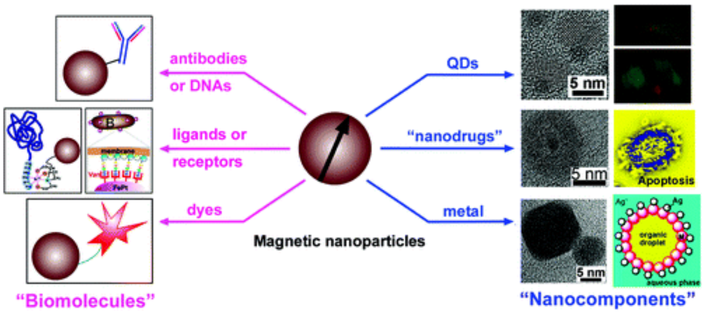
- Multifunctional Magnetic Nanoparticles: Design, Synthesis, and Biomedical Applications
  Gao, J.; Gu, H.; Xu, B. *Acc. Chem. Res.* **2009**, *42*, 1097–1107.
  Abstract:

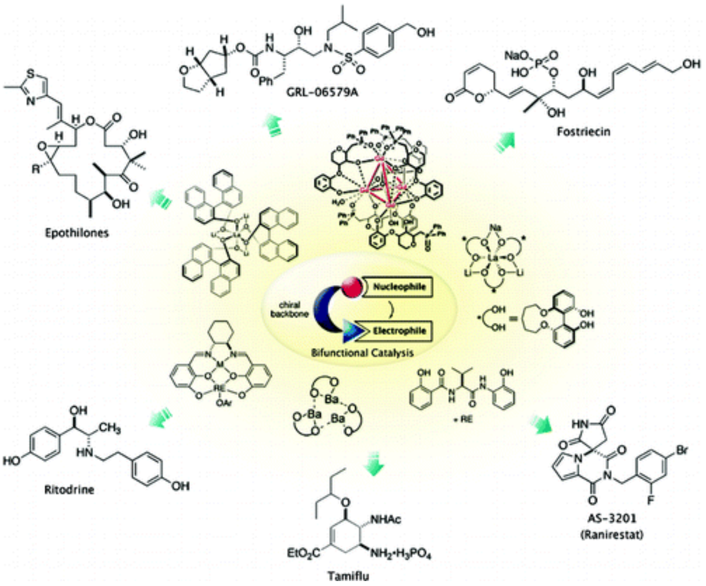


The combination of nanotechnology and molecular biology has developed into an emerging research area: nanobiotechnology. Magnetic nanoparticles are well-established nanomaterials that offer controlled size, ability to be manipulated externally, and enhancement of contrast in magnetic resonance imaging (MRI). As a result, these nanoparticles could have many applications in biology and medicine, including protein purification, drug delivery, and medical imaging.

Because of the potential benefits of multimodal functionality in biomedical applications, researchers would like to design and fabricate multifunctional magnetic nanoparticles. Currently, there are two strategies to fabricate magnetic nanoparticle-based multifunctional nanostructures. The first, molecular functionalization, involves attaching antibodies, proteins, and dyes to the magnetic nanoparticles. The other method integrates the magnetic nanoparticles with other functional nanocomponents, such as quantum dots (QDs) or metallic nanoparticles. Because they can exhibit several features synergistically and deliver more than one function simultaneously, such multifunctional magnetic nanoparticles could have unique advantages in biomedical applications.

In this Account, we review examples of the design and biomedical application of multifunctional magnetic nanoparticles. After their conjugation with proper ligands, antibodies, or proteins, the biofunctional magnetic nanoparticles exhibit highly selective binding. These results indicate that such nanoparticles could be applied to biological medical problems such as protein purification, bacterial detection, and toxin decorporation. The hybrid nanostructures, which combine magnetic nanoparticles with other nanocomponents, exhibit paramagnetism alongside features such as fluorescence or enhanced optical contrast. Such structures could provide a platform for enhanced medical imaging and controlled drug delivery. We expect that the combination of unique structural characteristics and integrated functions of multicomponent magnetic nanoparticles will attract increasing research interest and could lead to new opportunities in nanomedicine.

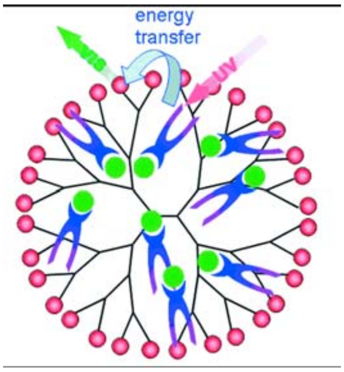
- Recent Progress in Asymmetric Bifunctional Catalysis Using Multimetallic Systems
  Shibasaki, M.; Kanai, M.; Matsunaga, S.; Kumagai, N. *Acc. Chem. Res.* **2009**, *42*, 1117–1127.
  Abstract:



The concept of bifunctional catalysis, wherein both partners of a bimolecular reaction are simultaneously activated, is very powerful for designing efficient asymmetric catalysts. Catalytic asymmetric processes are indispensable for producing enantiomerically enriched compounds in modern organic synthesis, providing more economical and environmentally benign results than methods requiring stoichiometric amounts of chiral reagents. Extensive efforts in this field have produced many asymmetric catalysts, and now a number of reactions can be rendered asymmetric. We have focused on the development of asymmetric catalysts that exhibit high activity, selectivity, and broad substrate generality under mild reaction conditions. Asymmetric catalysts based on the concept of bifunctional catalysis have emerged as a particularly effective class, enabling simultaneous activation of multiple reaction components. Compared with conventional catalysts, bifunctional catalysts generally exhibit enhanced catalytic activity and higher levels of stereodifferentiation under milder reaction conditions, attracting much attention as next-generation catalysts for prospective practical applications.

