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Discussion

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Concluding remarks

Soft nanotechnology: "structure" *vs.* "function"

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This paper offers a perspective on "soft nanotechnology"; that is, the branch of nanotechnology concerned with the synthesis and properties of organic and organometallic nanostructures, and with nanofabrication using techniques in which soft components play key roles. It begins with a brief history of soft nanotechnology. This history has followed a path involving a gradual shift from the promise of revolutionary electronics, nanorobotics, and other futuristic concepts, to the realization of evolutionary improvements in the technology for current challenges in information technology, medicine, and sustainability. Soft nanoscience is an area that is occupied principally by chemists, and is in many ways indistinguishable from "nanochemistry". The paper identifies the natural tendency of its practitioners—exemplified by the speakers at this Faraday Discussion—to focus on synthesis and structure, rather than on function and application, of nanostructures. Soft nanotechnology has the potential to apply to a wide variety of large-scale applied (information technology, healthcare cost reduction, sustainability, energy) and fundamental (molecular biochemistry, cell biology, charge transport in organic matter) problems.

1. Introduction

1.1 What is "soft" nanoscience?

"Soft" is a word famously introduced into science by Pierre-Gilles de Gennes to refer to organic matter.[1] He was concerned primarily with the physics of polymers; nanotechnology can write its own definition. For the sake of this Discussion, we define it both in terms of what it is *not*—that is, *not* the nanoscience of "hard" materials such as metals, ceramics, or inorganic semiconductors; *e.g.*, the materials of primary concern in classical condensed matter physics—and in terms of what it *is*—the nanoscience of organic and organometallic matter, including molecules and structures in biology.

Within this definition, however, all nanostructures (hard and soft) share some characteristics: (i) some critical smallest dimension (*e.g.*, ≤100 nm); (ii) dimensions small enough to be "all—or mostly—surface"; (iii) the possible emergence of quantum properties at temperatures approaching room temperature; and (iv) small enough in number of particles to show non-Boltzmann statistics. The dimensions of nanostructures place soft nanoscience at the border between the science of large molecules and molecular aggregates (*e.g.*, polymers and vesicles) and small microfabricated structures such as the nanometer-scale wires in microprocessors, or biologically derived structures such as virus particles or the ribosome.

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1.2 History

The history of "soft" nanoscience in some ways recapitulates the history of nanoscience. In very general terms, all new technologies seem to follow a similar course. There is an initial period of exaggerated expectation (expectation usually unconstrained by experimental experience and reality), a following phase of disappointment as reality creeps in, and then a phase of growing focus on the areas in which the technology has immediate potential (Fig. 1). Both nanoscience and soft nanoscience have now passed through the first two periods, and have entered adolescence. Both are clearly interesting and important new fields of science and technology, and broad areas of application are emerging or have developed.[2] Still, much of the practical impact of the field of nanoscience has so far come in one area—information technology—and that impact is due to the extension of existing technologies by brilliant engineering, rather than from the introduction of radically new technologies.

The original expectations for nanoscience—including soft nanoscience—included revolutionary electronics (including the often controversial[3–9] topic of devices based on transport in single organic molecules,[10,11] ultradense microprocessors and memories, and quantum computers[12]); futuristic speculations concerning so-called "nanobots" and nanoscale machines; revolutionary materials with extraordinary applications (*e.g.*, buckytubes and the "space elevator",[13] or quantum dots and cancer-targeted drugs[14]); and applications in biomedicine relying on particles small on the scale of the cell.[15]

What has emerged is not a completely distinct list, but a list with substantial overlap and a completely distinct flavor.[16] At the top of the list is information technology and nanoelectronics. Developments in "conventional" microfabrication—short-wavelength light sources and immersion optics—have moved microfabrication to design rules in the deep nanoscale region (currently 45 nm);[17] extreme ultraviolet lithography,[18] double patterning lithography,[19] and multiple electron-beam (maskless) writing[20] have the potential to push the limit even further.[21] This technology is, of course, remaking the world through the internet and globalization. There is an enormous range of opportunities for nanoscience in technologies concerned with the production of energy and with global stewardship;[22] these range from heterogeneous catalysis to improved membranes for separation of water and gases.[23] The intuition that soft nanotechnology *must* be important in biology—based on the fact that the cell is micron-size in scale—seems inevitably to be correct,[24] although

