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Dynamic Nanoparticle Assemblies

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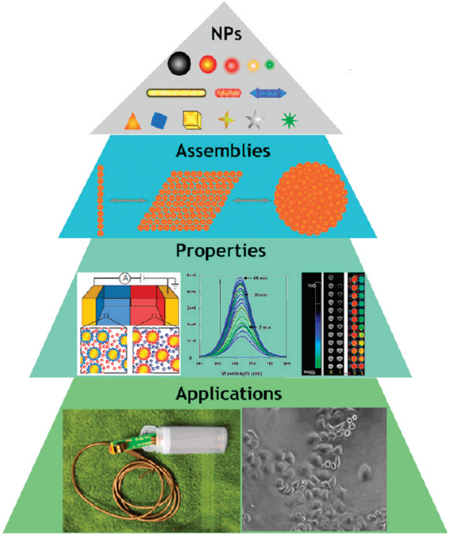
CONSPECTUS



Although nanoparticle (NP) assemblies are at the beginning of their development, their unique geometrical shapes and media-responsive optical, electronic, and magnetic properties have attracted significant interest. Nanoscale assembly bridges multiple levels of hierarchy of materials: individual nanoparticles, discrete molecule-like or virus-like nanoscale agglomerates, microscale devices, and macroscale materials. The capacity to self-assemble can greatly facilitate the integration of nanotechnology with other technologies and, in particular, with microscale fabrication. In this Account, we describe developments in the emerging field of dynamic NP assemblies, which are spontaneously form superstructures containing more than two inorganic nanoscale particles that display the ability to change their geometrical, physical, chemical, and other attributes. In many ways, dynamic assemblies can represent a bottleneck in the "bottom-up" fabrication of NP-based devices because they can produce a much greater variety of assemblies, but they also provide a convenient tool for variation of geometries and dimensions of nanoparticle assemblies.

Superstructures of NPs (and those held together by similar intrinsic forces)are classified into two groups: *Class 1* where media and external fields can alter shape, conformation, and order of stable super structures with a nearly constant number of NPs or *Class 2* where the total number of NPs changes, while the organizational motif in the final superstructure remains the same. The future development of successful dynamic assemblies requires understanding the equilibrium in dynamic NP systems. The dynamic nature of Class 1 assemblies is associated with the equilibrium between different conformations of a superstructure and is comparable to the isomerization in classical chemistry. Class 2 assemblies involve the formation or breakage of linkages between the NPs, which is analogous to the classical chemical equilibrium for the formation of a molecule from atoms. Finer classification of NP assemblies in accord with established conventions in the field may include different size dimensionalities: discrete assemblies (artificial molecules) and one-dimensional (spaced chains), two-dimensional (sheets), and three-dimensional (superlattices, twisted structures) assemblies. Notably, these dimensional attributes must be regarded as primarily topological in nature because all of these superstructures can acquire complex three-dimensional shapes.

We discuss three primary strategies used to prepare NP superstructures: (1) anisotropy-based assemblies utilizing either intrinsic force field anisotropy around NPs or external anisotropy associated with templates or applied fields, (2) assembly methods utilizing uniform NPs with isotropic interactions, and (3) methods based on mutual recognition of biomolecules, such as DNA and antigen–antibody interactions.

We consider optical, electronic, and magnetic properties of dynamic superstructures, focusing primarily on multiparticle effects in NP superstructures as represented by surface plasmon resonance, NP–NP charge transport, and multibody magnetization. Unique properties of NP superstructures are being applied to biosensing, drug delivery, and nanoelectronics. For both Class 1 and Class 2 dynamic assemblies, biosensing is the most dominant and well-developed area of dynamic nanostructures being successfully transitioned into practice. We can foresee the rapid development of dynamic NP assemblies toward applications in harvesting of dissipated energy, photonics, and electronics. The final part of this Account is devoted to the fundamental questions facing dynamic assemblies of NPs in the future.

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Introduction

A wide variety of individual nanoparticles (NPs) were synthesized by different methods of nanoscale synthesis. Although the synthetic challenges to make intricate nanoscale shapes still persist, many basic shapes of common materials used in nanotechnology became routine. Instead, challenges related to making the complex structures using NPs as building blocks emerged. Nanoparticle superstructures offer even greater variety of nano/microscale systems than individual NPs and enable investigations of collective behavior/properties. The research on nanoparticle assemblies is constantly increasing (Figure 1), and there are many reasons to believe that it will continue with increasing rate.

One of the most intriguing parts of the research continuum on NP assemblies is dynamic superstructures. Dynamic NP assemblies can be defined as *spontaneously formed superstructures containing more than two inorganic nanoscale particles that display ability to change their geometrical, physical, chemical, and other attributes.* Dynamic NP assemblies are scientifically attractive because they

- open the pathway to understanding collective interactions in NP assemblies
- increase diversity of NP assemblies
- enable functional tuning/optimization of superstructures
- facilitate integration with microscale technologies
- mimic characteristic processes in live organisms.

With respect to practical applications, dynamic assemblies are potentially suitable for

- a variety of sensor devices
- stimuli-responsivze optoelectronic materials
- drug delivery vehicles
- energy harvesting

Other applications based on stimuli- and media-dependent restructuring, aka "smart" nanomaterials, should also be considered. In this Account, we summarize recent progress in dynamic NPs assemblies. Properties and emerging applications of dynamic NPs assemblies are also briefly discussed.

Classification

Considering current and constantly emerging new examples of dynamic processes (Figure 1), we can tentatively identify two classes of dynamic NP assemblies.