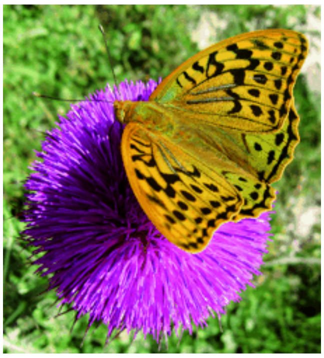
In this Account, we describe recent advances in enantioselective catalysis with bifunctional catalysts. Since our identification of heterobimetallic rare earth−alkali metal−BINOL (REMB) complexes, we have developed various types of bifunctional multimetallic catalysts. The REMB catalytic system is effective for catalytic asymmetric Corey−Chaykovsky epoxidation and cyclopropanation. A dinucleating Schiff base has emerged as a suitable multidentate ligand for bimetallic catalysts, promoting catalytic *syn*-selective nitro-Mannich, *anti*-selective nitroaldol, and Mannich-type reactions. The sugar-based ligand GluCAPO provides a suitable platform for polymetallic catalysts; structural elucidation revealed that their higher order polymetallic structures are a determining factor for their function in the catalytic asymmetric Strecker reaction. Rational design identified a related ligand, FujiCAPO, which exhibits superior performance in catalytic asymmetric conjugate addition of cyanide to enones and a catalytic asymmetric Diels−Alder-type reaction. The combination of an amide-based ligand with a rare earth metal constitutes a unique catalytic system: the ligand−metal association is in equilibrium because of structural flexibility. These catalytic systems are effective for asymmetric amination of highly coordinative substrate as well as for Mannich-type reaction of α-cyanoketones, in which hydrogen bonding cooperatively contributes to substrate activation and stereodifferentiation. Most of the reactions described here generate stereogenic tetrasubstituted carbons or quaternary carbons, noteworthy accomplishments even with modern synthetic methods. Several reactions have been incorporated into the asymmetric synthesis of therapeutics (or their candidate molecules) such as Tamiflu, AS-3201 (ranirestat), GRL-06579A, and ritodrine, illustrating the usefulness of bifunctional asymmetric catalysis.

- Adducts between Dansylated Poly(propylene amine) Dendrimers and Anthracene Clips Mediated by Zn^{II} Ions: Highly Efficient Photoinduced Energy Transfer
  Branchi, B.; Ceroni, P.; Balzani, V.; Bergamini, G.; Klärner, F.-G.; Vögtle, F. *Chem. Eur. J.* **2009**, *15*, 7876-7882.
  Abstract:



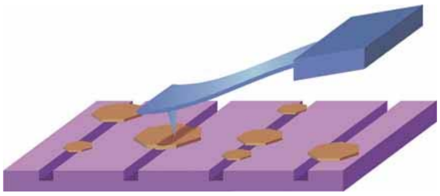
Give us a glue! The self-assembly of anthracene-functionalized clips (purple-blue) and dansylated (red) dendrimers from the first up to the fourth generation, which is driven by Zn^{II} ions (green) as the "glue", leads to an energy transfer from the excited state of anthracene to yield the fluorescent excited state of dansyl.

- Seeking the Chemical Roots of Darwinism: Bridging between Chemistry and Biology
  Pross, A. *Chem. Eur. J.* **2009**, *15*, 8374-8381.
  Abstract:



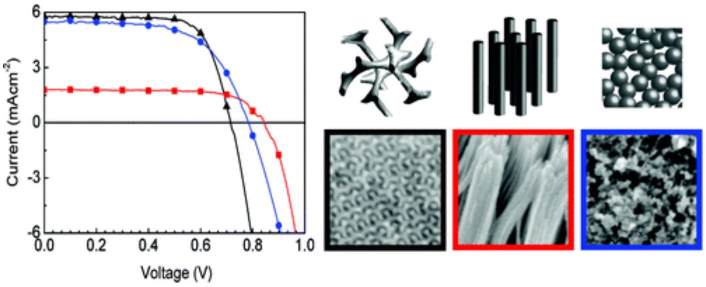
Darwin and the second law of thermodynamics: The suggestion that there are two distinct kinds of stability in nature - replicative and "regular" - leads to the integration of Darwinian theory within chemical kinetic theory, to the unification of chemical emergence and biological evolution, and to the proposal of a second law analogue in the world of replicating systems.

