cellular RVEs.[15] Isotropic stresses (such as uniform pressure) can change the volume (expanding or contracting). Dipolar stresses can induce motion.

So far, we are describing bulk behaviors as we did in the cases of inactive matter. That is, we have tacitly assumed that the active materials studied are not spatially confined or walled in. But, an important feature of some active materials (including what goes on inside the cell) is the spatial confinement of the processes. This confinement or spatially bounded behavior can have dramatic effects on behaviors and classifications of the active materials we have been considering. Needleman and Dogic (2017) say that

chaotic dynamics is a generic feature of intrinsically unstable active nematics. By contrast, although the mitotic spindle is well described as an active nematic system, it retains a uniform alignment throughout its entire structure because of its finite size. This observation clearly demonstrates that boundary effects also strongly influence the behaviours of active nematics. (p. 9)

In "Physical Basis of Spindle Self-Organization," Brugués and Needleman (2014a) develop a (minimal) liquid crystal model for understanding the self-organizing processes inside the spindle. The model assumes that the orientation of the microtubules and their density are cross-correlated or coupled. As such, the model allows for a higher-scale description of the dynamics inside the spindle. They employ sophisticated experimental techniques to determine values for *spatiotemporal correlation functions* of microtubule density, of microtubule orientation, and of stresses. Their model reproduces the experimentally determined values of these correlation functions. It is a continuum model described by nematic
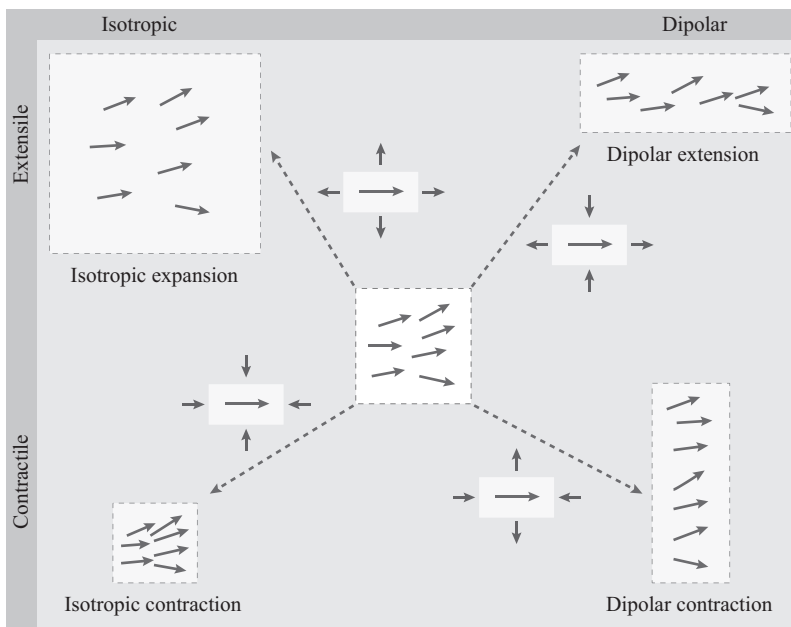
Figure 11.10
Stresses in active materials (Needleman & Dogic, 2017).

and polar fields, which result from the collective effects of local microtubule interactions that are determined by lower-scale effects of motor proteins and cross-linkers. Thus, they construct a mesoscale model that allows for qualitative and quantitative predictions of spindle behaviors, some of which are pictured in figures 11.8a, 11.8b, and 11.8c. Specifically, their measurements of the various correlation functions and of the generation and propagation of stress in the spindle are "consistent with spindle self-organization arising from the local interactions of microtubles, mediated by crosslinkers and motors, and microtubule polymerization dynamics" (Brugués & Needleman, 2014a, p. 18499).

In this model, the orientation of the microtubules is determined by nematic interactions, and the polar field convects the microtubule concentration and polarity magnitude. The magnitude of the nematic field is taken to be constant throughout the spindle, while the magnitude of the polarity field depends on motor activity and self-advection. (Brugués & Needleman, 2014b, p. 1)

The takeaway here is that continuum models of active materials, just as with inactive materials, can be very fruitful. Mesoscale parameters and fields can code for complex molecular scale behaviors, and the continuum minimal models can be shown to be quantitatively and qualitatively accurate. It remains to be seen, I believe, whether justifications of such models of the kind provided by homogenization theory (and the renormalization group) will be possible in the active matter case. Further questions include describing the role of boundaries and confinement in active matter systems. In the case of the spindle discussed here, the ordered structures seem to depend upon the constraints that exist within the cytoskeleton. However, flocks of birds and schools of fish appear to generate their own boundaries (amorphous as they may be). Are there ways of explaining the emergence of such features? Does it make sense to say that for some active matter systems, boundaries are emergent?

