Active Biomimetic Systems with Mobile Nanostructures

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Summary

Biological systems contain a large variety of nanostructures and colloids built up from macromolecules and supramolecular assemblies. The corresponding structure formation processes – polymerization and aggregation – have been used for a long time in order to construct a large variety of biomimetic nanostructures such as polymers and association colloids.

Another fundamental aspect of self–organization in biological systems is their ability to *reorganize and to reconstruct their spatial structure on the nano– and microscale*. This capability is based on *active nanostructures* such as growing filaments and moving molecular motors. The integration of these active components into supramolecular assemblies leads to 'smart' microsystems which are able to respond to and to 'survive' in a changing environment.

This talk reviews recent progress in the construction of active biomimetic systems which represent simplified models for the rather complex biological systems. Three examples will be discussed in some detail: (i) Force generation by growing filaments; (ii) Transport by molecular motors; and (iii) Active assemblies of motors and filaments. The talk also advertises the vision that these active systems provide the foundations for a new, mobile nanotech. Potential applications include nanoscale manufacturing, sorters for nanoparticles, and switchable networks or scaffolds of filaments.

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1. Introduction: Biological and Biomimetic Nanostructures

Biological systems are complex and contain many levels of self–organization. The most fundamental level corresponds to the nanodomain of biocolloids which extends from molecules to cells and which may be regarded as the twilight zone between matter and life.

The smallest structures within this nanodomain consist of molecular building blocks or monomers. These monomers can be divided into several subsets which contain chemically similar but distinct elements. These elements can be connected by covalent bonds which leads to the formation of *polymers* such as proteins, nucleic acids, polysaccharides, and lipids.

Biopolymers form supramolecular assemblies such as filaments, membranes, and ribosomes. Filaments are usually built up from a single protein component whereas membranes typically contain a large number of lipid components as well as protein and polysaccharide components. Ribosomes are formed by the self–assembly of proteins and RNA. Finally, different types of assemblies interact and form 'super–assemblies'. A simple example is provided by a lipid vesicle bound to a filament via a motor protein.

On the one hand, all of these biological structures represent nanostructures (or colloids) in an aqueous environment. On the other hand, all nanostructures (or colloids), which are dispersed in water, may be regarded as *biomimetic*.

There are several different strategies in order to construct biomimetic nanostructures which resemble their biological counterparts. First, one may use the basic construction principles used in biological systems – polymerization and aggregation – but simplify the chemical composition. This strategy leads (i) to polymers, which consist only of a single type of monomer, and (ii) to lipid bilayers, which contain only a few types of lipid molecules. Secondly, one may focus on certain biological subsystems which contain only a relatively small number of components. Thirdly, one may construct hybrid systems which contain a combination of natural and synthetic components.

These biomimetic construction methods have produced a wide variety of different nanostructures (or colloids). The next challenge for biomimetics in the nanodomain is to couple these structures to active processes which resemble those used for the free energy transduction in biological cells.

2. Thermodynamics and Nanomachines

Consider a nanocompartment which contains a mixture of different molecules. The compartment is kept at constant temperature and pressure. To be precise, let us focus on time scales for which we can ignore the exchange of molecules between the nanocompartment and its environment. In such a situation, the 2nd law of thermodynamics imposes certain constraints on all processes which may occur in the compartment. First, any spontaneous process must be *exergonic*, i.e.,

it must decrease the free enthalpy of the system. In practise, such a process may be rather slow and one then needs a catalyst in order to speed it up. Secondly, any *endergonic* process, which *increases* the free enthalpy of the system, must be coupled to another, exergonic one.

As an example, let us consider the assembly of polypeptides (or proteins) from amino acids. In the absence of any free energy transduction, this assembly process is endergonic and, thus, cannot occur spontaneously. In biological cells, this assembly is performed by nanomachines, aminoacyl–tRNA synthetases and ribosomes, which couple peptide bond formation to the exergonic hydrolysis of ATP and GTP. As a result of this free energy transduction, ribosomes can assemble about 20 amino acids per second.

Since the formation of a peptide bond is endergonic, its cleavage is exergonic (if one ignores the possible shielding of the bond by folding of the chain). This is true in general: if the forward process is endergonic, the backward process is exergonic and vice versa. This has direct implications for any nanomachine which undergoes a *cyclic* sequence of processes: Any such cycle must involve at least one exergonic process.

3. Biological Complexity and Biomimetic Models

The hydrolysis of ATP (or of other nucleoside triphosphates) can drive many different processes such as: synthesis of DNA and RNA; protein folding by chaperones; ion transport across membranes via pumps; treadmilling of filaments; movement of cytoskeletal motors along filaments; disassembly of clathrin cages; etc. In addition, biological systems use other exergonic processes such as the growth of filaments arising from the nonequilibrium between the molecular building blocks and the linear aggregates. The growing filaments can exert localized forces onto particles and membranes.