- Deformation Measurements on Thin Clay Tactoids
  Kunz, D. A.; Max, E.; Weinkamer, R.; Lunkenbein, T.; Breu, J.; Fery, A. *Small* **2009**, *5*, 1816 – 1820.
  Abstract:



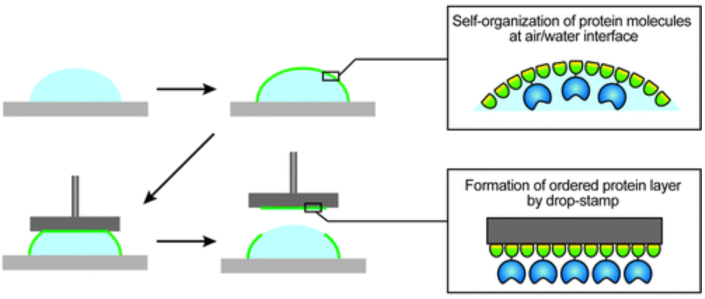
Applying a synthetic fluorohectorite that shows giant lateral extensions, a microscopic bending test is performed using atomic force microscopy (see image). Due to the significantly weaker bonding strength between neighboring lamellae along the stacking direction, the C_{33} elastic constant of synthetic $Na_{0.5}$-fluorohectorite is found to be lower than those reported for micas, which falls within the expected trend.

- Block Copolymer Morphologies in Dye-Sensitized Solar Cells: Probing the Photovoltaic Structure−Function Relation
  Crossland, E. J. W.; Nedelcu, M.; Ducati, C.; Ludwigs, S.; Hillmyer, M. A.; Steiner, U.; Snaith, H. J. *Nano Lett.* **2009**, *9*, 2813–2819.
  Abstract:



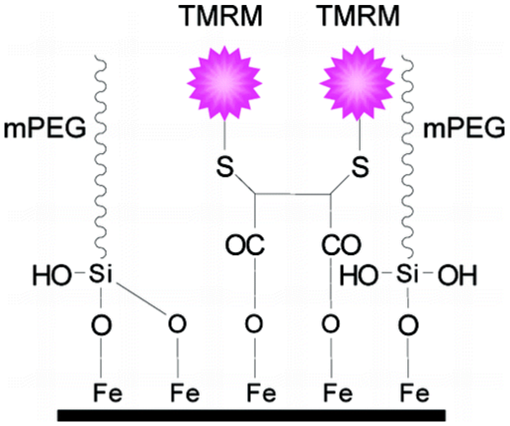
We integrate mesostructured titania arrays into dye-sensitized solar cells by replicating ordered, oriented one-dimensional (1D) columnar and three-dimensional (3D) bicontinuous gyroid block copolymer phases. The solar cell performance, charge transport, and recombination are investigated. We observe faster charge transport in 1D “wires” than through 3D gyroid arrays. However, owing to their structural instability, the surface area of the wire arrays is low, inhibiting the solar cell performance. The gyroid morphology, on the other hand, outperforms the current state-of-the-art mesoporous nanoparticle films.

- The Amphiphilic Protein HFBII as a Genetically Taggable Molecular Carrier for the Formation of a Self-Organized Functional Protein Layer on a Solid Surface
  Asakawa, H.; Tahara, S.; Nakamichi, M.; Takehara, K.; Ikeno, S.; Linder, M. B.; Haruyama, T. *Langmuir* **2009**, *25*, 8841–8844.
  Abstract:



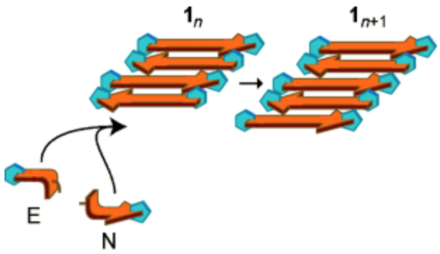
A “drop-stamp method” has been developed for the design and fabrication of molecular interfaces. The amphiphilic protein HFBII, isolated from filamentous fungi, was employed as a genetically taggable molecular carrier for the formation of a structrally ordered layer of functional protein molecules on a solid surface. In this study, the interfacial behavior of maltose-binding protein tagged with HFBII (MBP-HFBII fusion protein) at both the air/water and water/ solid interfaces was investigated.Arigid molecular layer of MBP-HFBII fusion protein was successfully formed through the drop-stamp procedure by employing an intermixed system, in which HFBII molecules are intermingled as nanospacers to prevent the intermolecular steric hindrance of the fusion protein. The results show that the drop-stamp method can be utilized in the high-throughput fabrication of structurally ordered molecular interfaces.