Class 1 encompasses superstructures that change their shape, conformation, size, topology, etc. The total number of the NPs does not change appreciably.

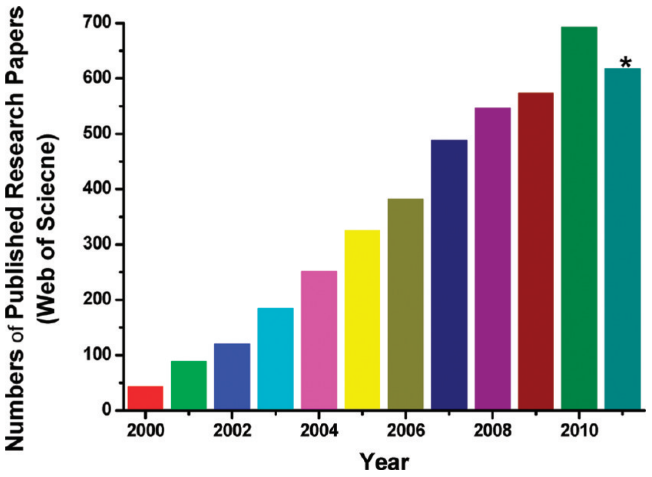

FIGURE 1. Research papers on NP assemblies (Source: Web of Science).

Class 2 encompasses superstructures in which the total number of NPs in superstructures greatly changes while the organizational motif remains the same.

Within each class one can also distinguish superstructures that are different in their spatial and topological characteristics: discrete assemblies[1,2], extended one-dimensional (1D),[3,4] two-dimensional (2D),[5] and three-dimensional (3D) assemblies.[6,7] The dimensionality classification follows the accepted terminology in the current literature and refers primarily to topology of NP "connections" within the assemblies rather than their actual geometry. For instance, NP chains are typically referred to as 1D assemblies and correspond to the case when most NPs have two neighbors. It is implicitly understood, however, that in solutions and on surfaces they can acquire complex 3D and 2D conformations. Similarly, the number of neighbors in flexible NP sheets is limited to, for instance, six particles localized within the equatorial plane but the sheets can acquire many 3D shapes.

Understanding equilibrium and kinetic effects[8] is exceptionally important for all dynamic and more so than for static NP systems. Note there are also dynamic superstructures responsive to external stimuli in a nonequilibrium fashion, which eventually result in static assemblies. Interparticle fusion to form the mesocrystals[7] and conformational transition of flat ribbons into twisted ribbons upon illumination[6] exemplify such systems.

The differences between Class 1 and 2 dynamic superstructures are fundamental. Class 1 assemblies are associated with equilibrium between different conformations of a superstructure. The transitions between them can be compared with isomerization in classical chemistry. Class 2 assemblies involve formation or breakage of linkages

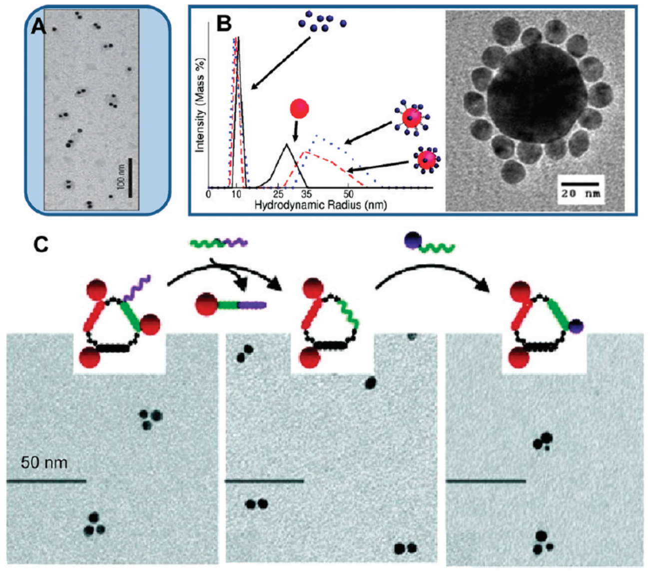

FIGURE 2. DNA-based discrete assemblies. (A) NP dimers; (B) reconfigurable satellite assemblies with hydrodynamic diameters in hairpin and extended states; (C) NP triangles and dimers from 15 and 5 nm NPs. Reproduced with permission from refs 2, 25 and 26. Copyright 2010 Nature Publishing Group; Copyright 2008 and 2007 American Chemical Society.

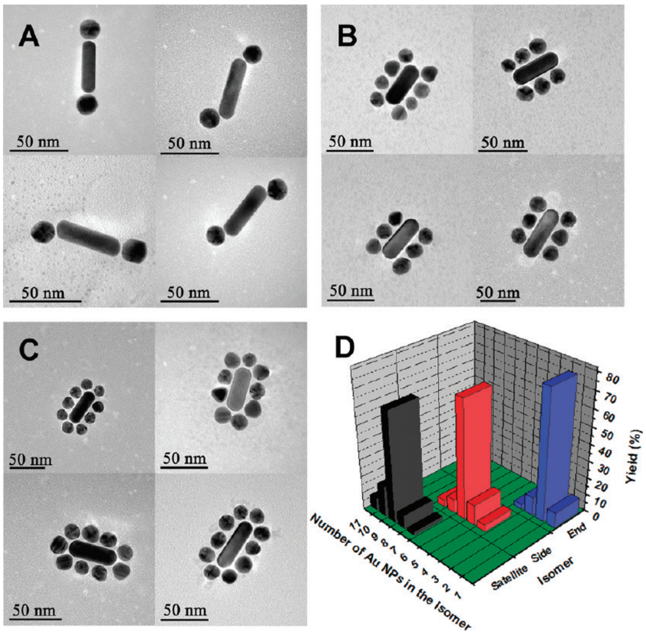

FIGURE 3. TEM images of DNA-based regioselective discrete assemblies: (A) *End*, (B) *Side*, and (C) *Satellite* assemblies with (D) yield analysis. Reproduced from ref 27. Copyright 2012 American Chemical Society.

between NPs. They can be compared with equilibrium in synthetic reactions.