I do think answers to these questions are forthcoming and depend upon a phenomenon quite common in condensed matter physics—the important fact that long-range correlations can form even among systems whose components interact only locally. Early flocking models (e.g., Vicsek et al., 1995) modeled individuals interacting in response to their immediate neighbors. Such "agent-based" models (akin to Ising models) were able to simulate quite interesting behaviors, including phase transitions from disordered to ordered states. More recently, in the vein of Brugués and Needleman's approach, continuum hydrodynamic descriptions of flocks have been presented with an important focus on correlations (see Toner et al., 2005). *The key to successful mesoscopic continuum modeling of both active and inactive systems is to have an understanding of the nature of the relevant RVE.* Spatial and temporal correlation functions allow for just such an understanding.

11.4 Conclusion

The conception of biological levels of organization is problematic, as witnessed by (at least some of) the chapters in this volume. But a conception of properties or dominant behaviors at various spatial (and temporal) scales appears to be widespread across various sciences.[16] An important aspect of such a conception is the fact that when behaviors appear at widely separated scales, it is possible to model them largely independently of features that exist at different scales. Multiscale modelers take advantage of this relative autonomy of behaviors at separated scales to gain explanatory insight into the nature of different systems.

Much work has been done to understand how such scale-relative behaviors can relate to one another in single systems. In section 11.2, I have characterized some of this work by focusing on the extremely important concept of a representative volume element (RVE). This is a mesoscale concept that can be exploited to try to determine the continuum scale behaviors of materials whether they be samurai swords or earthen dams. For the latter, the makeup of the RVE can easily be determined by digging with a shovel. For the former, various forms of microscopy will likely be necessary. In the case of fluids (as studied in statistical mechanics and thermodynamics), information about the RVEs can be theoretically probed using various spatial and temporal correlation functions whose values can be subjected to empirical tests.[17] It turns out that some of the most important information about RVEs for upscaling is geometrical and topological, which is exactly the kind of information encoded in the correlation functions.

It is extremely interesting that one can actually, in certain contexts, treat biological structures and processes using some of the same techniques. The field of active matter is brand new and brings with it a new set of modeling challenges. In the last section, I provided an all-too-brief discussion of the multiscale modeling of active materials. The specific focus was on understanding the behaviors of the mitotic spindle using a continuum approach that is quite analogous to that discussed in the section on inactive materials. The analog of atoms or molecules is microtubules and molecular motor proteins. The analog of RVEs with their encoding of geometric and topological features of inactive materials is the nematic and polar fields within a spindle. Active materials can generate their own stresses and strains (unlike inactive materials). As a result, they are typically more complex than inactive materials. Yet, because of scale separation, the resulting upper-scale behaviors can be nicely modeled without detailed knowledge of the lower-scale behaviors of microtubules and molecular motors. The multiscale methods of materials science generalize nicely to the cases of active materials despite the radically different behaviors active materials can exhibit.

Acknowledgments

Notes

1. The continuum hydrodynamic equations are partial differential equations. The equations of molecular dynamics are ordinary differential equations. These are of completely different mathematical type. See Batterman (2009) for more details.

2. Of course, this energy is typically provided by the environment.

3. See Batterman (2013, section 3, pp. 269–273) for a discussion of this situation and the controversy surrounding the proper derivation of the Navier–Cauchy equations.

4. It is also an idealization that sometimes is not warranted.

5. For a discussion concerning the similarities between this feature of material parameters and so-called order parameters that are introduced to account for symmetry behaviors of condensed matter systems, see Batterman (2019).

6. γ, γ_i are *material parameters*. The following discussion shows how one can connect between such continuum parameters and mesoscale properties of RVEs.

7. The ensuing discussion follows Cioranescu and Donato (1999).

8. $v \in H$ are knowns as "test functions."

9. A lot of difficult mathematics is involved in demonstrating that this limit exists, that the values for the temperatures u^ε converge to an effective temperature, and that there exists an effective limit conductivity γ_{eff} to which the γ^ε converges. This mathematics is called "homogenization theory."

10. It is beyond the scope of the present chapter to address these interesting investigations in any further detail. See Milton (2002, chap. 21) for a brief overview.

11. Clearly, these are loaded terms. We need to see whether the phenomena described truly warrant such descriptors.

12. The discussion here largely follows Needleman and Dogic (2017).

13. There are three types of cytoskeletal motors—myosin, kinesin, and dynein. They direct different types of motion (yielding different kinds of shapes), as can be seen in figure 11.8.

14. For a ferromagnet, the order parameter is the net magnetization of the material. As the ferromagnet is heated, the net magnetization (reflecting a preferred spatial direction) weakens as the spins begin to point in all directions. Above a critical temperature, the system is paramagnetic with full rotational symmetry.

15. Needleman and Dogic (2017, p. 6) note that this figure is schematic in that the individual filaments appear to be the units experiencing the active stresses. In cells, the units might be pairs of filaments, asters, or bundles of different kinds.

16. Suggestions along these lines can be found in the groundbreaking work of Bill Wimsatt. See Wimsatt (this volume) for a summary and discussion of many issues relating to levels and scales.

17. Such experimental tests involve X-ray and neutron scattering, among other techniques.

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