- Easy Route to Functionalize Iron Oxide Nanoparticles via Long-Term Stable Thiol Groups
  Maurizi, L.; Bisht, H.; Bouyer, F.; Millot, N. *Langmuir* **2009**, *25*, 8857–8859.
  Abstract:



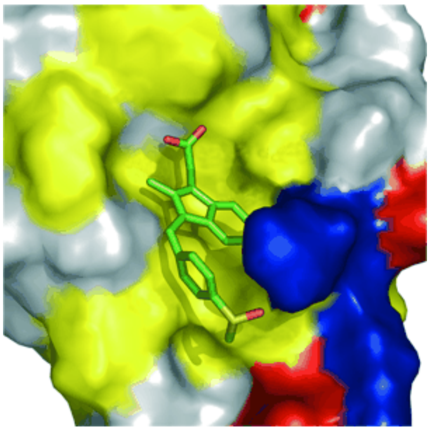
The functionalization of superparamagnetic iron oxide nanoparticles (SPIOs) by meso-2,3-dimercaptosuccinic acid (DMSA) was investigated. Under ambient conditions, the thiol groups from DMSA are not stable and do not allow a direct functionalization without storage in stringent conditions or a chemical regeneration of free thiols. In this study, we have developed a protocol based on poly(ethylene glycol) (PEG) grafting of SPIO prior to DMSA anchoring. We have observed that PEGhelps to increase the stability of thiol groups under ambient conditions. The thiol functionalized SPIOs were stable under physiological pH and ionic strength as determined by Ellman's essay and allowed us to graft a thiol reactive fluorescent dye: tetramethylrhodamine-5-maleimide (TMRM).

- Self-Replicating Amphiphilic **β**-Sheet Peptides
  Rubinov, B.; Wagner, N.; Rapaport, H.; Ashkenasy, G. *Angew. Chem. Int. Ed.* **2009,** *48*, 6683 – 6686.
  Abstract:



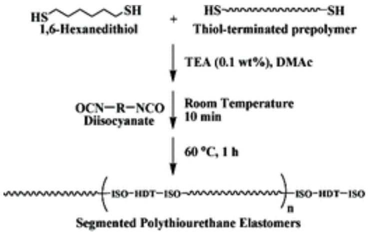
Simple peptides can do that too: Synthetic amphiphilic peptides **1**, formed of electrophilic (E) and nucleophilic (N) precursors, are close analogues of the Glu-(Phe-Glu)$_n$ molecules. The peptides form soluble one-dimensional β-sheet aggregates in water (see picture), and serve to significantly accelerate chemical ligation and self-replication.

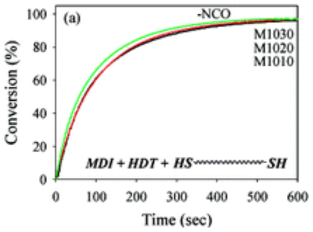
- Sulindac Inhibits Canonical Wnt Signaling by Blocking the PDZ Domain of the Protein Dishevelled
  Lee, H.-J.; Wang, N. X.; Shi, D.-L.; Zheng, J. J. *Angew. Chem. Int. Ed.* **2009,** *48*, 6448 –6452.
  Abstract:



A new application: The nonsteroidal anti-inflammatory drug sulindac interacts directly and specifically with the PDZ domain of the protein Dishevelled (Dvl), which is a key intracellular component of the Wnt signaling pathways. Sulindac binds to the conventional peptide-binding pocket of the domain (see picture), and may exert a cancer chemoprotective effect by blocking it, thereby inhibiting canonical Wnt signaling.

- Segmented Polythiourethane Elastomers through Sequential Thiol-Ene and Thiol-Isocyanate Reactions.
  Shin, J.; Matsushima, H.; Chan, J. W.; Hoyle, C. E. *Macromolecules* **2009**, *42*, 3294-3301.
  Abstract :

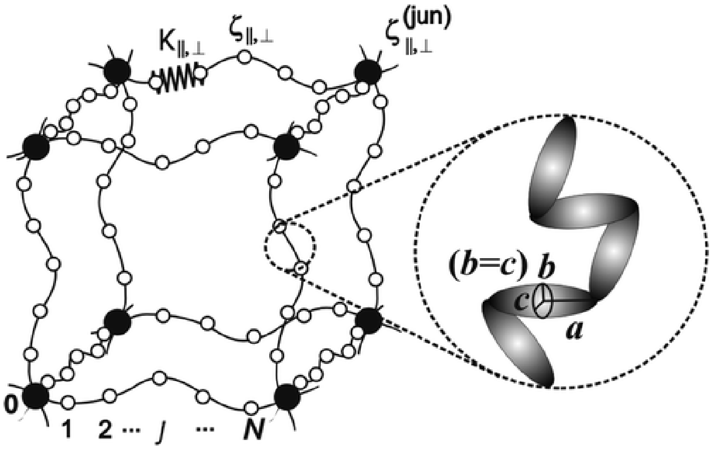




Highly elastic polythiourethanes were synthesized through sequential thiol reactions involving 1,6-hexanedithiol (HDT), 1,4-butanediol diacrylate (BDDA), and several diisocyanates (ISO). Thiol-terminated prepolymers prepared by the phosphine-catalyzed thiol Michael addition of HDT and BDDA form flexible thioether oligomers which were then incorporated as soft segments into polythiourethane main chains through a triethylaminecatalyzed thiol-isocyanate reaction with HDT and ISO to give polymers with both hard and soft segments. Real-time FTIR, used to investigate the kinetic conversion profiles of both reactions, and NMR showed that both the thiol Michael addition and the thiol-isocyanate reactions are very fast and efficient, having the chemical attributes generally associated with thiol-ene radical click reactions. The effects of the soft and hard segment length, soft/hard segment weight ratio, and chemical structure of the ISO on thermal and dynamic thermal mechanical properties was characterized in terms of microphase separation determined by DSC and