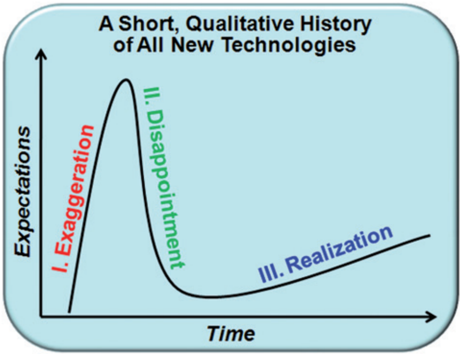

Fig. 1 The expectations of a new technology as a function of time. (I) In the beginning, there is a period of exaggerated expectations, during which exciting—but sometimes irreproducible—results and unrealistic claims are made. (II) When these high expectations go unmet, a period of disappointment sets in. (III) There is then a return to the fundamental aspects of the technology; science is linked with applications; new tools are developed; and real commercial investment begins.

the details of the applications in which nanoscience plays a role in fundamental biology remains to be established. The physical chemistry of systems containing small numbers of molecules or particles, and having most of these particles on or close to a surface, is just beginning to be explored.[25] And the quantum phenomena that emerge in small systems is very much *terra incognito*. So, the list of opportunities for the emerging and maturing field of soft nanoscience is long.

2. Focus of the Faraday Discussion

2.1 Nanochemistry and soft nanochemistry: *structure* and *function*

One of the characteristics of soft nanoscience is that it has developed in the hands of scientists with backgrounds in organic and organometallic chemistry; this group is particularly inclined philosophically to synthesis. As a consequence, the field has seen an explosion of work—often derived from prior themes in molecular synthesis—that has generated a broad range of new types of nanostructures: colloids, vesicles, polymers, molecular aggregates, self-assembled monolayers (SAMs),[26] and other small structures.[27] A characteristic of this work has been its focus on the *structure* rather than on *function*.

Historically, among the sciences, chemistry has been uniquely expert in synthesis of molecular and supramolecular structures, but less concerned with the functions of the structures that were synthesized. The enormous competence in organic synthesis that has emerged in the last century has made it possible to synthesize almost any small molecule. The justification for this work has often been its utility in pharmaceutical chemistry, although most of the work in that difficult and important field is done by biologists, pharmacologists, physiologists, and doctors, rather than by chemists. Similarly, the important field of polymer science has flourished because polymers are an important class of materials; chemists synthesized polymers, but others developed the applications for them. Soft nanochemistry is in a similar state. Chemistry is developing an exciting array of new synthetic techniques, but the field is still at the stage of "a solution chasing a problem". It is evident that one can make a wide variety of previously unmakable nanoscale structures.[27] The questions now are "Who cares?" and "What are they good for?"

2.2 Research interests of the attendees of this Faraday Discussion

This Faraday Discussion showed a broad spectrum of work, representative—in the usual non-representative way characteristic of a well-assembled conference—of the work going on in soft nanoscience. The range of topics offered a broad view of the topics being actively considered by the field. We classify these into eight groups; this classification certainly is not a uniquely correct sorting, but it gives a crude sense for what this group thought to be sufficiently important in soft nanoscience that it was worth pursuing.

(i) Biology. Jones[28] opened the conference around this theme, and a number of others reinforced his message concerning the almost unlimited opportunities offered by biology to nanoscience.

(ii) Nanoactuation, nanomotion, and nanomechanics. Sen[29] (redox motors), Sushko[30] (cantilevers and SAMs), and Schulten[31] (nanopores) focused on this subject (one that represents a *new* direction in chemistry).