Synthesis

Three primary strategies were used to synthesize static and dynamic NP superstructures. Historically the first was based on anisotropy of NP interactions with each other (intrinsic) or templates or external fields (extrinsic).[9–13] The second strategy is based on drying highly uniform NPs with isotropic interactions.[14–16] Such assemblies were made from semiconductor,[14] metal,[15,17] and magnetic[16] NPs. Interestingly, they can also be made from nonspherical NPs, for instance, from gold nanorods[18] and mixtures of NPs with different shapes.[19] The third and probably the most widespread strategy is the method utilizing biomolecules, when NPs are assembled following mutual recognition of biomolecules using DNA[20,21] or antigen–antibody pairs.[22] DNA is arguably the most attractive platform for dynamic assembly due to the base-pairing regularity and relatively simple synthetic strategies. They are also attractive to many applications especially sensing.[23] Both DNA and proteins give both Class 1 and Class 2 assemblies as well as different degrees of reversibility in the superstructures.[8]

Discrete Assemblies refer to nanoscale superstructures made from a finite and typically small number of NPs. Most of them take advantage of biomacromolecular linkages.[24] They allow for reconfigurable topology and conformational changes of superstructures. The assembly of NP dimers via hybridization of partially complementary single-stranded DNA (ssDNA) is the simplest case of such dynamic superstructures (Figure 2). The distance between adjacent NPs in them can also be modified by switching between distinct conformational states.[2]

Discrete dynamic Class 1 superstructures can also be built using hairpin DNA sequences[2,25] (Figure 2B). The interparticle distance increased upon addition of complementary ssDNA. Precise control over the spatial assembly of homogeneous or heterogeneous NPs has been achieved using cyclic ssDNA as templates[26] to produce triangles and rectangles from individual NPs. Upon addition of a different specific ssDNA, these assemblies could be disassembled and reconfigured (Figure 2C).[2]

The next step in discrete DNA-based assemblies is exploration of increasing complexity of the superstructures. The first example of an assembly with NPs of different geometries is the assemblies from NPs and nanorods (NRs). They are made with >85% yield and regiospecific selectivity (Figure 3).[27] Incorporation of NRs stimulates strong Raman scattering and can be a convenient spectroscopic tool in addition to UV–vis spectroscopy to observe the dynamic behavior.

Self-organizing supraparticles also represent Class 1 discrete NP systems (Figure 4).[28] They can be made from a large