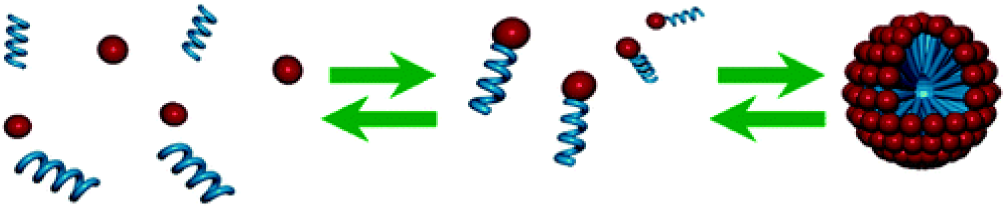
DMA. Tensile properties of the polythiourethanes were measured and correlated with the degree of microphase mixing between the soft and hard segments.

- Shear Dynamic Modulus of Nematic Elastomers: Modified Rouse Model.
  Toshchevikov, V. P.; Gotlib, Y. Y. *Macromolecules* **2009**, *42*, 3417-3429.
  Abstract :



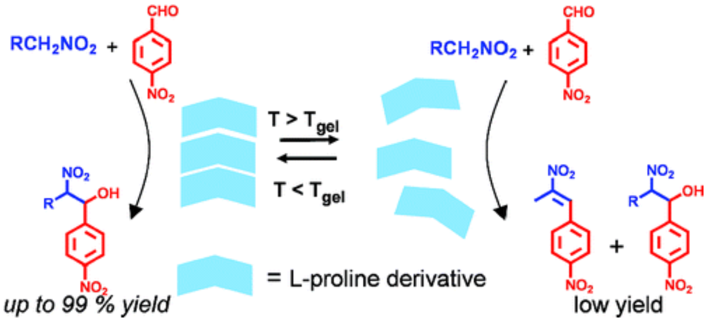
We develop a microscopic theory of dynamic mechanical properties of nematic elastomers taking the chain structure of network strands explicitly into account. We use an approach in which network strands are modeled as a sequence of Gaussian subchains, whose elasticity constants and friction coefficients are different for motions parallel and perpendicular to the LC-director: $K_\parallel \neq K_\perp$ and $\zeta_\parallel \neq \zeta_\perp$ (a modified Rouse model). We show that the dynamic modulus of an ordered nematic elastomer, $G^* = G' + iG''$, should demonstrate a frequency behavior very similar to that of usual (nonordered) rubbers; especially, it should display a frequency domain with a Rouse-like behavior, $G' \doteq G'' \sim \omega^{1/2}$, a feature which is confirmed by experiments. In contrast to the usual rubbers, nematic elastomers are characterized by the anisotropy of the dynamic mechanical behavior with respect to the LC director, **n**. In agreement with experiment we show that for prolate systems in the D-geometry (when **n** is parallel to the shear velocity) G'_D greatly decreases around the nematic isotropic phase transition, whereas in the V-geometry (when **n** is perpendicular to the shear plane) G_V' does not demonstrate such a singularity. We discuss the predictions of our theory for other geometries under shear deformation.

- Triggered Self-Assembly of Simple Dynamic Covalent Surfactants
  Minkenberg,C. B.; Florusse, L.; Eelkema, R.; Koper, G. J. M.; Esch, Jan H. *J. Am. Chem. Soc.* **2009**, *131*, 11274–11275.
  Abstract:



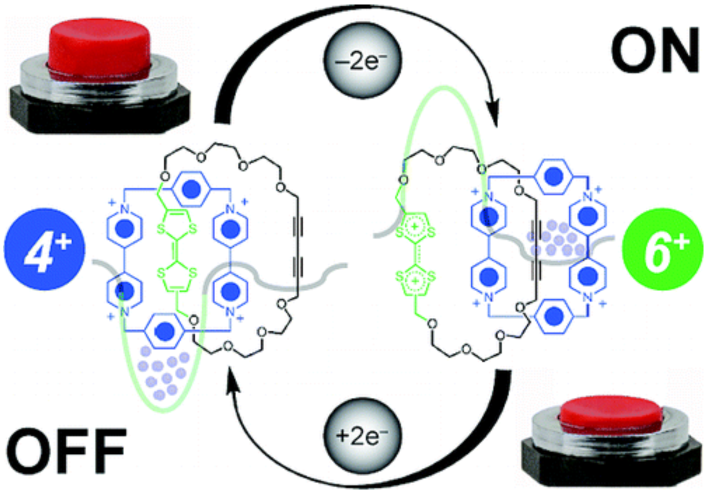
A prototype surfactant system was developed with the unique feature that it can be switched between an aggregated, amphiphilic state and a nonaggregated, nonamphiphilic state using external stimuli. This switchable surfactant system uses the reversible formation of a dynamic covalent bond for pH- and temperature-triggered on/off self-assembly of micellar aggregates by reversible displacement of the equilibrium between nonamphiphilic building blocks and their amphiphilic counterparts. The potential for application in controlled-release systems is shown by reversible uptake and release of an organic dye in aqueous media.

