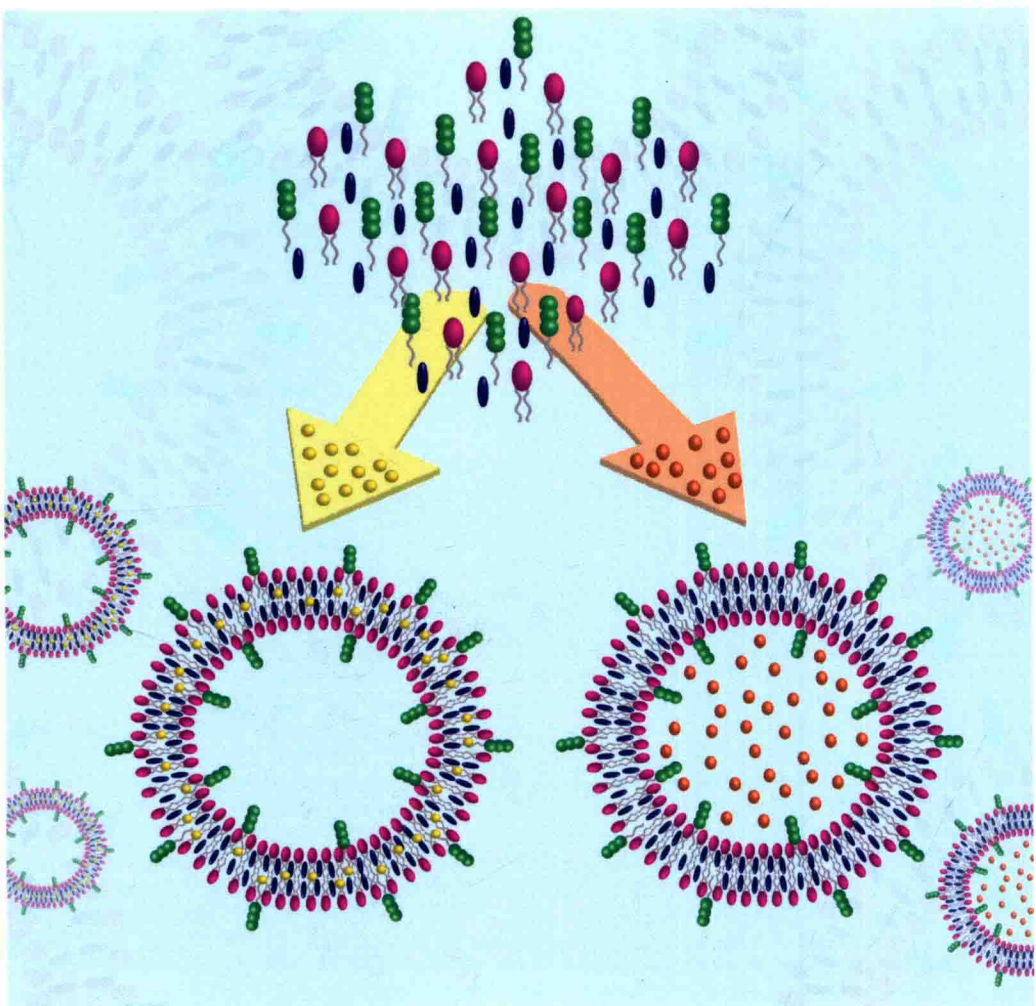
Faraday Discussions Vol 166

Self-Assembly of Biopolymers



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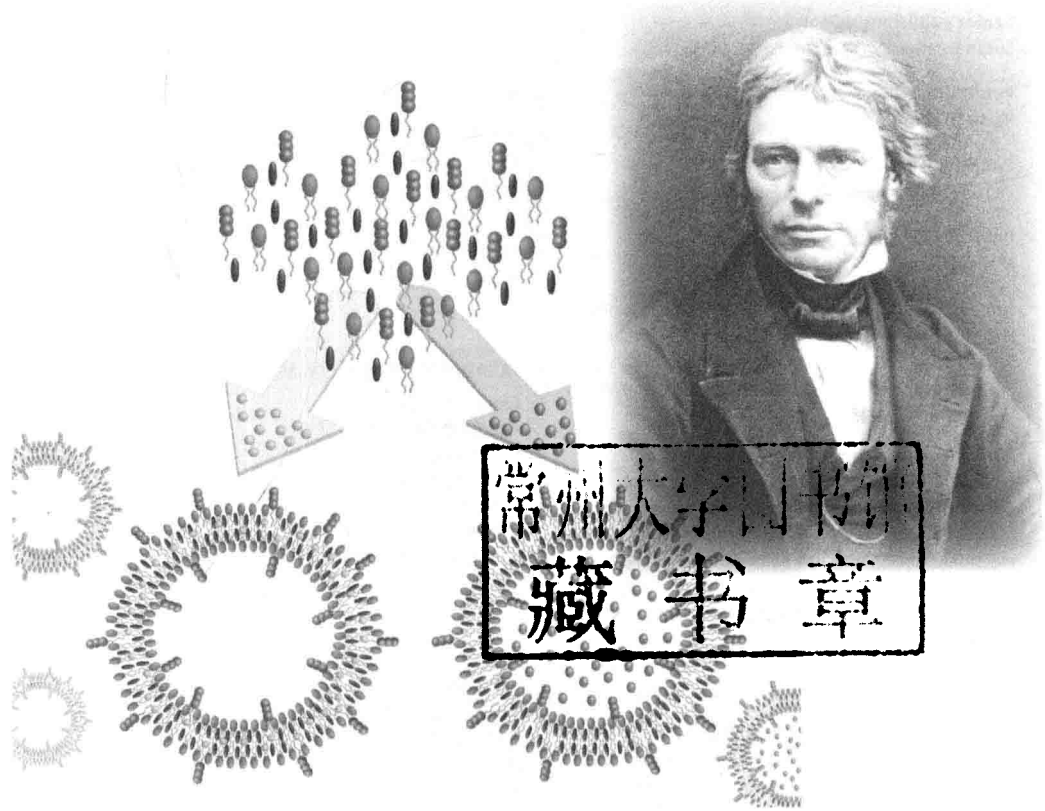
Self-Assembly of Biopolymers

University of Bristol, UK
16–18th September 2013



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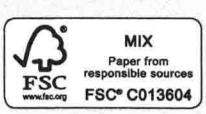

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Self-Assembly of Biopolymers