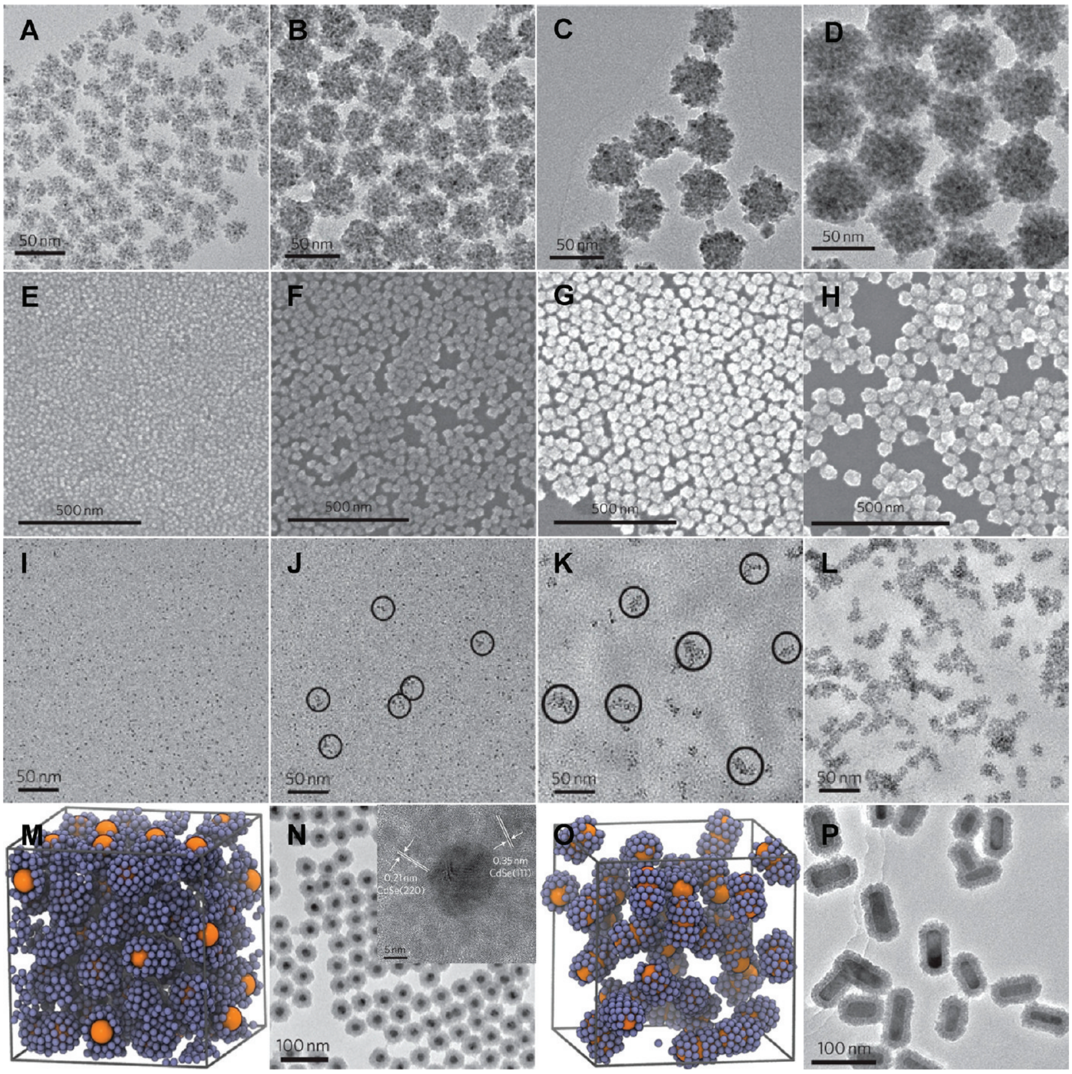

FIGURE 4. TEM (A–D) and SEM (E–H) of CdSe supraparticles of different sizes. (I–L) Intermediate stages of formation and corresponding (M, O) computer simulations and (N, P) TEM images of core–shell supraparticles from CdSe and Au NPs. Reproduced with permission from ref 28. Copyright 2011 Nature Publishing Group.

number of materials. Their existence and the fact that they can be exceptionally uniform are the manifestations of the dynamic assembly–disassembly process. They are formed in a self-limiting growth process that is governed by the equilibrium of repulsive–attractive interactions that makes possible fabrication of complex assemblies with great ease. Ultimately, they display similarities in size, core–shell structure, and self-organization behavior with viruses.

One-Dimensional Assemblies. One-dimensional dynamic NP chains can be constructed using all three assembly strategies. A discernible similarity between the 1D Class 2 self-assembly of Au NRs and polymerization was pointed out by Kumacheva.[29] Linear, branched, and cyclic ensembles of NRs were obtained in a DMF/water mixture (Figure 5). To reduce the surface energy of the system in the poor solvent, the hydrophilic NRs tethered with hydrophobic PS molecules organized into chains.[30] NRs were assembled into rings, nanochains, bundles, nanospheres, and bundled nanochains merely by changing the water content in different organic solvents. Antibody–antigen interactions can also be used to assemble Au NRs into 1D superstructures.[31] Extended Class 2 chains from end-modified NRs were observed in the presence of an antigen (Figure 6b,d). Chains from ZnO pyramids assembled by excluded volume interactions present a system with rich dynamic behavior and transitions of the assembly motif between head-to-tail, parallel, and antiparallel patterns.[32]

A distinct example of Class 1 dynamic 1D NP assembly is the hybrid Au NP + CdTe NW superstructures assembled via bifunctional PEGs acting as molecular springs. The dynamic