- Switchable Perfomance of an l-Proline-Derived Basic Catalyst Controlled by Supramolecular Gelation
  Rodriguez-Llansola, F.; Escuder, B.; Miravet, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 11478–11484.
  Abstract:



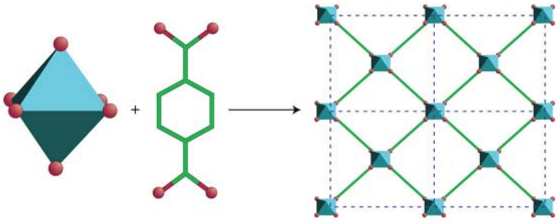
An l-proline-derived low molecular weight gelator forms gels in nitromethane and nitroethane and acts as a basic catalyst for the Henry nitroaldol reaction of these solvents with 4-nitrobenzaldehyde and 4-chlorobenzaldehyde. The reported catalyst is efficient only upon aggregation into self-assembled fibrillar networks. The formation of the gels is associated to a basicity boost of the l-proline residues. Gel dissociation blocks the catalytic efficiency for the nitroaldol reaction but enhances a reaction pathway leading to alkenes. Because of the reversible nature of supramolecular gels, subtle temperature changes allow for a reversible sol–gel transition associated to an activation of the catalyst. The catalytic gel from nitroethane is significantly more active than the one from nitromethane probably because of its different structure as revealed by X-ray diffraction and thermal stability studies. The results shown indicate that in solution the l-proline moiety catalyzes the reaction of nitroalkanes with aldehydes via iminium intermediates while efficient nitroaldol reactions are promoted in the gel phase through an ionic pair type mechanism. The fact that upon aggregation the amino acid-based molecule used as gelator plays both a structural (gel formation) and catalytic role is interesting for the point of view of life origin studies.

- A Push-Button Molecular Switch
  Spruell, J. M.; Paxton, W. F.; Olsen, J.-C.; Benitez, D.; Tkatchouk, E.; Stern, C. L.; Trabolsi, A.; Friedman, D. C.; Goddard, W. A.; Stoddart, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 11571–11580.
  Abstract:



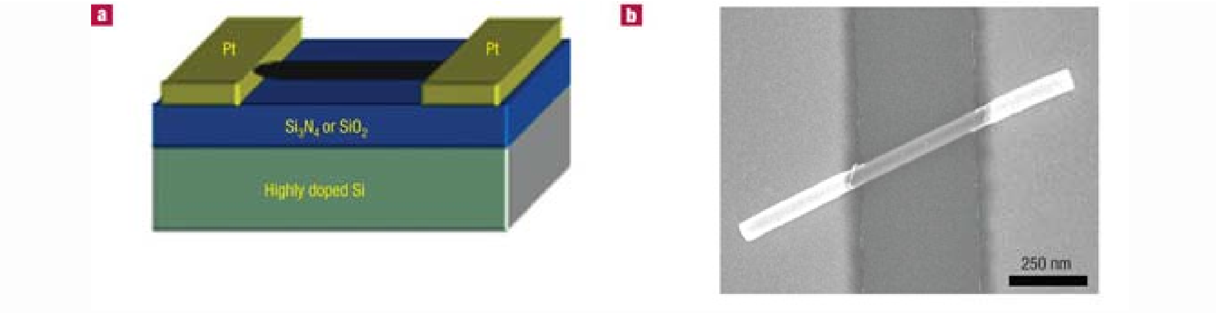
The preparation, characterization, and switching mechanism of a unique single-station mechanically switchable hetero[2]catenane are reported. The facile synthesis utilizing a “threading-followed-by-clipping” protocol features Cu^{2+}-catalyzed Eglinton coupling as a mild and efficient route to the tetrathiafulvalene-based catenane in high yield. The resulting mechanically interlocked molecule operates as a perfect molecular switch, most readily described as a “push-button” switch, whereby two discrete and fully occupied translational states are toggled electrochemically at incredibly high rates. This mechanical switching was probed using a wide variety of experimental techniques as well as quantum-mechanical investigations. The fundamental distinctions between this single-station [2]catenane and other more traditional bi- and multistation molecular switches are significant.

- Crystal structure prediction from first principles
  Woodley, S. M.; Catlow, R. *Nature Materials* **2008**, *7*, 937-946.
  Abstract:



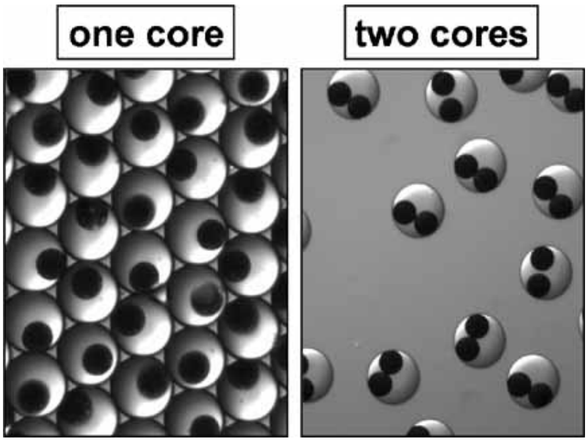
The prediction of structure at the atomic level is one of the most fundamental challenges in condensed matter science. Here we survey the current status of the field and consider recent developments in methodology, paying particular attention to approaches for surveying energy landscapes. We illustrate the current state of the art in this field with topical applications to inorganic, especially microporous solids, and to molecular crystals; we also look at applications to nanoparticulate structures. Finally, we consider future directions and challenges in the field.

