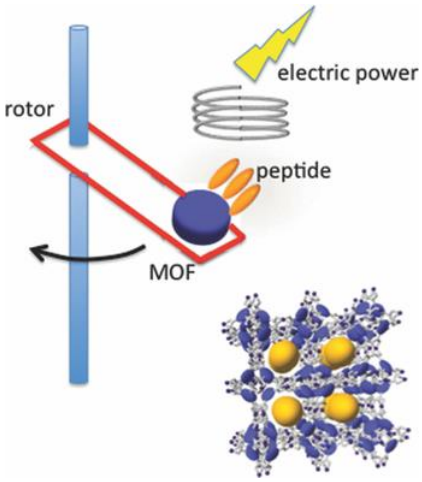
- Peptide Assembly-Driven Metal–Organic Framework (MOF) Motors for Micro Electric Generators

  Ikezoe, Y.; Fang, J.; Wasik, T. L.; Uemura, T.; Zheng, Y.; Kitagawa, S.; Matsui, H. *Adv. Mater.* **2015**, *27*, 288–291.

  Abstract:

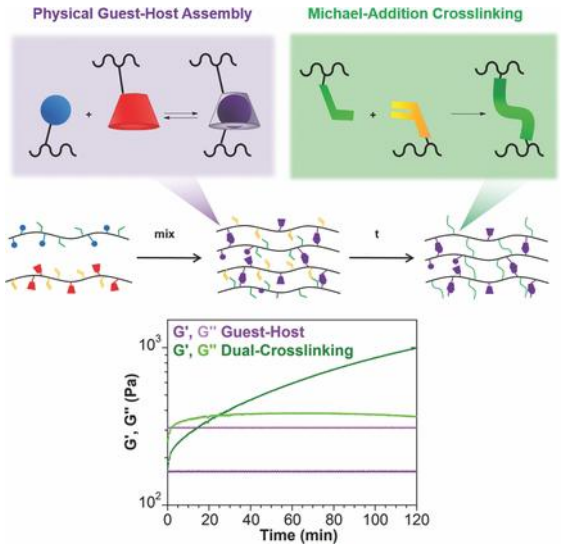


Peptide–metal–organic framework (Pep-MOF) motors, whose motions are driven by anisotropic surface tension gradients created via peptide self-assembly around frameworks, can rotate microscopic rotors and magnets fast enough to generate an electric power of 0.1 μW. A new rigid Pep-MOF motor can be recycled by refilling the peptide fuel into the nanopores of the MOF.

- Shear-Thinning Supramolecular Hydrogels with Secondary Autonomous Covalent Crosslinking to Modulate Viscoelastic Properties In Vivo

  Rodell, C. B.; MacArthur, J. W.; Dorsey, S. M.; Wade, R. J.; Wang, L. L.; Woo, Y. J.; Burdick, J. A. *Adv. Funct. Mater.* **2015**, *25*, 636–644.

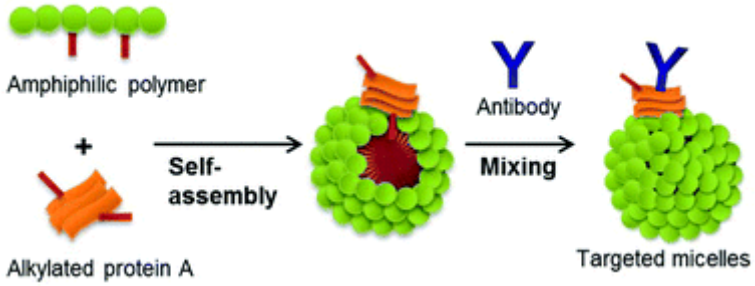
  Abstract:



Clinical percutaneous delivery of synthetically engineered hydrogels remains limited due to challenges posed by crosslinking kinetics—too fast leads to delivery failure, too slow limits material retention. To overcome this challenge, supramolecular assembly is exploited to localize hydrogels at the injection site and introduce subsequent covalent crosslinking to control final material properties. Supramolecular gels are designed through the separate pendant modifications of hyaluronic acid