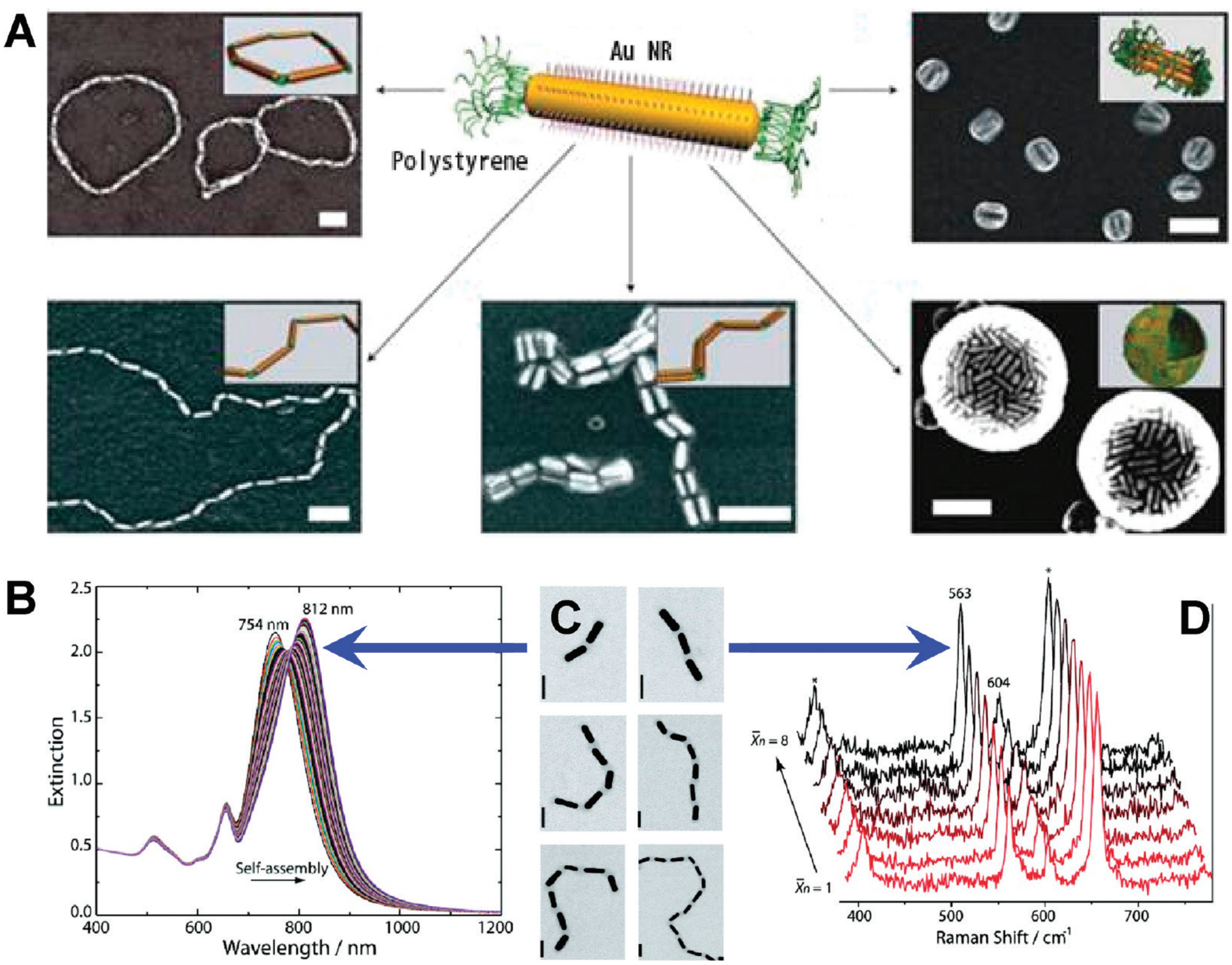

FIGURE 5. (A) Self-assembly of polymer-modified NRs. (B) Absorption spectra, (C) TEM images, and (D) SERS spectra as they assemble. Reproduced from refs 30 and 50**.** Copyright 2007 Nature Publishing Group. Copyright 2011 American Chemical Society.

behavior manifests in them as solvent and temperature response of PEG chains altering the distance between the NPs (Figure 7). The conformation of the PEG and NP–NW distance is altered with increase of the temperature.[33]

2D Assemblies. Fluid–fluid interfaces offer many opportunities to make dynamic 2D assemblies where the NPs are in constant movement at the interface and bulk phase(s).[9–13] These interfacial assemblies rapidly reach equilibrium, which rapidly reach equilibrium, which can also manifest as NP size selectivity.[34]

Spontaneous assembly of 2D sheets as static systems was achieved for CdTe NPs.[5] The structure of NP sheets was compared with the structure of proteins and other biomacromolecules and resembled the assembly of S-proteins[35] or chaperonines. Adjustment of the strength of the attractive interactions can lead to true Class 1 or Class 2 dynamic systems.[36]

3D Assemblies. Thee-dimensional dynamic assemblies can be formed using biological linkages[19,21,37,38] and isotropic[19,39] and anisotropic NP interactions.[7] Their formation can be induced by pH,[40] redox reaction, polarity of solvent,[30] or illumination with light.[6] As such, microscale helical twisted ribbons are formed in Class 1 irreversible dynamic process from straight ribbons.[6] The change of conformation occurs in ribbons due to photooxidation-induced mechanical strain in the assembled structures. Uniquely shaped assemblies (ellipsoidal clouds, dog-bone agglomerates, and ribbon bunches) undergo dynamic transitions in the same system (Figure 8).

Polymeric hydrogels are typical representatives of "smart" dynamic materials. Due to intrinsic anisotropy of NPs manifesting in formation of chains, it is also possible to fabricate gels from NPs,[41] but their dynamics are still to be investigated well. Along with irreversible transitions described by Eycmuller,[42] the reversible sol–gel transitions of fluorescent hydrogels from CdTe NPs induced by sonication