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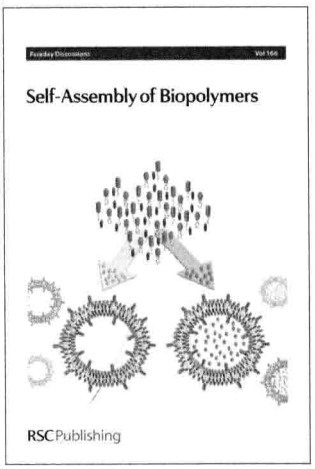

Cover

See Tekinay, Guler, *et al.*, *Faraday Discuss.*, 2013, **166**, 269–283.

Liposamal delivery systems can be functionalized with amphiphilic peptides for enhanced cell uptake.

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INTRODUCTORY LECTURE

PAPERS AND DISCUSSIONS

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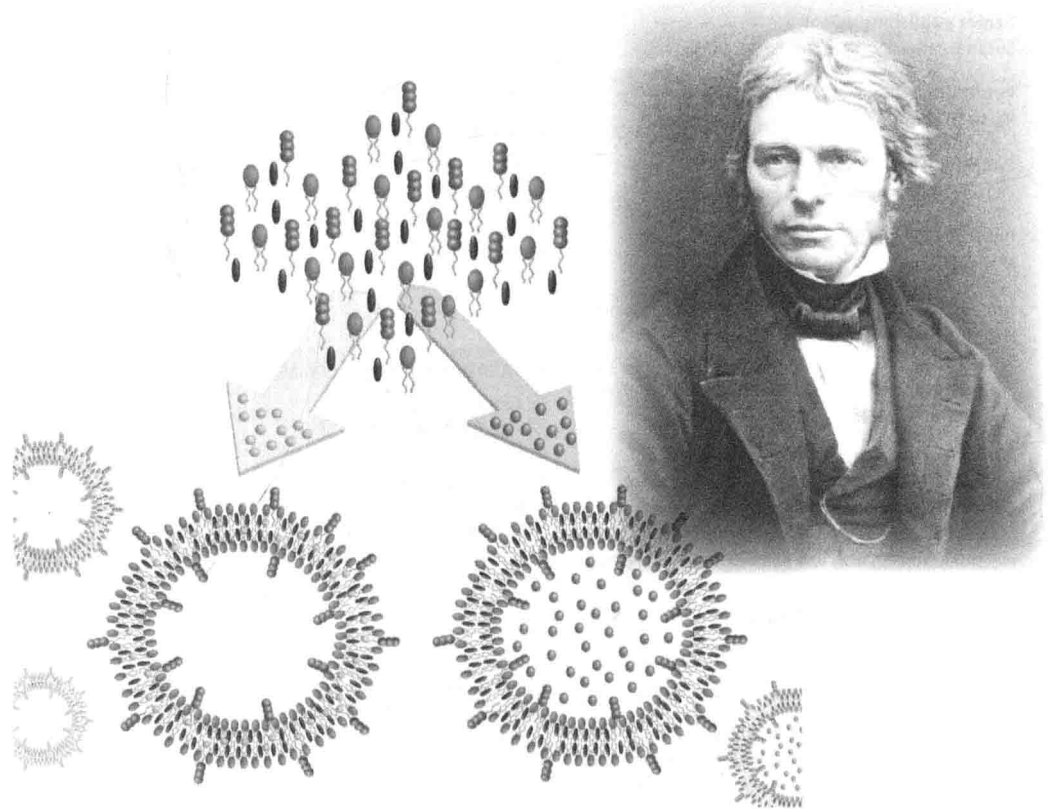