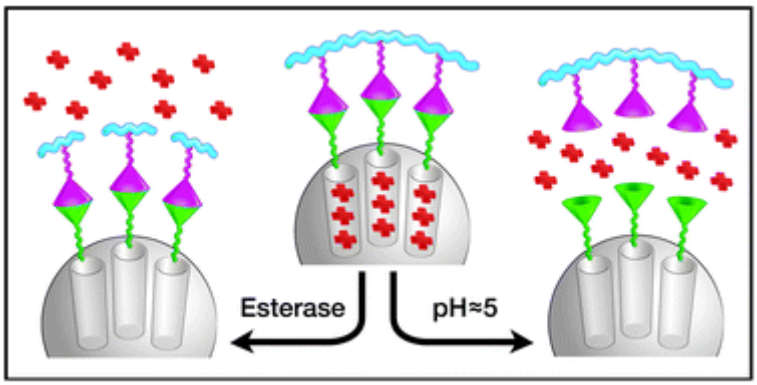
(HA) by the guest–host pair cyclodextrin and adamantane, enabling shear-thinning injection and high target site retention (>98%). Secondary covalent crosslinking occurs via addition of thiols and Michael-acceptors (i.e., methacrylates, acrylates, vinyl sulfones) on HA and increases hydrogel moduli (E = 25.0 ± 4.5 kPa) and stability (>3.5 fold in vivo at 28 d). Application of the dual-crosslinking hydrogel to a myocardial infarct model shows improved outcomes relative to untreated and supramolecular hydrogel alone controls, demonstrating its potential in a range of applications where the precise delivery of hydrogels with tunable properties is desired.

- Bacteria-mimicking nanoparticle surface functionalization with targeting motifs
  Lai, M.-H.; Clay, N. E.; Kimb, D. H.; Kong, H. *Nanoscale* **2015**, *7*, 6737 – 6744.
  Abstract:



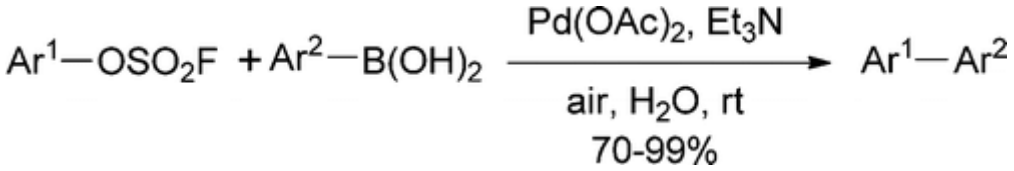
In recent years, surface modification of nanocarriers with targeting motifs has been explored to modulate delivery of various diagnostic, sensing and therapeutic molecular cargo to desired sites of interest in in vitro bioengineering platforms and in vivo pathologic tissue. However, most surface functionalization approaches are often plagued by complex chemical modifications and effortful purifications. To resolve such challenges, this study demonstrates a unique method to immobilize antibodies that can act as targeting motifs on the surfaces of nanocarriers, inspired by a process that bacteria use for immobilization of the host's antibodies. We hypothesized that alkylated Staphylococcus aureus protein A (SpA) would self-assemble with micelles and subsequently induce stable coupling of antibodies to the micelles. We examined this hypothesis by using poly(2-hydroxyethyl-co-octadecyl aspartamide) (PHEA-g-C18) as a model polymer to form micelles. The self-assembly between the micelles and alkylated SpA became more thermodynamically favorable by increasing the degree of substitution of octadecyl chains to PHEA-g-C18, due to a positive entropy change. Lastly, the mixing of SpA-PA-coupled micelles with antibodies resulted in the coating of micelles with antibodies, as confirmed with a fluorescence resonance energy transfer (FRET) assay. The micelles coated with antibodies to VCAM-1 or integrin αv displayed a higher binding affinity to substrates coated with VCAM-1 and integrin αvβ3, respectively, than other controls, as evaluated with surface plasmon resonance (SPR) spectroscopy and a circulation-simulating flow chamber. We envisage that this bacteria-inspired protein immobilization approach will be useful to improve the quality of targeted delivery of nanoparticles, and can be extended to modify the surface of a wide array of nanocarriers.