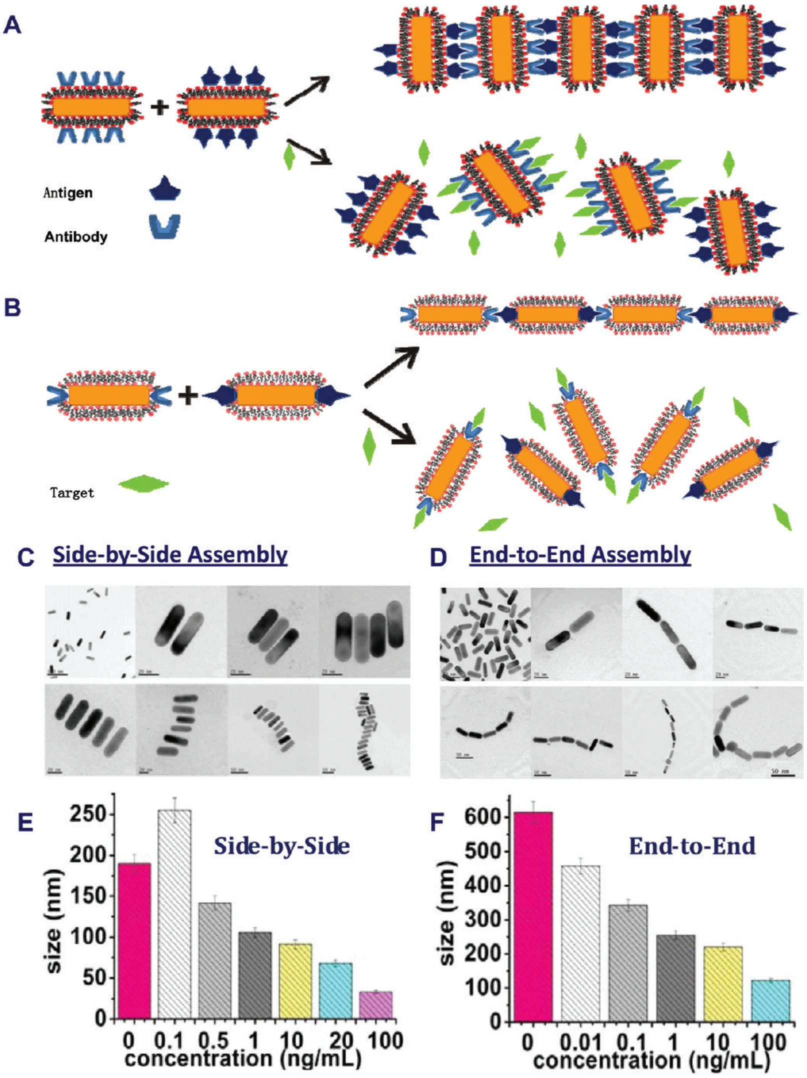

FIGURE 6. Schematics of (A) side-by-side and (B) end-to-end NR assemblies for toxin detection, (C, D) representative TEM images, and (E, F) hydrodynamic diameter of assemblies at different concentrations of microcystin-LR. Reproduced from ref 31. Copyright 2010 Wiley.

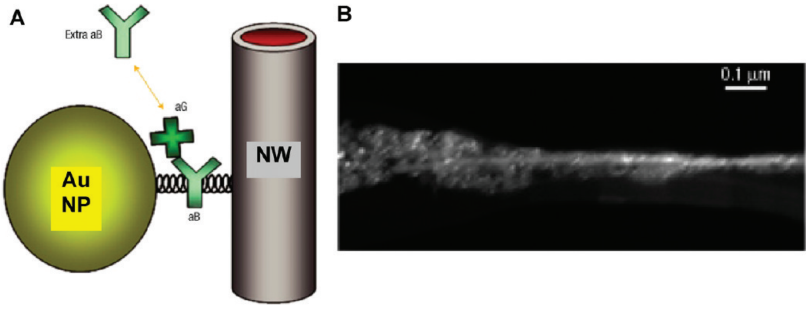

FIGURE 7. (A) Schematics and (B) TEM image of dynamic assemblies with molecular springs. Reproduced from ref 65. Copyright 2007 Nature Publishing Group.

(Figure 9) accompanied by reversible emission-color switching are also possible.[43]

The 3D character of NP assemblies can also originate from the special shape of individual NPs that can acquire extreme anisotropy and anisometry; however, assemblies from them remain challenging due to "jammed" states. It was possible however for octapod-shaped NPs (Figure 10) precisely due to unfreezing these states into dynamic equilibrium.[7]

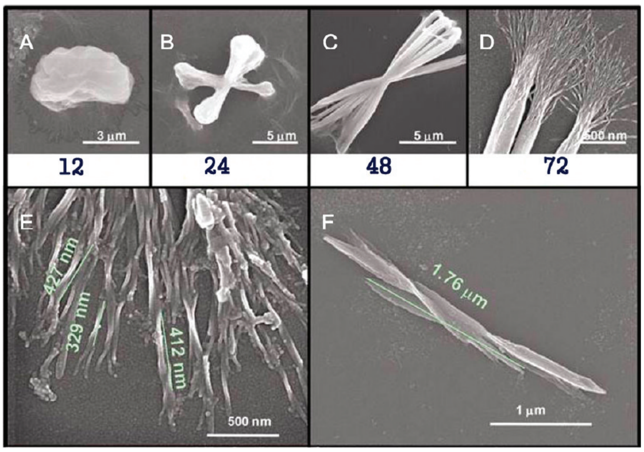

FIGURE 8. SEM images of intermediate NP superstructures and twisted ribbons after (A) 12, (B) 24, (C) 48, and (D) 72 h of assembly and (E, F) twisted ribbons prepared at different light intensities: (E) 61 and (F) 21 mW. Reproduced from ref 6. Copyright 2010 American Association for the Advancement of Science.

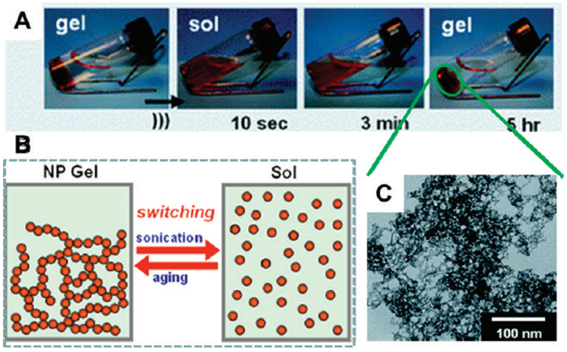

FIGURE 9. (A) Photographs and (B) schematic of CdTe sols and gels before and after sonication with corresponding (C) TEM image of CdTe gels. Reproduced from ref 43. Copyright 2011 Royal Society of Chemistry.

Properties

Well-characterized dynamic NP systems are still not very common. However, the optical, electrical, and magnetic properties of both static and dynamic assemblies often overlap. Therefore in discussing properties we used examples of both dynamic and a limited number of static assemblies to illustrate promising research directions.

Optical Properties. The energy of the surface plasmon resonance (SPR) bands is dependent on the number of NPs[27] and their shape, orientation, and distance.[44] All these effects have been extensively investigated by Mirkin,[45] El-Sayed,[46] Alivisatos,[44] Liz-Marzan,[21,38] Gang,[2] Mulvaney,[47] Kumacheva,[30] Xia,[48] and many others. Great examples can be found for chains made of gold NPs exhibiting strong red-shift when assembled. For NRs, the shift can be vastly different for the longitudinal plasmon band and transverse plasmon depending on the assembly fashion (Figure 6).[31]

SERS is of particular interest for NP assemblies with SPR. High SERS intensity originates from the dramatic amplification of the electromagnetic fields in the gaps between the plasmonic particles.[18,48,49] The geometry of NP assembles is therefore of great importance. Kumacheva reported that SERS intensity varied nonlinearly with the aggregation number.[50] The field intensity was the highest for NR assemblies containing three NRs.