- Electronic two-terminal bistable graphitic memories
  Li, Y.; Sinitskii, A.; Tour, J. M. *Nature Materials* **2008**, *7*, 966-971.
  Abstract:



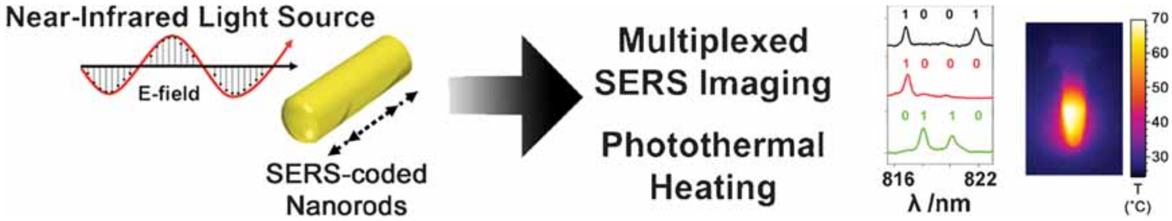
Transistors are the basis for electronic switching and memory devices as they exhibit extreme reliabilities with on/off ratios of 10^4–10^5, and billions of these three-terminal devices can be fabricated on single planar substrates. On the other hand, two-terminal devices coupled with a nonlinear current–voltage response can be considered as alternatives provided they have large and reliable on/off ratios and that they can be fabricated on a large scale using conventional or easily accessible methods. Here, we report that two-terminal devices consisting of discontinuous 5–10 nm thin films of graphitic sheets grown by chemical vapour deposition on either nanowires or atop planar silicon oxide exhibit enormous and sharp room-temperature bistable current–voltage behaviour possessing stable, rewritable, non-volatile and non-destructive read memories with on/off ratios of up to 10^7 and switching times of up to 1 µs (tested limit). A nanoelectromechanical mechanism is proposed for the unusually pronounced switching behaviour in the devices.

- Microfluidic Assembly of Magnetic Hydrogel Particles with Uniformly Anisotropic Structure
  Chen, C.-H.; Abate, A. R.; Lee, D.; Terentjev, E. M.; Weitz D. A. *Adv. Mater.* **2009,** 3201-3204.
  Abstract:



Monodisperse magnetic particles are templated from double emulsions formed using sequential flow-focus drop formation. The microfluidic drop formation allows the particles to be formed with high monodispersity and with consistently anisotropic internal structure. This structural anisotropy gives rise to magnetic anisotropy, allowing the particles to be rotated by a magnetic field.

- SERS-Coded Gold Nanorods as a Multifunctional Platform for Densely Multiplexed Near-Infrared Imaging and Photothermal Heating
  von Maltzahn, G.; Centrone, A.; Park, J.-H.; Ramanathan, R.; Sailor, M. J.; Hatton, T. A.; Bhatia S. N. *Adv. Mater.* **2009,** 3175-3180.
  Abstract:

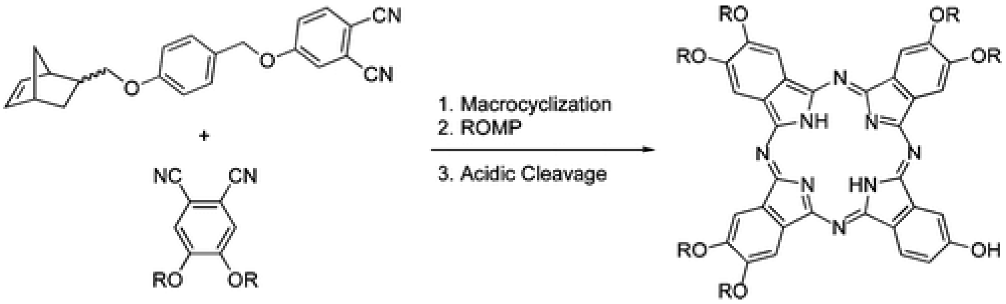


Screening nanorods coated with a mixture of SERS active molecules and biocompatible polymer identifies three formulations that may be uniquely distinguished in vivo over a spectral bandwidth of only 6 nm in the near-infrared (a spectral multiplexing density over an order of magnitude greater than attainable with semiconductor quantum dots, organic fluorochromes, and Raleigh scattering nanoparticle imaging approaches), while providing intense photothermal heating for cancer therapy.

