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Perspectives

Designing dynamic functional molecular systems

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ABSTRACT

The design and construction of dynamic functional molecular systems, which mimic some of the properties of living systems, pose a huge contemporary challenge. Recent developments in supramolecular self-assembly, molecular switches, motors and machines, and chemical reaction networks, offer an excellent basis for integrating dynamic properties in molecular systems. In this perspective, we discuss different approaches towards dynamic functional molecular systems covering areas such as translated motion, dissipative self-assembly, self-regulation and biohybrid systems. The selected examples illustrate the level of control and complexity that can be achieved at present in this rapidly growing and exciting field of research.

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1. Introduction

A distinctive feature of synthetic chemistry is its amazing creating power as is evident from the wealth of molecules and materials that enable proper functioning of our modern society. From drugs to dyes, cables and cars to displays and detergents, it is the creativity in designing structure and function along length scales, ranging from small molecules to mesoscopic and macromolecular materials, where chemistry shows its nearly unlimited opportunities for exploration. The total synthesis of many of the most complex natural products is a clear testimony of the often ingenious way synthetic chemists have mastered chemical reactivity, functionality and covalent assembly of complex structures. With the advent of supramolecular chemistry, the stage is set for non-covalent assembly and molecular recognition processes far beyond the level of the individual molecules reminiscent to many phenomena in biological systems. In recent years a new dimension has been added with the introduction of dynamic covalent chemistry providing a stepping stone to adaptive and potentially evolutionary behavior.

A closer look at the molecules of life itself immediately leads to the realization that biomolecules do not function in isolation but are usually part of complex molecular systems that operate in a highly dynamic manner. Membrane transport, the process of vision, muscle movement, ribosomal peptide synthesis or bacterial flagellar rotation are just a few examples of the "machinery of life"[1] and the delicate interplay of complex biomolecular assembly and specific well controlled dynamic processes that ultimately allow a

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specific biological function. Beyond the mere "synthesis for function" it is the design of dynamic functional molecular systems that offers great challenges for contemporary chemistry and molecular nanoscience. The recent progress in the development and application of molecular switches, motors and machines, provides a superb basis for the exploration of dynamic properties in molecular systems.

Moving from molecules to dynamic molecular systems, it is evident that the emphasis in the chemical design strategy shifts to complex and multicomponent molecular assemblies and responsive behavior. Besides the obvious precise design of molecular structure and its synthesis, control over organization, specific functions and/or tasks, the multi-molecular ensemble, interface phenomena and hierarchical levels, are some of the main aspects to deal with. Design, synthesis and reactivity are cornerstones in the approach but integration of structure and function, control of assembly and intrinsic dynamic properties are equally important. As the ultimate goal is dynamic and responsive function, it is essential to consider from the onset questions associated with triggering, addressing and sensing. Here the molecular designer can exploit a wide variety of chemical and physical triggers including pH, ion binding, redox, chemical conversion and light. Numerous opportunities arise when the suite of chemical catalysis methodology is to be exploited, i.e. coupling chemical conversions to control of dynamic functions. It should be reminded that biomolecular motor-driven mechanical processes in Nature are almost exclusively governed by catalytic conversions of chemical fuels (e.g. ATPase rotary motor). The study of dynamic behavior allows also the development of molecular systems that operate far from thermodynamic equilibrium akin of many natural processes. Other important challenges associated with dynamic molecular systems are cooperative or collective behavior, amplification of motion along many length scales (i.e. molecular, supramolecular, mesoscopic, microscopic, macroscopic) and interfacing to the micro-macro-worlds including control of hard-soft interfaces. Once the design principles are established and control over dynamic functions is achieved, the stage is set for autonomous processes as well as emerging and adaptive behavior. Signal transduction, molecular information processing, feedback mechanism and self-repair mechanisms are all major challenges ahead. Despite the complexity of the envisioned systems and the intricate interplay of multiple functions, the prospects in a more distant future for soft robotics, smart materials and numerous biomedical applications are particularly bright.