Chirality is a geometrical and optical property that describes an object whose mirror image is non-superimposable with the original. This property represents one of the most interesting research areas for dynamic NP assemblies due to high sensitivity to small geometrical changes. Alivisatos demonstrated dynamic Class 1 NP assemblies in a chiral tetrahedral configuration in 2009.[51] Kotov and Xu made dynamic NP assemblies with strong chirality (Figure 11)[1] associated with formation of trimer and tetramer assemblies also in 2009 observing chiral "wave" in plasmonic part of the spectrum. Liz-Marzan observed chiral effects in helical NR assemblies in 2011.[52] A circular dichroism (CD) band representing the superstructures appeared in the 400–700 nm region coinciding with SPR. While the origin of these CD bands is still being investigated, the strong chirality of plasmonic superstructures could be a pathway to negative refractive index materials (NIMs). Class 1 assemblies of plasmonic and semiconductor particles can also help realization of NIMs serving as an energy "pump" for NIMs in the visible range.[53,54]

Electronic Properties. The grand challenge of nanoscale electronics is to self-organize NPs, NRs, NW, etc. in a specific configuration. Care needs to be taken to attain high crystallinity of the superstructures and avoid gaps because electron transport can be strongly frustrated by the grain boundaries[55] and gaps made by structure-determining ligands.[56] Considerable attention in NP assemblies for nanoelectronics was focused on ordered 2D metallic NP structures exemplified by single electron transistors. Two-dimensional assemblies of 5.4 nm dodecanethiol-protected Au NPs assembled at an air–water interface[57] revealed Coulomb blockade effect at 4.2 K. Dynamic nature of these assemblies resulted in large noise.

The assemblies from anisotropic NPs with minimal surface coating are advantageous because they allow for more facile charge transfer from one NP to another. Spontaneous recrystallization of NP chains into monocrystalline NWs observed for CdTe[3] is also very encouraging for solar cells.

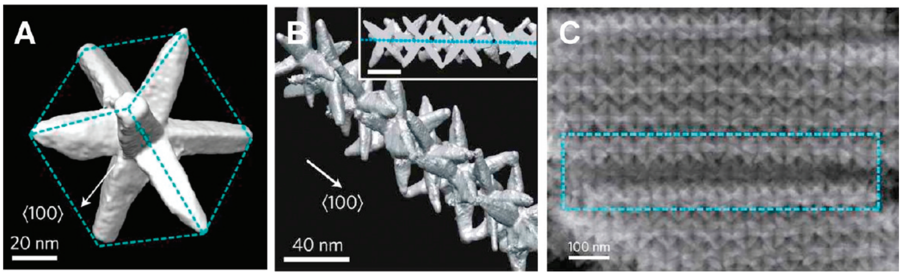

FIGURE 10. Three-dimensional TEM of individual octapod NPs (A) and an octapod NP chain (B). (C) SEM of octapod sheets. Reproduced from ref 7. Copyright 2011 Nature Publishing Group.

Assembly of NP superlattices and subsequent removal of the insulating coatings around NPs demonstrated by Talapin and Shevchenko presents an alternative pathway[58] and unusual electronic properties.[59]

Magnetic Properties. The best examples of magnetic studies in Class 2 superstructures can be probably found in the works by Pileni. They reported differences in the magnetic properties of single Co NPs and NP chains.[60] Magnetic measurements showed increases in the remnant magnetization and coercivity for the 1D Co chains, due to the orientation of the NPs' magnetic moments in the direction of the magnetic field. External magnetic field organizing cobalt NPs in dynamic architectures provides a convenient tool for tuning the collective magnetic response, which is interesting for magnetic storage devices.

Applications

Sensors. Over the past decade, the application of dynamic NP assemblies as sensors has been widely investigated.[61,62] Most of these studies involve Class 2 NP superstructures with strong plasmonic resonance. They utilize the shift of the SPR band and the color change of the NP dispersion from red to blue or *vice versa* in presence of analytes associated with change of the total number of NPs in the assembly. The works of Mirkin demonstrated their exceptional sensitivity for biomedical purposes, with detection limit of 10 fmol of oligonucleotide.[45] El-Sayed used oral cancer cells as the template to assemble NRs conjugated to anti-epidermal growth factor receptor antibody for Raman signal enhancement.[46]

The challenges for detection of environmental pollutants and toxins could be as hard as those for cancer. Rapid assessment of minute amounts of toxins is much needed[31] for environmental sensors.[62,63] For example, Au NR ensembles with side-by-side and end-to-end attachment motifs have been prepared for detection of microcystin-LR, a widespread toxin that results in liver failure or cancer. The method based on Class 2 superstructures from NRs had a detection limit of 5 pg/mL making it more sensitive than enzyme-linked immunosorbent assay (ELISA). The detection time was 15−20 min, which is 36−48-fold faster than ELISA. The use of magnetic NPs with antigens allows one to improve the detection limit to 0.6 ppb.[64]

The photoluminescence of Class 1 superstructures made from semiconductor NWs with metal NPs connected by molecular springs with antibodies transduced protein concentration into the change of emission wavelength.[65] The advantage the wavelength read-out is the elimination of internal standards.