- Unexpected De-Arylation of a Pentaaryl Fullerene
  Clavaguera, S.; Khan, S. I.; Rubin, Y. *Org. Lett.* **2009**, *11*, 1389–1391.
  Abstract:

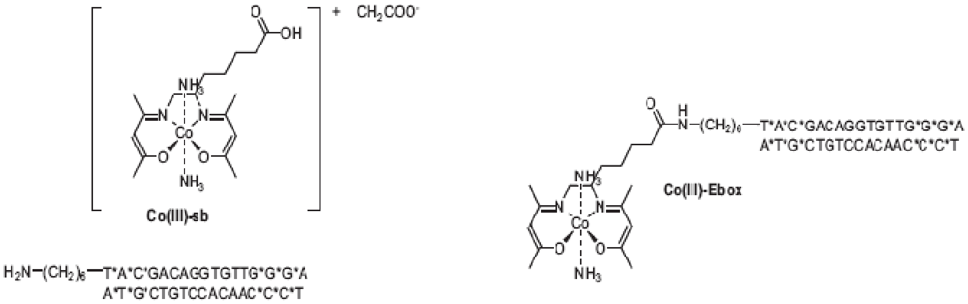
A triphenylamine-derived pentaaryl fullerene undergoes an unusual oxidative dearylation under basic conditions to give tetraarylated epoxy fullerene in high yield. The structure of the product was confirmed by single crystal X-ray diffraction. A mechanism is proposed to account for the loss of the addend and the subsequent formation of the epoxide group.

- Asymmetric Phthalocyanine Synthesis by ROMP-Capture-Release
  Chen, X.; Salmon, T. R.; McGrath, D. V. *Org. Lett.* **2009**, *11*, 2061–2064.
  Abstract:



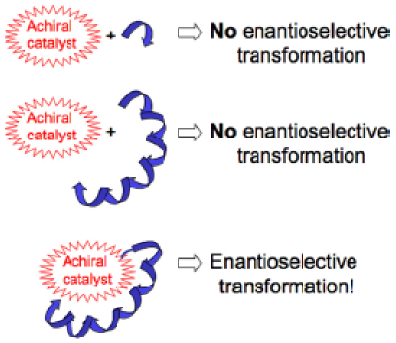
Statistical condensation of norbornenyl-tagged phthalonitrile **3** (Pn A) and 4,5-di-4-methoxyphenoxyphthalonitrile **4** (Pn B) followed by ring-opening metathesis polymerization (ROMP) of Pcs AB_3 and B_4 produced asymmetric Pc-appended polymers. Acidic cleavage of the resulting polymers afforded 2,3,9,10,16,17-hexa-(4-methoxyphenoxy)-23-hydroxy Pc **9**. A more soluble 2,3,9,10,16,17-hexa-4-pentylphenoxy-23-hydroxy Pc **13** was synthesized by the same strategy and modified with sebacoyl chloride demonstrating that the unmasked hydroxyl site is reactive as a nucleophile.

- Targeted inhibition of Snail family zinc finger transcription factors by oligonucleotide-Co(III) Schiff base conjugate
  Harney, A. S.; Lee, J.; Manus, L. M.; Wang, P.; Ballweg, D. M.; LaBonne, C.; Meade, T. J. *Proc. Nat. Acad. Sci.* **2009**, *106*, 13667–13672.
  <u>Abstract:</u>



A transition metal complex targeted for the inhibition of a subset of zinc finger transcription factors has been synthesized and tested in *Xenopus laevis*. A Co(III) Schiff base complex modified with a 17-bp DNA sequence is designed to selectively inhibit Snail family transcription factors. The oligonucleotide-conjugated Co(III) complex prevents Slug, Snail, and Sip1 from binding their DNA targets whereas other transcription factors are still able to interact with their target DNA. The attachment of the oligonucleotide to the Co(III) complex increases specificity 150-fold over the unconjugated complex. Studies demonstrate that neither the oligo, or the Co(III) Schiff base complex alone, are sufficient for inactivation of Slug at concentrations that the conjugated complex mediates inhibition. Slug, Snail, and Sip1 have been implicated in the regulation of epithelial-to-mesenchymal transition in development and cancer. A complex targeted to inactivate their transcriptional activity could prove valuable as an experimental tool and a cancer therapeutic.

- Folded biomimetic oligomers for enantioselective catalysis
  Maayan, G.; Ward, M. D.; Kirshenbaum, K. *Proc. Nat. Acad. Sci.* **2009**, *106*, 13679–13684.
  <u>Abstract:</u>



Many naturally occurring biopolymers (i.e., proteins, RNA, DNA) owe their unique properties to their well-defined three-dimensional structures. These attributes have inspired the design and synthesis of folded architectures with functions ranging from molecular recognition to asymmetric catalysis. Among these are synthetic oligomeric peptide (‘‘foldamer’’) mimics, which can display conformational ordering at short chain lengths. Foldamers, however, have not been explored as platforms for asymmetric catalysis. This report describes a library of synthetic helical ‘‘peptoid’’ oligomers that enable enantioselective transformations at an embedded achiral catalytic center, as illustrated by the oxidative kinetic resolution of 1-phenylethanol. In an investigation aimed at

elucidating key structure–function relationships, we have discovered that the enantioselectivity of the catalytic peptoids depends\ on the handedness of the asymmetric environment derived from the helical scaffold, the position of the catalytic center along the peptoid backbone, and the degree of conformational ordering of the peptoid scaffold. The transfer of chiral information from a folded scaffold can enable the use of a diverse assortment of embedded achiral catalytic centers, promising a generation of synthetic foldamer catalysts for enantioselective transformations that can be performed under a broad range of reaction environments.