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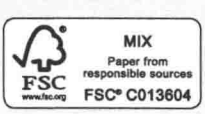

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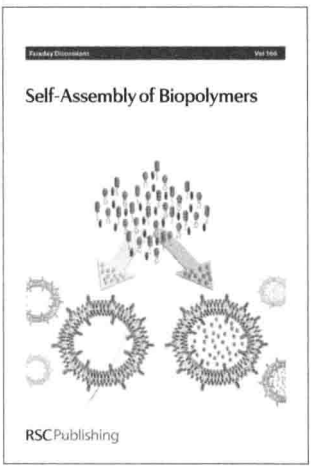

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PAPER

Self-assembly of biomolecular soft matter

Samuel I. Stupp,*[abcd] R. Helen Zha,[a] Liam C. Palmer,[b] Honggang Cui[a] and Ronit Bitton[d]

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DOI: 10.1039/c3fd00120b

Self-assembly programmed by molecular structure and guided dynamically by energy dissipation is a ubiquitous phenomenon in biological systems that build functional structures from the nanoscale to macroscopic dimensions. This paper describes examples of one-dimensional self-assembly of peptide amphiphiles and the consequent biological functions that emerge in these systems. We also discuss here hierarchical self-assembly of supramolecular peptide nanostructures and polysaccharides, and some new results are reported on supramolecular crystals formed by highly charged peptide amphiphiles. Reflecting on presentations at this Faraday Discussion, the paper ends with a discussion of some of the future opportunities and challenges of the field.

1. Introduction to the field

Self-assembly has fascinated a very large number of scientists over the past decade. If this bio-inspired strategy could be generally implemented in synthetic systems, it would have a profound impact on new materials and devices, as well as help in the discovery of new behaviors, even emergent ones, in abiotic systems. Fig. 1 shows the number of papers dealing with self-assembly published over the past decade and the various fields of science associated with them. Chemistry, materials science, and physics dominate. In life sciences, not surprisingly, self-assembly as a strategy for fabrication of functional systems is taken for granted. To the physical scientist, the following phenomena are truly amazing examples of dynamic self-assembly involving molecular and supramolecular programming: protein folding, formation of receptor rafts for signaling on cell membranes, alignment of muscle fibers over macroscopic length scales, assembly of the ribosome as an efficient protein-making machine, reversible filaments of the cytoskeleton, hierarchical structure of articular cartilage with spatially varying orientations of collagen fibers to create a remarkably tough tissue with low coefficient of friction, and many others.

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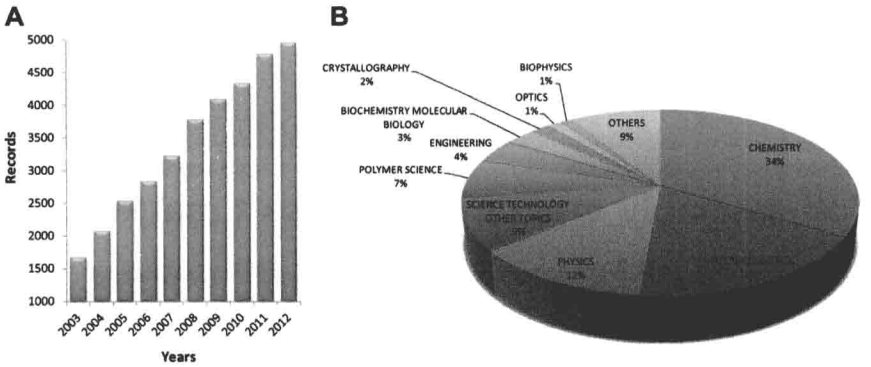

Fig. 1 Analysis of publications using the term "self-assembly" over the past decade (2003–2012). This record was obtained from the Web of Science database using the keyword "self-assembly" as the search topic. (A) Bar graph reveals a continuous growth in publications per year over this period. (B) Pie chart shows the percentage of these publications categorized by research area.