(iii) Vesicles. Parnell[32] (encapsulation) and Matile[33] (polyarginine and anions) demonstrated some of the new possibilities that derive from one of the oldest fields in chemistry.

(iv) Molecular recognition was a theme that entered a number of discussions, with work by Matile,[33] Colquhoun[34] (non-biological sequences), and Mao[35] (DNA-based structural assembly) being prominent.

(v) Polymers—as expected for molecules at the border between "molecular" and "nano"—were components of many discussions, including those of Piñol[36] (structures formed from block copolymers), Hayes[37] (self-healing structures) and Ikkala[38] (fibrils).

(vi) Synthesis of molecules and aggregates showed the continuing skill of chemists in connecting atoms—both covalently and non-covalently—in new ways. Discussions including an important component of synthetic methods were those of Huskens[39] (templated molecular recognition), Mao[35] (DNA-based synthesis), Ikkala[38] (hierarchical self-assembly), Woolfson[40] (synthesis exploiting alpha-helices), Aida[41] (templated self-assembly), and van Esch[42] (self-assembly based on orthogonal interactions).

(vii) Properties. Chan[43] (hydrophobicity of surfaces), Hayes[37] (self-healing systems), Vendruscolo[44] (solubilities), Ulijn[45] (aggregation), and Aida[41] (self-healing) were all concerned with various aspects of the properties of soft-nanostructures.

(viii) Interfaces. Kornyshev[46] described his work on soft, charged interfaces.

Another conference, and another group of scientists, would certainly have provided a different distribution of interests among the attendees. Nonetheless, the focus in this group was clearly on large molecules, molecular aggregates and small particles, and on their synthesis and properties, rather than on the identification and exploitation of problems whose solutions might require such structures. It was, thus, a structure-focused discussion, rather than a function-focused discussion.

3. Expectations of soft nanotechnology

3.1 What does the rest of the world expect from nanotechnology? Does *soft* nanotechnology have a special role?

Technology proceeds both forward and backward: that is, from science and knowledge forward to applications, and from problems backward to technology for their solutions. There are many areas in which the capabilities offered by nanotechnology and the problems important to society and technology are sufficiently close that there is a clear opportunity for nanoscience to form the basis for nanotechnology, and nanotechnology to contribute to the solution of large-scale societal problems. Some of these will be particularly appropriate for soft, chemistry-based nanotechnology; others undoubtedly will be best treated by hard, physics-based nanotechnology.

Electronics. The extension of "conventional" microfabrication based on silicon and photolithography into the nanoscale region has been startlingly rapid, and has moved to sizes and complexities that were unimaginable twenty years ago.[21] When nanoscience emerged as a separate discipline, the perceived difficulties of making very small electronic systems were one of the sets of stimuli for its development, and the fabrication of microprocessors, computer memory, and other components of information systems was considered to be a possible area of application for *radical* nanotechnology, including soft forms of nanotechnology (*e.g.*, transistors—or even more exotic devices—based on single organic molecules).[5,47] It now seems unlikely that electronics and information technology will be an area in which radical soft nanotechnology will play an important role; technology based on extensions of the existing hard methods are so advanced, and the scale of investment required to develop new methods where they can be accepted in manufacturing so enormous, that it is improbable that it will make economic sense to develop an entire new technology for one or two generations of microprocessors. It is, however, always possible—in fact, probable—that soft nanotechnology and soft device physics will discover devices, processes, or functions that cannot be duplicated by hard methods. The use of step-and-flash imprint lithography, developed by Willson;[48] phase-shifting lithography using elastomeric masks;[49] and chemical-mechanical polishing[50] are three examples. There will almost certainly be others in the future.[51] Nonetheless, the theme of continuing development of classical methods of microfabrication—with chemical innovation, perhaps, in photoresists,[52] fluids with high indices of refraction,[17] and other chemical processes required by these methods, and especially now in technologies which lower costs—will continue, and, barring some presently unforeseen innovation, information technology will not represent the opportunity for radical nanotechnology that it once seemed.[21]