Class 1 superstructures could be used as intracellular probes. Incubation of label-free NP−NR assemblies with HeLa cells indicated sufficient Raman intensity enhancement to detect lipids of mitochondria and provided the first proof-of-concept data for the possibility of real-time probing of local organelle environments in live cells.[27]

Drug Delivery. Site-specific delivery and controlled release of drugs to physiological targets remain major challenges for therapeutics of cancer and other diseases. Since dynamic NP superstructures are sensitive to external conditions, they are attractive for targeted drug delivery and mitigation of chemotherapy side effects. Nanostructures can also incorporate multiple therapeutic and targeting agents. Potential applications of dynamic superstructures in drug delivery[66,67] can be exemplified by DNA nanotubes incorporating capsules or compartments along their length (Figure 12).[66] They open when specific DNA strands are added releasing the cargo.

Nanoelectronics. Self-assembly processes could potentially be a cost-efficient manufacturing approach for nanoelectronics. Self-organization of NPs at solid interfaces was successfully used in light-emitting devices.[68] Stochastic agglomerates of colloidal particles emerged as an alternative to single-crystalline photovoltaic (PV) devices for dye- and NP-sensitized solar cells.[69] Greater conversion efficiency values are expected for NP PV elements after optimization

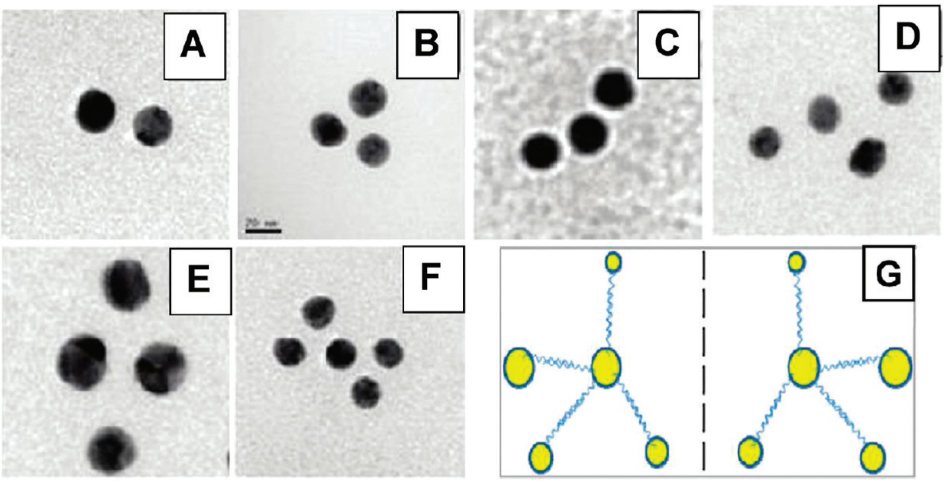

FIGURE 11. TEM images of early PCR products and schematics of their chiral isomers. Reproduced from ref 1. Copyright 2009 American Chemical Society.

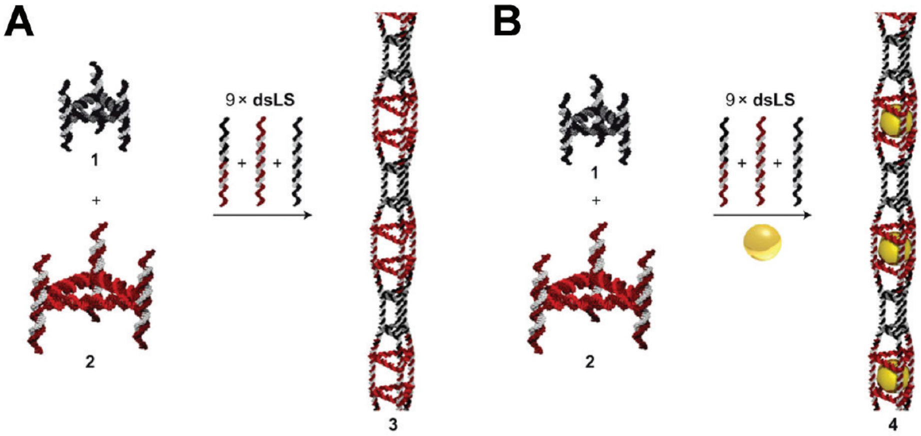

FIGURE 12. DNA nanotubes (A) without and (B) with encapsulated NPs. Reproduced from ref 66. Copyright 2010 Nature Publishing Group.

of both the absorption of incident photons and carrier collection pathways which is likely to require nonplanar assembly geometries.[70]

Particular attention must be given to NP assemblies for PVs. Self-assembly approaches were not articulated well for NP-based PVs; however, a number of devices were demonstrated using self-assembly of conducting polymers. PV devices require materials with complex nanoscale architectures that facilitate charge transport, maximize light absorption, and minimizing charge carrier entrapment. Potentially NP superstructures for PVs and other areas of nanoelectronics can replicate organization of photosynthetic centers in plants and bacteria.

Conclusions

Further work should also address the following questions: (1) How should building blocks and ligands be chosen (or designed) for the formation of dynamically self-assembled superstructures? (2) How can dynamic assembly processes be monitored in real time? (3) How do laws of thermodynamics apply to these assemblies? (4) How close do the dynamic superstructures emulate the functions of living cells? There is also a high probability that the dynamic processes in NP superstructures will display unpredictable behavior due to collective interactions between NPs and entropy–enthalpy compensation effects. All these questions have both fundamental and practical importance and can sustain the development of this field for decades to come.

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BIOGRAPHICAL INFORMATION

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FOOTNOTES

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The authors declare no competing financial interest.

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