- Esterase- and pH-responsive poly(β-amino ester)-capped mesoporous silica nanoparticles for drug delivery
  Fernando, I. R.; Ferris, D. P.; Frasconi, M.; Malin, D.; Strekalova, E.; Yilmaz, M. D.; Ambrogio, M. W.; Algaradah, M. M.; Hong, M. P.; Chen, X.; Nassar, M. S.; Botros, Y. Y.; Cryns, V. L.; Stoddart, J. F. *Nanoscale* **2015**, *7*, 7178–7183.
  Abstract:



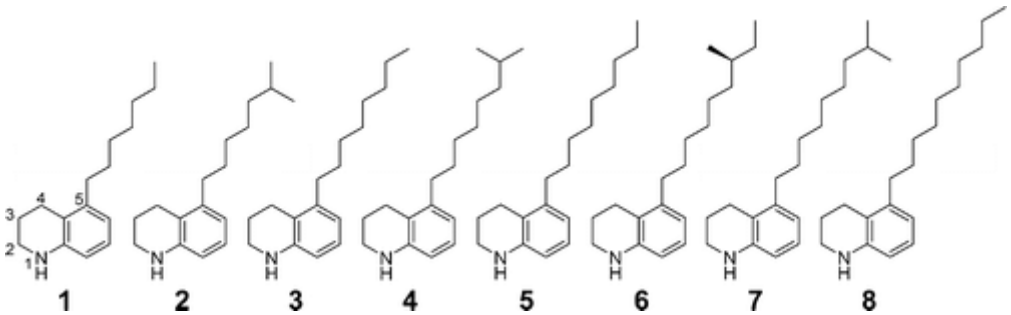
Gating of mesoporous silica nanoparticles (MSNs) with the stimuli-responsive poly(β-amino ester) has been achieved. This hybrid nanocarrier releases doxorubicin (DOX) under acidic conditions or in the presence of porcine liver esterase. The DOX loaded poly(β-amino ester)-capped MSNs reduce cell viability when tested on MDA-MB-231 human breast cancer cells.

- Palladium-Catalyzed, Ligand-Free Suzuki Reaction in Water Using Aryl Fluorosulfates
  Liang, Q.; Xing, P.; Huang, Z.; Dong, J.; Sharpless, K. B.; Li, X.; Jiang, B. *Org. Lett.* **2015**, *17*, 1942–1945.
  Abstract:



Aryl fluorosulfates were prepared by a simple method and employed as coupling partners in the Suzuki–Miyaura reaction. The cross-coupling reactions were performed in water under air at room temperature without ligands or additives such as surfactants or phase-transfer reagents and proceeded smoothly to give excellent yields. Aryl fluorosulfates could also be used as alternatives to halides or triflates in other coupling reactions.

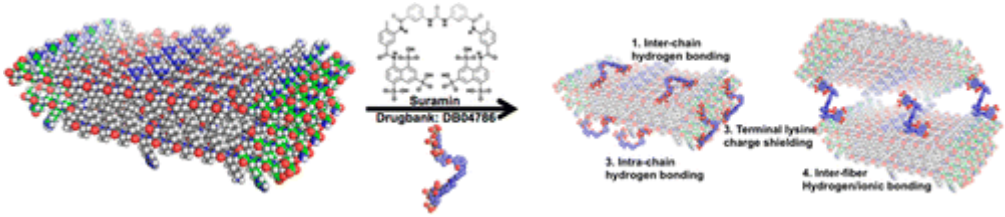
- 5-Alkyl-1,2,3,4-tetrahydroquinolines, New Membrane-Interacting Lipophilic Metabolites Produced by Combined Culture of Streptomyces nigrescens andTsukamurella pulmonis
  Sugiyama, R.; Nishimura, S.; Ozaki, T.; Asamizu, S.; Onaka, H.; Kakeya, H. *Org. Lett.* **2015**, *17*, 1918–1921.
  Abstract:



Eight novel 5-alkyl-1,2,3,4-tetrahydroquinolines (5aTHQs) bearing different side chains have been isolated from a combined culture of Streptomyces nigrescens HEK616 and Tsukamurella pulmonis TP-B0596. The chemical structures including the absolute configuration were elucidated by spectroscopic analysis and total synthesis. 5aTHQs inhibited the growth of wild-type fission yeast

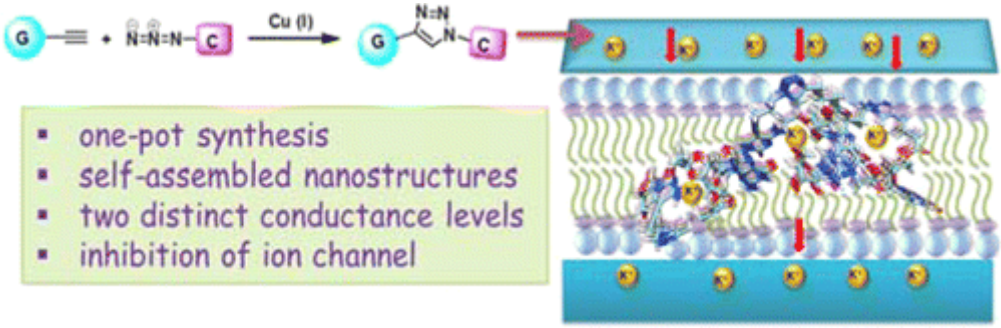
while only weakly inhibiting the growth of several mutant strains synthesizing premature ergosterol. These results demonstrate that 5aTHQs are novel antifungals that may target cell membranes.

- Drug-Triggered and Cross-Linked Self-Assembling Nanofibrous Hydrogels
  Kumar, V. A.; Shi, S.; Wang, B. K.; Li, I-C.; Jalan, A. A.; Sarkar, B.; Wickremasinghe, N. C.; Hartgerink, J. D. *J. Am. Chem. Soc.* **2015**, *137*, 4823-4830.
  Abstract:



Self-assembly of multidomain peptides (MDP) can be tailored to carry payloads that modulate the extracellular environment. Controlled release of growth factors, cytokines, and small-molecule drugs allows for unique control of in vitro and in vivo responses. In this study, we demonstrate this process of ionic cross-linking of peptides using multivalent drugs to create hydrogels for sustained long-term delivery of drugs. Using phosphate, heparin, clodronate, trypan, and suramin, we demonstrate the utility of this strategy. Although all multivalent anions result in good hydrogel formation, demonstrating the generality of this approach, suramin led to the formation of the best hydrogels per unit concentration and was studied in greater detail. Suramin ionically cross-linked MDP into a fibrous meshwork as determined by scanning and transmission electron microscopy. We measured material storage and loss modulus using rheometry and showed a distinct increase in G' and G" as a function of suramin concentration. Release of suramin from scaffolds was determined using UV spectroscopy and showed prolonged release over a 30 day period. Suramin bioavailability and function were demonstrated by attenuated M1 polarization of THP-1 cells compared to positive control. Overall, this design strategy has allowed for the development of a novel class of polymeric delivery vehicles with generally long-term release and, in the case of suramin, crosslinked hydrogels that can modulate cellular phenotype.

- A DNA-Inspired Synthetic Ion Channel Based on G-C Base Pairing
  Das, R. N.; Kumar, Y. P.; Schütte, O. M.; Steinem, C.; Dash, J. *J. Am. Chem. Soc.* **2015**, *137*, 34-37.
  Abstract:



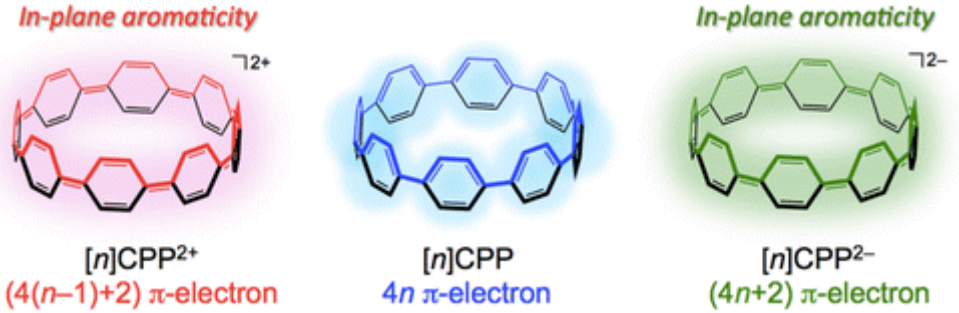
A dinucleoside containing guanosine and cytidine at the end groups has been prepared using a modular one-pot azide-alkyne cycloaddition. Single channel analysis showed that this dinucleoside predominantly forms large channels with 2.9 nS conductance for the transport of potassium ions

across a phospholipid bilayer. Transmission electron microscopy, atomic force microscopy, and circular dichroism spectroscopy studies reveal that this dinucleoside can spontaneously associate through Watson-Crick canonical H-bonding and π-π stacking to form stable supramolecular nanostructures. Most importantly, the ion channel activity of this G-C dinucleoside can be inhibited using the nucleobase cytosine.

- In-Plane Aromaticity in Cycloparaphenylene Dications: A Magnetic Circular Dichroism and Theoretical Study

  Toriumi, N.; Muranaka, A.; Kayahara, E.; Yamago, S.; Uchiyama, M. *J. Am. Chem. Soc.* **2015**, *137*, 82-85.

  Abstract:

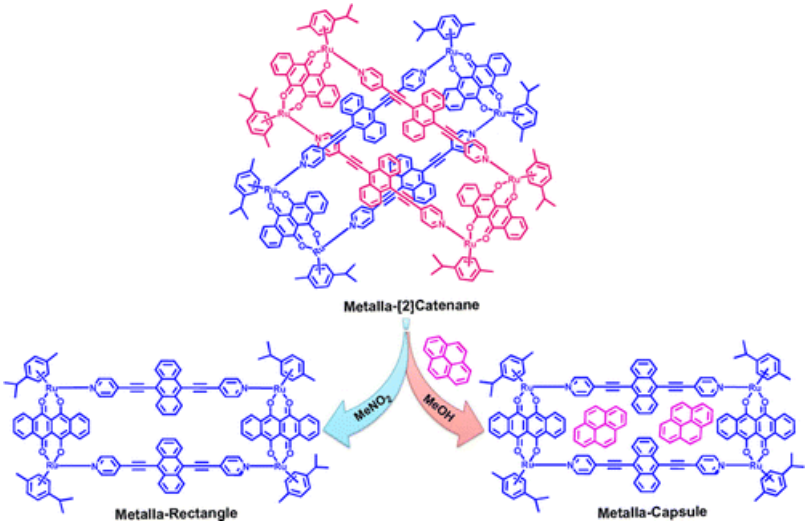


The electronic structures of [8]cycloparaphenylene dication ([8]CPP^{2+}) and radical cation ([8]CPP$^{\bullet+}$) have been investigated by magnetic circular dichroism (MCD) spectroscopy, which enabled unambiguous discrimination between previously conflicting assignments of the UV–vis–NIR absorption spectral bands. Molecular orbital and nucleus-independent chemical shift (NICS) analysis revealed that [8]CPP^{2+} shows in-plane aromaticity with a (4*n* + 2) π-electron system (*n* = 7). This aromaticity appears to be the origin of the unusual stability of the dication. Theoretical calculations further suggested that not only [8]CPP^{2+} but also all [*n*]CPP (*n* = 5–10) dications and dianions exhibit in-plane aromaticity.

