Introduction

The past decade has witnessed an unprecedented expansion of the involvement of theoretical physicists in biologically related problems. This has been driven by several factors, including the vast amount of new data emerging from new quantitative experimental methods, such as gene sequencing and advanced imaging methods; the increasing computational capabilities available to physicists for dealing with complex problems; and the realization that work on biological problems can have important spin-offs for problems in physics and materials science. The increased interest of physicists in biologically related problems is evidenced by the large number of theoretical condensed matter physicists and materials scientists currently migrating to these problems, as several different sub-communities have realized that their approaches have a potential impact on biology. The large number of positions in biological physics that have been advertised in recent years by United States university physics departments is another indicator of the increased involvement of physicists with biology. This development has been more rapid than that in engineering-based materials departments, in which a steady influx of biological influence has been felt for a longer time. For this reason, the discussion in this report is focused in the direction of biological physics. The biology community is also increasingly interested in expanding the number of individuals with quantitative *hard-science* backgrounds working on biological problems, as is evidenced by the increasing prevalence of well-attended computational sessions at biology meetings, and the existence of government-funded programs supporting collaboration between biologists and quantitatively trained individuals. Physics and materials science departments see increased undergraduate and graduate interest in biological physics and are struggling to accommodate this, often with insufficient qualified faculty.

The physical science theory community is well poised to make important contributions to the study of biological problems, and biologically based materials. One of these contributions is the *physics approach*. This means searching for the single relation or phenomenon at the heart of a problem, rather than attempting a complete quantitative description of all the details of the problem. Physicists have traditionally sought underlying trends and unifying principles in complex systems. The *physics approach* can involve defining a paradigm model. It also includes the search for general results, such as the fluctuation-dissipation theorem of statistical mechanics, which cut across a broad range of systems. Or it can consist of the use of astutely chosen reduced variables in analyzing data, to more clearly establish relationships between quantities of interest. Such methods can have enormous payoffs when combined with the increasingly precise data emerging from quantitative experimental biology. The methods of condensed-matter and materials theory are particularly well suited to the study of biological and biologically-derived systems.

The major part of the workshop effort was devoted to examining examples of past successes in the interaction between theory and biological physics/materials, and examining prospects for the future. For this purpose, it was deemed necessary to divide up the field into subfields of manageable size, and the workshop participants were correspondingly divided into discussion teams. The subfields chosen (with necessarily fuzzy boundaries) were **Biomolecules, Supramolecular Assemblies**, and **Systems Biology**. An additional workgroup examined issues relating to **Education and Infrastructure**. The following report is also structured along these lines. The workshop included substantial amounts of time devoted to small-group discussions, as well as large-group discussions (see workshop schedule in Appendix B). Because of the breadth of biological physics and materials, it is impossible to give an exhaustive survey of either past successes or future research areas. Thus each section below gives a few examples of past successes and possible future research directions.

Some of the general areas treated by physicists moving into biological problems include protein folding, biomolecular phase transitions, membrane phases, bioinformatics, and applications of spatially-extended dynamical systems to biology. The specific examples that were discussed demonstrate numerous past successes of theory in the study of biomolecules and supra-molecular assemblies. These include the structure of double-stranded DNA, protein structure determination, evaluation of low-energy vesicle shapes, and random-walk treatments of DNA moving through pores. They have involved the use of a tremendous range of methodologies, over a very broad range of length scales. Systems biology is emerging and strengthening as a vital area. Almost all theoretical techniques that have been developed for condensed matter/materials problems appear to have potential applications in biological problems.

The involvement of theory in biological physics and materials leads to both answers to biological questions, and enrichment of the fields of condensed-matter and materials theory by the study of biological problems or biologically based materials. An example of the former is the evaluation of red blood cell shapes via minimization of an energy function including elastic terms. An example of the latter is the study of diffusion in random potentials. This was motivated in a general way by biological issues, and has subsequently enriched condensed-matter and materials theory. Biomimetic materials, which use biological components or their analogues to construct materials with unique properties, also demonstrate the spin-offs possible from the study of biological systems. The workshop participants felt that the entire spectrum of interactions between the disciplines should be strongly supported.

Two scientific themes occurred repeatedly throughout all the discussions: *non-equilibrium thermodynamics*, and *molecular self-assembly*.

Condensed matter/materials theory has generally focused on equilibrium problems, and a solid conceptual base exists for treating such problems. However, most biological phenomena are inherently *non-equilibrium*. Cells continuously consume the energy currency ATP, and this is the origin of much of their highly dynamic behavior. Spatiotemporal gradients of key chemical concentrations are ubiquitous in biology. The conversion of chemical energy into mechanical energy, required for several essential cell processes, is also a non-equilibrium phenomenon. The structure and properties of living organisms and ecosystems are determined not by a global-optimization procedure, but rather by the interaction of evolutionary dynamics with a changing environment. Thus the study of biology and biological materials could have a large impact on condensed-matter and materials physics by accelerating the development of an underlying conceptual structure for studying non-equilibrium phenomena.

Self-assembly is seen on an enormous range of length scales, including the reliable folding of proteins, the undirected growth of motility organelles such as flagella, viral capsid assembly, and the packaging of DNA. The self-assembly is often very accurate – as for example in the assembly of the hook in bacterial flagella which stops at a very well-defined length. In none of these cases is the dynamics or the perfection of the self-assembly well understood, and there is very little predictive methodology for establishing what structures can be formed. Understanding self-assembly would have very important ramifications for physics and materials science. Self-assembling materials may well be a major thrust in future materials development and understanding how biological systems assemble as accurately as they do would surely help spur this technology forward.

Having determined that the interaction between theory and biological physics/materials can have important benefits for both the physical-science and biology communities, the workshop participants addressed the question of how this interaction can best be encouraged. These discussions are summarized in the **Education and Infrastructure** section. There is a pronounced shortage of individuals who have a command of both the theoretical methods of the physical sciences, and the language of biology. This shortage is evident both in the experience of physics and materials science departments which have hired or attempted to hire in biological physics, and of investigators seeking to hire postdoctoral research associates. Measures that could alleviate this shortage include increased support for postdoctoral training in biological physics and mid-career research field transitions, the establishment of regional research and training centers, and expansion of educational programs such as summer schools. There is also a shortage of research funding for individuals working at the interface between the biological and physical sciences – there has been a tendency for this work to “slip between the cracks” at NSF, and it is important that mechanisms be found to support this emerging community.