In the living cell, all of these different processes of free energy transduction are 'entangled' and form complex networks involving many different molecular species. In order to gain a deeper and more quantitative understanding, one has to construct biomimetic model systems to which one can apply the experimental and theoretical methods of physics and chemistry. The systematic study of these model systems will then enable us to improve their design, to optimize their performance, and to increase their reliability.

As described in the following sections, such biomimetic model systems are now available for several active processes.

4. Force Generation by Growing Filaments

The simplest mechanism which leads to active force generation is based on growing filaments. In biological systems, this type of force generation is provided by actin filaments (or F–actin) and microtubules. Actin filaments, which grow by

aggregation of actin monomers (or G–actin), have a diameter of about 8 nanometer and can have a length of up to 20 micrometers. Microtubules built up from tubulin dimers have a diameter of about 25 nanometer and can have a length of up to hundreds of micrometers.

The presumably simplest model system consists of a *single* filament which grows against an obstacle. If the obstacle is immobilized, the growth of the filament may be stalled or the filament may buckle. The latter process has been recently observed for single microtubules. The corresponding stall force was estimated to be of the order of 10 piconewton.

Force generation by single actin filaments has not been determined so far. However, a relatively simple assay has been found which leads to the propulsion of micrometer beads by thick actin 'tails' containing a large number of branched filaments. The growing 'tails' push the beads with a velocity of about 100 – 200 nanometer per second.

5. Transport by Molecular Motors

In all animal and plant cells, one observes heavy traffic of vesicles and other types of nanoparticles. This transport is based on molecular motors which move along filaments via discrete steps. A single molecular motor needs about 10 milliseconds in order to make a single step of about 10 nanometers. Processive motors such as dimeric kinesin and myosin V make about a hundred steps before they detach from the filament. The corresponding walking distance is of the order of one micrometer.

It is now possible to construct biomimetic transport systems based on filaments and motors. The filaments are immobilized on a substrate surface. The motors are attached to cargo particles which can be manipulated by optical tweezers (or laser traps). It is useful to have several active motors per cargo particle since the walking distance grows essentially as $\exp(n)$ with the number n of active motors.

The strong attraction between filaments and processive motors leads to an overcrowding of the filaments and, thus, to traffic jams. As a consequence, the motor current along the filament exhibits a maximum at an optimal motor concentration in the surrounding solution. In addition, transport systems with many motors exhibit nonequilibrium phase transitions at which the state of these systems can be switched by a small change in an appropriate control parameter. Particularly interesting phase transitions arise in systems with two motor species which move into opposite directions.

6. Active Assemblies of Motors and Filaments

Many active processes in biological cells are based on the mutual displacement of filaments by motors. The relative displacement of microtubules, for example, is crucial for the formation of the mitotic spindle during cell division. Likewise,

actin–myosin complexes form 'nano–muscles' which play an important role for cell adhesion and cell locomotion.

Several biomimetic systems have been studied which contain both mobile motors and mobile filaments. For microtubules which are crosslinked by kinesin motors, the activity of the motors leads to stationary patterns of filaments which have the form of asters or vortices. For actin filaments which are crosslinked by myosin motors, on the other hand, the filaments are crosslinked in the absence of motor activity but become disassembled when this activity is switched on.

In the microtubule–kinesin system, the free energy transduction arising from the motor activity leads to a transformation from a disordered mixture into highly ordered states. For the actin/myosin system, on the other hand, the motor activity transforms partially ordered states into disordered mixtures.

7. Perspectives for Mobile Nanotech

More than fourty years ago, the theoretical physicist Richard Feynman gave an after dinner talk in which he pointed out that there is 'Plenty of Room at the Bottom' (where 'Bottom' means 'Nanodomain'). His main source of inspiration was biological information storage in the DNA which corresponds to one bit of information in about 1 cubic nanometer. He then estimated that, using this information density, one could store all knowledge of mankind, contained to about 25 million books, on a dust particle with a diameter below one millimeter!

Modern information technology has come a long way in order to fulfill this vision. Indeed, the memory sticks, which we now use with our laptops, store Gigabytes and are smaller than matchboxes. There are several promising candidates for new principles of information storage (including carbon nanotubes) which will further increase the density of information storage.

In his talk, Feynman also speculated about the possibility to assemble nanostructures 'atom by atom' and about nanomachines such as 'nano–surgeons' which one could simply swallow. Two decades later, Eric Drexler and the Foresight Institute rediscovered these ideas and proposed a variety of possible designs for such nanomachines and 'nanorobots'. If one looks at those designs, one clearly sees that they are inspired by the engineering of macroscopic devices: the Foresight nanomachines resemble macroscopic machines scaled down into the nanodomain.

The main message of this talk is that the most promising candidates for future nanomachines are biomimetic ones. As described above, we now have several examples where we can construct active biomimetic systems with mobile nanostructures. These model systems should have many possible applications. Some examples are: (i) Active force generation by growing filaments could be employed for nanoscale manufacturing; (ii) Active transport systems based on molecular motors could be used for sorting out molecules and colloidal particles; and (iii) Active pattern formation based on assemblies of motors and filaments could lead to switchable networks or scaffolds for nanoparticles and cells.