Here we discuss approaches towards dynamic functional systems and provide a perspective in areas ranging from molecular motion, responsive materials, dissipative and self-regulatory systems to dynamic bio-hybrid systems. The examples presented are not exhaustive but an illustration of the level of control of complex functions and dynamic properties that can be achieved in this young but rapidly emerging field.

2. From molecular to macroscopic motion

Among the most fascinating dynamic functional molecular systems are those in which motion at the molecular level translates into movement at the macroscopic scale. Initially, the driving force behind this research objective was to prove that molecular switches and motors can perform work.[2] However, because of the rapid progress in this field, functional applications of these systems are now becoming within reach. For example, in soft robotics since soft matter is the most frequently used material in this research.

The group of Ikeda showed that the photoinduced structural changes in azobenzene switches can be harnessed to achieve macroscopic motion, i.e. the directed bending of a thin polymer film.[3] The thin film was prepared by co-polymerization of azobenzene-containing liquid crystalline monomers with a diacrylate crosslinker affording a liquid crystalline film consisting of small domains. Each domain is composed of many azobenzene units, which are all aligned in the same direction, although on average, for all the domains, the alignment is randomly distributed. Irradiation with linearly polarized light, led to the *trans*-to-*cis* isomerization of only the azobenzene moieties aligned with the light's polarization direction. This isomerization resulted in a decrease in size of the liquid crystalline domains and hence, a contraction of the volume at the illuminated surface, which consequently led to bending of the film. The polymer film could be used as a transmission belt to power a rotary motor with light (Fig. 1a).[4] This example beautifully illustrates how motion at the molecular scale can induce macroscopic movement and moreover, how azobenzene photoswitches can be used to convert light energy into mechanical work.

Inspired by this work and also related studies conducted by Broer and co-workers,[5,6] the group of Katsonis took the next step in the development of these materials.[7] The addition of a small amount of chiral dopant to the azobenzene containing liquid crystalline matrix afforded thin films with extraordinary properties. Depending on the angle at which these films were cut, ribbon-like structures with either left or right handed helicity and varying pitch were obtained. The responsive behavior of these ribbons upon irradiation depended on their morphology: They either exhibited a winding or an unwinding motion, or displayed an inversion of their handedness. The group of Katsonis nicely demonstrated how this feature could be used to construct a functional device.[7] A ribbon with mixed helicities, where one half contracts upon irradiation while the other part expands, was able to perform work in the form of moving two magnets (Fig. 1b).

Our group presented a different approach to amplify molecular motion using the unique properties of liquid crystalline materials.[8] Instead of covalent functionalization, the doping of a nematic liquid crystal with small quantities of enantiopure molecular motor, resulting in the formation of a cholesteric phase, proved to be sufficient to control the liquid crystal properties. When the liquid crystal was placed on top of a glass slide covered with a unidirectionally aligned polyimide layer, photoisomerization of the chiral motor dopant led to a rotational reorganization of the cholesteric texture, which could be used to power the rotation of a microsized glass rod (Fig. 1c).

In addition to the use of light, chemical stimuli can be used to achieve macroscopic mechanical work via molecular motion. Skeletal muscles are a good example of how chemically-induced molecular motion can be harnessed to achieve function. Sauvage and co-workers conducted pioneering work on mimicking the action of muscles in a fully synthetic system.[9] In his daisy-chain rotaxane based system, the addition of Cu^{+} and Zn^{2+} ions led to an extending and contracting motion. Stoddart et al. demonstrated how this type of motion, in a rotaxane assembled on gold, induced by chemical oxidation and reduction, could be used to enable bending and straightening of a cantilever (Fig. 1d).[10]

One of the benefits of light-driven rotary molecular motors compared to bistable switches (e.g. azobenzene) is that they exhibit repetitive unidirectional motion. This feature is highly beneficial when continuous molecular motion is desired, for example, in the system developed by the group of Giuseppone who integrated a light-driven molecular motor into a polymeric PEG gel via a quadruple Click reaction (Fig. 2a).[11] The rotation of the motor led to the braiding of the polymer chains, resulting in gel shrinkage. In this way, light energy could be stored into the gel as potential energy with an efficiency of about 0.15%. However, it was impossible to harvest this energy as the process of braiding the polymeric