Biomedicine. If there *is* an important nanotechnological component to biomedicine, it seems almost inevitable that it will involve soft components.[53–56] The cell, and everything in it, are soft materials: that is, organic molecules in complex, functional configurations.[57] So far, however, the clear applications of nanostructures in biology and biomedicine have been surprisingly limited. One area that has demonstrated substantial promise is imaging. Quantum dots (for fluorescence microscopy at the cellular level),[58] and superparamagnetic colloids (for MRI contrast enhancement at the scale of localized tissues and organelles) have already demonstrated value;[59] other applications will certainly emerge. A second area where nanoscience and nanotechnology have already made important contributions is high-throughput analysis and array-based screening.[60,61] Although the components in these systems are now usually microscale—certainly larger than nanoscale as commonly defined—the future may well hold nanoscale components for biomedical assays,[62] and in any event the surface chemistry and surface functionalization that are required in the systems even now plausibly fall in the area of soft nanotechnology.[63] A third area with significant potential is in sensing based on either localized surface plasmonic effects in metallic nanostructures[64,65] or electrochemical gating of chemically prepared nanowires.[66]

New materials. Chemistry has always been uniquely skilled at synthesizing or generating new molecules, aggregates of molecules, and materials. There is every reason to think that the current high level of research activity in soft nanotechnology and soft nanomaterials science will produce new or improved systems. Among the successes of soft nanotechnology in materials science to date have been SAMs,[26] buckytubes,[67,68] quantum dots,[69] systems for chemical vapor deposition and atomic layer deposition,[70] methods for controlled synthesis of colloids,[71] and many others. This area is one in which chemistry will continue to excel, and in which the most important question is not “Can it be made?” but “What is the application?”

Energy. Nanotechnology is already ubiquitous in the production and use of energy.[72,73] Essentially all liquid fossil fuels are processed into useful forms by catalytic conversion over heterogeneous catalysts whose areas of catalytic activity are nanoscale.[74] Separations through nanoscale structures (usually fabricated in polymers) are crucial throughout the technology of energy production, and involve molecule-selective diffusion through polymer-based membranes, with or without discrete pores.[75] Thin-film solar photovoltaic cells—those based on amorphous silicon, CdTe, and other inorganic and organic semiconductors—rely on processes of charge separation and collection on the length scale of 5–100 nm.[76,77] All of these areas already constitute important fields of chemical technology and condensed matter science, but the rapid development of nanoscience offers the opportunity to re-examine them, and to develop new activities, new functions, and new levels of control.

4. Big problems

4.1 Inevitabilities

Beyond these well-defined technical problems, there is a bigger and more diffuse set—perhaps a dozen at any given time—of problems broadly important to society that require solutions that combine technology, economics, politics, sociology, law, and policy. Soft nanotechnology is now becoming sufficiently mature that it is appropriate to examine these very large-scale societal needs to see if some aspect of "nano" might offer options or partial solutions. We give four examples for illustration.

Sustainability: energy, water, and the environment. The problem of sustainability is often phrased and focused around energy. Sustainability is a large collection of different problems and is, of course, much more complicated than simply finding new methods of *producing* energy. There are many potential approaches to energy production, which include many untapped sources of fossil fuel (provided that problems of global climate change allow their use). Nuclear power generation can, in principle, also be expanded. Alternative sources of energy—especially renewable sources such as wind and solar—may fill important niches.[78]

Global warming and greenhouse gases (CO_2, CH_4, NO_x, and others) pose limitations to the growth of some of these technologies, and non-technical issues (*e.g.*, limiting proliferation of nuclear weapons) might make us wish to limit others. And if global warming is anthropogenic (and possibly even if it isn't), our ability to generate energy from fossil fuels will probably be severely limited.

Conservation has barely been exploited,[79] but it too will have technological solutions. Fig. 2 illustrates the flows of energy from sources to uses in the USA, and emphasizes the opportunities for conservation. While engineering development of this complex system continues, nanoscience has the potential to invent new materials (*e.g.* for coatings, catalysts, friction- and corrosion-resistant surfaces, and membranes). There could be as much potential for technological innovation in saving energy as there is in the production of more "new energy". Telecommuting and video conferencing are examples of technological alternatives to transportation, which is the largest consumer of distributed energy.