The self-assembly of synthetic systems relies on components designed to spontaneously order into a "functional" structure with little or no intervention from humans or machines.[1] As stated above, this process takes its inspiration from biology and can occur at molecular to macroscopic length scales. Non-covalent interactions such as hydrogen bonding, π–π stacking, metal–ligand interactions, electrostatic forces, dipole–dipole interactions, hydrophobic forces, and steric forces can now be used as part of a "supramolecular code" to design simple self-assembling materials, relative to biological systems.[2] These so-called simple structures can be equilibrium structures and thus regarded as "static" at specific temperatures, pressures, or environments. However, they can also be highly metastable and exist in non-equilibrium states. In the early stages of the self-assembly field, systems that could be regarded as nano-sized materials in which relatively small molecules aggregated through short range interactions were investigated. The assemblies created were nanoscale supramolecular objects such as non-centrosymmetric clusters of molecules,[3] ribbons,[4] tubes,[5] helices,[6,7] among others. More complex systems in terms of structure and function could be accessed by dissipative systems which require energy input in the form of "fuels"[8] or external forces. In these systems it may be possible, as observed in biology, to achieve higher complexity levels of self-organization. Other systems may require a structural template, such as in biomineralization processes. One of the grand challenges in the field of self-assembly is to develop strategies to create hierarchical structures, also commonly observed in biological systems. So far examples of hierarchical self-assembly have been discovered,[9] but the principles to design them rationally are effectively not known.

In the biopolymers space, the subject of this Faraday Discussion, the systems of interest are polypeptides, nucleic acids, polysaccharides, biologically synthesized condensation polymers, and supramolecular polymers built from biomolecular structural units such as peptides and oligonucleotides. Hybrid combinations of these systems could greatly expand the scope of the field. These macromolecules and supramolecular structures have potential for biocompatibility or bioactivity since they are built from biomolecular units. Peptides,

polypeptides, and proteins naturally contain many self-assembling motifs and a high potential for function.[10,11] New opportunities for functional materials have opened up with biosynthetic strategies which incorporate artificial amino acids or non-peptide backbones.[12,13] It is in fact now possible to express artificial proteins with non-canonical amino acids using bacteria.[14] The self-assembly of designed oligonucleotides has recently become a highly active area initiated by Seeman and co-workers, yielding programmed structures of arbitrary shapes driven by Watson–Crick pairing.[15,16] Very recently, these strategies have been used to design artificial DNA and RNA sequences for use in nanotechnology applications.[15–18] Oligosaccharides, in contrast to oligonucleotides and peptides, are difficult to synthesize with specific sequences but offer great potential to create systems with chemically encrypted biological information and thus potential for many important biological functions. One example of utilizing polysaccharides in self-assembly is the formation of complex supramolecular pseudorotaxane polymers using cyclodextrins (cyclic oligosaccharides) and small molecules.[19] Great progress has been made in oligosaccharide synthesis[20,21] but the preparation of more complex polysaccharide systems will require further synthetic innovation.

Many macromolecules with biological structural units have been synthesized and studied over the past few decades as covalent polymers, generating an enormous body of literature that is not covered here. However, the greatest potential for biomolecular soft matter with structural complexity and function lies with self-assembling systems in which supramolecular structure can be programmed. So far, this opportunity is on the horizon with peptide-based systems, which will eventually integrate with glycochemistry and oligonucleotides. This paper as well as many of the presentations at this Faraday Discussion are focused on peptide systems, particularly those that can create self-assembling structures across multiple scales.

Peptides offer a great structural tool for the science of self-assembly and for our understanding of proteins. At the same time, their synthesis is relatively simple and well developed (provided they are not too long) even though their purification can be challenging. It is also important that peptide-based systems can allow some degree of rational control based on current knowledge over molecular conformations and intermolecular interactions through the primary sequence of amino acids. This allows the possibility of interpreting the supramolecular complexity that often emerges in these systems. With regard to crafting function, the potential of peptides is enormous since they are the central signaling language of biology. This also provides the opportunity to create functional systems that are directly inspired by biology. The potential for biological interactions with other macromolecules, such as nucleic acids and polysaccharides, further augments the value of peptides. Thus, peptides can form the basis of systems programmed for useful applications in medicine, catalysis, energy related technologies, manipulation of microorganisms, and many other areas. On the structural side, the challenges include a deep understanding of the competition between inter-peptide *vs.* peptide-water interactions and also of the competition of hydrogen bonding, electrostatics, and hydrophobic contacts. These issues are critical for the development of a supramolecular code for peptides that can predict self-assembly of nanoscale and larger hierarchical architectures. Architectures known so far include, cylindrical fibers, spheres, lamellae, twisted ribbons, flat ribbons/tapes/belts, tubes, and helical ribbons. On