- Selective Synthesis of Ruthenium(II) Metalla[2]Catenane via Solvent and Guest-Dependent Self-Assembly

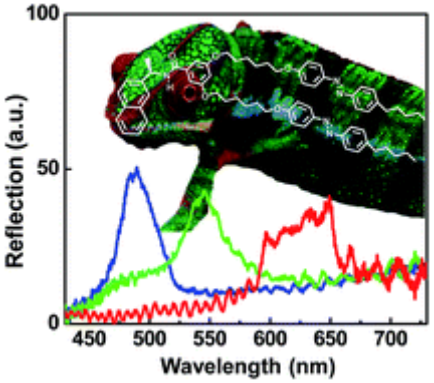
  Lee, H.; Elumalai, P.; Singh, N.; Kim, H.; Lee, S. U.; Chi, K.-W. *J. Am. Chem. Soc.* **2015**, *137*, 4674–4677.

  Abstract:



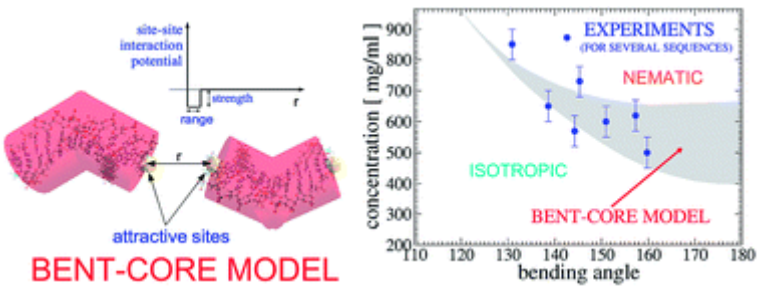
The coordination-driven self-assembly of an anthracene-functionalized ditopic pyridyl donor and a tetracene-based dinuclear Ru(II) acceptor resulted in an interlocked metalla[2]catenane, $[M_2L_2]_2$, in methanol and a corresponding monorectangle, $[M_2L_2]$, in nitromethane. Subsequently, guest template, solvent, and concentration effects allowed the self-assembly to be reversibly fine-tuned among monorectangle and catenane structures.

- Multi-responsible chameleon molecule with chiral naphthyl and azobenzene moieties
  Kim, D.-Y.; Lee, S.-A.; Park, M.; Choi, Y.-J.; Kang, S.-W.; Jeong, K.-U. *Soft Matter* **2015**, *11*, 2924-2933.
  Abstract:



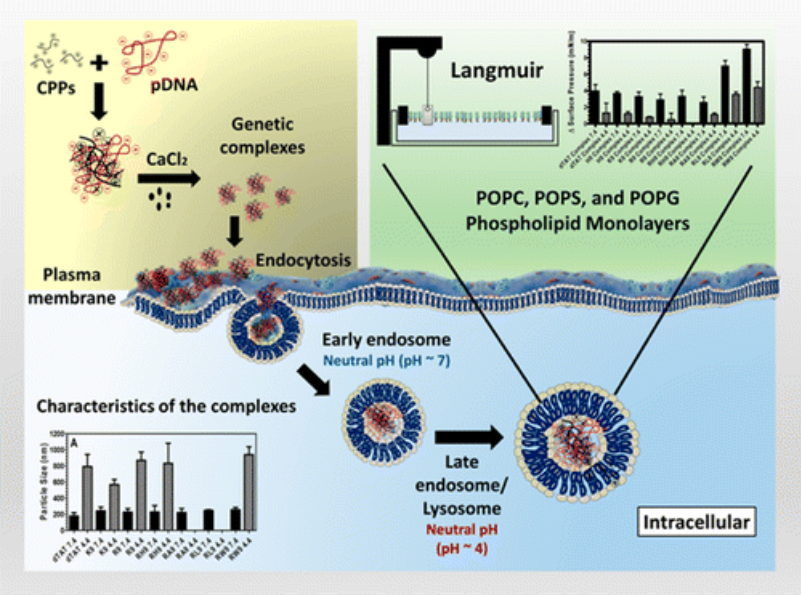
A photochromic chiral molecule with azobenzene mesogens and a (R)-configuration naphthyl moiety (abbreviated as NCA_2M) was specifically designed and synthesized for the demonstration of chameleon-like color changes responding to multitudinous external stimuli, such as temperature, light and electric field. The basic phase transition behaviors of NCA_2M were first studied by the combination of differential scanning calorimetry (DSC) and polarized optical microscopy (POM). Based on the structure-sensitive X-ray diffraction results obtained at different temperatures, it was comprehended that the NCA_2M molecule exhibited the tilted version of highly ordered smectic crystal phase with 5.45 nm layer thickness. Chiral nematic (N*) liquid crystals (LC) with helical superstructures were formed by doping the NCA_2M photochromic chiral molecule in an achiral nematic (N) LC medium. By controlling the helical pitch length of N*-LC with respect to temperature, light and electric field, the wavelength of selectively reflected light from the N* photonic crystal was finely tuned. The light-induced color change of N*-LC film was the most efficient method for covering the whole visible region from blue to green and to red, which allowed us to fabricate remote-controllable photo-responsive devices.