There presently are no solutions (other than the practically untested option of underground or underwater carbon sequestration) for disposal of carbon dioxide.[80] Alternative approaches may involve conversion of carbon dioxide into other materials, and large-scale processes based on chemical conversions will probably require new heterogeneous catalysts.[81]

Production of usable water (for agriculture and drinking) may, in fact, be a substantially more pressing short-term (<50 year) problem globally than energy production.[82] The separations involved in increasing the quality of water depend on membranes, and the design and fabrication of dramatically improved membranes (and perhaps of materials for other separations technologies) will probably have an important component of soft nanotechnology.

Sustainability may also require global-scale technologies. One of the most interesting and disquieting is "geoengineering"—the intentional modification of global climate.[83,84] Some of the technologies for geoengineering depend on creating small particles to scatter light—either in the atmosphere, in the ocean, or on land—and on the consequent modification of earth's albedo. The role of aerosols, particulates, and bubbles are ubiquitous in considerations of the reflectivity of the earth.[85]

The need for understanding nanoscale materials in thinking about the range of problems in sustainability is thus almost limitless, but in no case is nanotechnology by itself a complete solution to a problem. Understanding the constraints on the problem, and thinking it through from a systems perspective, would do a great deal to increase the impact of research in nanotechnology intended to apply to sustainability.

Healthcare and cost control. The distribution of benefits in healthcare (to the poor minority in the developed world, and to majority in the developing world) will require, and is causing, a radical rethinking of medicine and healthcare.[86] Access, cost, and effectiveness are all important issues, and to change all three, in a way that benefits consumers of healthcare, requires a movement from the high-technology, high-cost, end-of-life focus of the developed world to simple, low-cost, public health measures that make priorities of prevention and early detection of disease.[83] Again, throughout a shift of this sort, there will be opportunities for

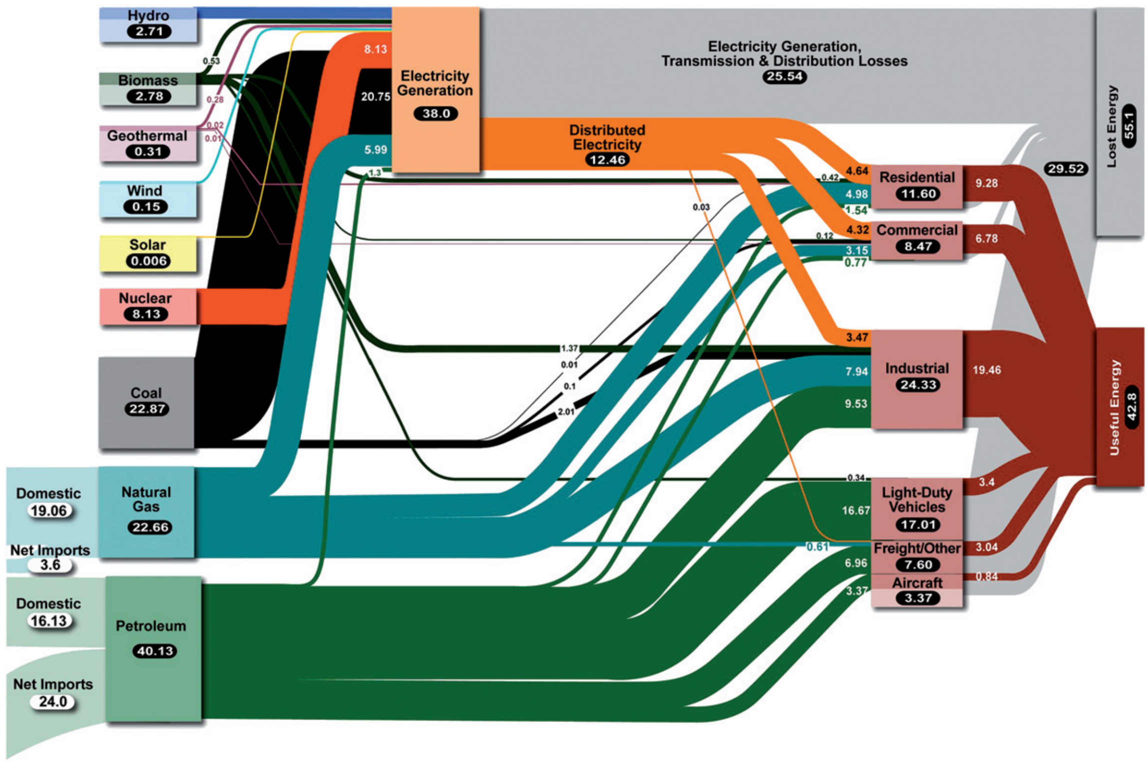

Fig. 2 Flowchart showing the origin and consumption of the energy produced in the US in 2005, including losses. The units are in quads; 1 quad = 10^{15} BTU = 1.055 EJ. Most of the energy is lost by transmission and conversion. The category "useful energy" conceals a large but incalculable fraction of energy that need not have been expended. (Source: Lawrence Livermore National Laboratory and US Department of Energy, 2005).

many new technologies, and no single one can make an enormous impact (although the availability of clean water and safe food, not smoking, exercise, weight control, and childhood vaccination provide a strong foundation).[87] For soft nanoscience, small systems and particles (for sensors, adjuvants, vaccines, systems for chronic healthcare monitoring, and others) have characteristics that suggest they could play an important role;[83] for nanotechnology in general, the marriage of information technology and medicine is probably the greatest opportunity.[88]

Megacities. In the future, much of the world's population will live in so-called "megacities": cities with populations of 20 to 40 million.[89] There is no clear technical strategy for managing populations of this magnitude, and the problems that they prose will be new. How does one provide clean water, clean air, safe food, transportation, personal security, education, work, and recreation for very large, very dense aggregates of people? We simply do not know, but it seems inevitable that micro- and nanoscience will be important parts of the services of such cities: for separations, inexpensive testing of water, food, and public health; as components of effective systems for public health; and as parts of many other technologies that are based in part upon small structures.

Information technology. We have offered the opinion that soft nanotechnology will probably not play a major part in radical change in high-performance information technology. There are, however, many other vitally important aspects of information technology where nanotechnology, and possibly soft nanotechnology, could plausibly play a role. These include consumer electronics for a wide variety of applications,[90] electronics for education, technologies related to healthcare such as implantable sensors,[91] very broadly distributed environmental sensors, intelligent buildings and cities for energy management,[92] and a range of others.

4.2 The next big thing?

Robotics. What will come after information technology and biotechnology? One possibility is robotics, which will, of course, have components from both information technology and biotechnology. The hardware of information technology (microprocessors, sensors, controllers) will unquestionably play a central role in the future development of robotic systems. Whether soft nanotechnology will be equally important will probably depend upon the emergence and ultimate importance of soft robotics.[93] Although most robotic systems are presently conceptually simple machines relying on sophisticated controllers, sensors, actuators, there is now great interest in developing robotic systems whose conceptual forbears are closer to squid or worms than to humans or donkeys.[92] These systems—with soft structures, and a requirement for flexibility—will benefit from soft electronics, and, we presume, from soft nanoscience.

The breadth of nanotechnology, including soft nanotechnology, is such that it is inevitable that these very large problems will involve solutions that incorporate some aspects of "nano". The question of whether chemistry can reach these solutions more efficiently by targeting the development of soft nanoscience to specific problems, or whether it is more efficient for chemists working in nanoscience to continue with relatively undirected programs in discovery, and for the engineers who work most directly on these problems then to reach back into nanoscience to find materials and components appropriate for their needs, remains to be seen.

5. Basic science: research problems for which soft nanoscience is uniquely suited

We have focused much of this summary and forecast on function and applications, in part because it seems that these areas are significantly less developed, and less of a focus, in the soft nanotechnology represented by this Faraday Discussion, than are exploratory academic studies focused on synthesis and properties. It is, however, important to understand that there are problems in fundamental science which will rely absolutely on understanding phenomenon that occur at the nanoscale for their solution. These problems constitute a long list, and include fundamental studies of heterogeneous catalysis, the nature of structures inside the cell, the role of nanoparticles in the environment, the relation between nanoscale structure and properties in materials, the nature and properties of nanoscale interfaces, options for actuation and sensing on the nanoscale, and synthetic techniques particularly appropriate to nanoscale science such as self-assembly and templated assembly. Simply for illustration, we briefly outline two problems in nanoscience that are especially important.

5.1 Molecular recognition and near-surface water

From a reductionist viewpoint, arguably the most important process in biology is molecular recognition. Everything—the formation of lipid membranes, the folding of proteins, the replication of DNA and reading of mRNA, the interaction of drugs with proteins, the activity of receptors and transporters, and so on—all rely on the recognition of one molecular surface by another. In the past, molecular recognition has been phrased as a scientific problem in terms of "lock and key". We now recognize that this formulation is fundamentally incorrect, in that it leaves out the medium, which is usually aqueous.[94,95] Understanding near-surface water (including, in particular, the water surrounding the functional surfaces of the drug, and the water filling the active site of its target protein) is perhaps the most important problem in biophysics.[96,97] The distances over which the phenomena involved extend, the interplay of enthalpy and entropy in these systems, the nature of interactions between hydrophobic surfaces and near-surface water, the interactions among electronically polarizable groups in an aqueous environment—all are nanoscale, soft, phenomenon. Soft nanoscience has an enormous opportunity to contribute to understanding the remarkable properties of liquid water within the first few nanometers of a molecular surface, and to do so—most importantly—using biological molecules and biological media.

5.2 Charge transport in organic matter

Photosynthesis supports almost all life on Earth. At the heart of photosynthesis is a series of energy and charge transport processes that convert the energy present in photons into reagents (ATP, NAD(P)(H)) and electrochemical gradients in photosynthetic plants, algae, and some bacteria.[98] Our understanding of charge transport in conductors and semiconductors is excellent; our corresponding understanding of charge transport in putative insulators (*e.g.*, within proteins and across membranes) is much less highly developed, both experimentally and theoretically.[99,100] Soft nanoscience offers the opportunity to study the fundamentals of charge transport across insulating systems relevant to photosynthesis, and to other areas of biology (*e.g.* oxidative metabolism)—and has begun to develop experimental systems relevant to these studies.[101,102]

6. Outlook: "nano" has moved; nano*chemistry* may need to adjust to keep up

This Faraday Discussion was successful in displaying a cross section of the interests and competencies of a central and distinguished group of soft nanoscientists, in laying out some of the opportunities in soft nanoscience, and in illustrating current activities of chemistry related to soft nanoscience and nanotechnology. It emphasized the skill of chemists in making things (whether on molecular or nanometer scale) and in studying chemical properties. It also betrayed a weakness of chemistry in thinking forward to function and applications in complex systems in which the chemistry of the starting materials was only a part of the problem. Synthesis, properties, function, applications—*all* are challenging to conceive and execute. Since chemistry is one of the central players in nanoscience, it could be very interesting, useful, important, and profitable for it to try to encompass the entire spectrum needed to go from fundamental understanding to societal benefit, rather than to leave the later links in this chain to other disciplines.

In the twenty-five years over which nanotechnology has grown as a recognizable subfield of science, its foci have shifted. Some of the original possibilities—radically new, small computers and machines—have been replaced by equally important but very different problems: focused extension or replacement of processes for fabricating silicon-based information processors, sustainability, energy production and conservation, imaging and genomics, and water. Ideally, soft (that is chemical) nanotechnology will become engaged in the most important of these problems, from their scientifically interesting beginning to their societally beneficial end.

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