- Self-assembly of mesogenic bent-core DNA nanoduplexes
  Nguyen, K. T.; Battisti, A.; Ancora, D.; Sciortino, F.; De Michele, C. *Soft Matter* **2015**, *11*, 2934-2944.
  Abstract:



Short cylinder-like DNA duplexes, comprising 6 to 20 base pairs, self-assemble into semi-flexible chains, due to coaxial stacking interactions between their blunt ends. The mutual alignment of these chains gives rise to macroscopically orientationally ordered liquid crystal phases. Interestingly, experiments show that the isotropic–nematic phase boundary is sequence-dependent. We perform all-atom simulations of several sequences to gain insights into the structural properties of the duplex and correlate the resulting geometric properties with the observed location of the isotropic–nematic phase boundary. We identify in the duplex bending the key parameter for explaining the sequence dependence, suggesting that DNA duplexes can be assimilated to bent-core mesogens. We also develop a coarse-grained model for the different DNA duplexes to evaluate in detail how bending affects the persistence length and excluded volume of the aggregates. This information is fed into a recently developed formalism to predict the isotropic–nematic phase boundary for bent-core mesogens. The theoretical results agree with the experimental observations.

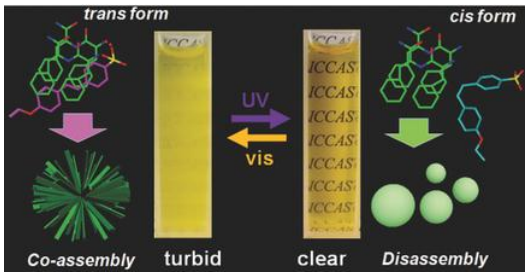
- Effect of Lipid Headgroup Charge and pH on the Stability and Membrane Insertion Potential of Calcium Condensed Gene Complexes
  Alhakamy, N. A.; Elandaloussi, I.; Ghazvini, S.; Berkland, C. J.; Dhar, P. *Langmuir* **2015**, *31*, 4232–4245.
  Abstract:



Noncovalently condensed complexes of genetic material, cell penetrating peptides (CPPs), and calcium chloride present a nonviral route to improve transfection efficiency of nucleic acids (e.g., pDNA and siRNA). However, the exact mechanisms of membrane insertion and delivery of macromolecule complexes to intracellular locations as well as their stability in the intracellular environment are not understood. We show that calcium condensed gene complexes containing different hydrophilic (i.e., dTAT, K9, R9, and RH9) and amphiphilic (i.e., RA9, RL9, and RW9) CPPs formed stable cationic complexes of hydrodynamic radii 100 nm at neutral pH. However, increasing the acidity caused the complexes to become neutral or anionic and increase in size. Using zwitterionic and anionic phospholipid monolayers as models that mimic the membrane composition of the outer leaflet of cell membranes and intracellular vesicles and pHs that mimic the intracellular environment, we study the membrane insertion potential of these seven gene complexes (CPP/pDNA/Ca^{2+} complexes) into model membranes. At neutral pH, all gene complexes

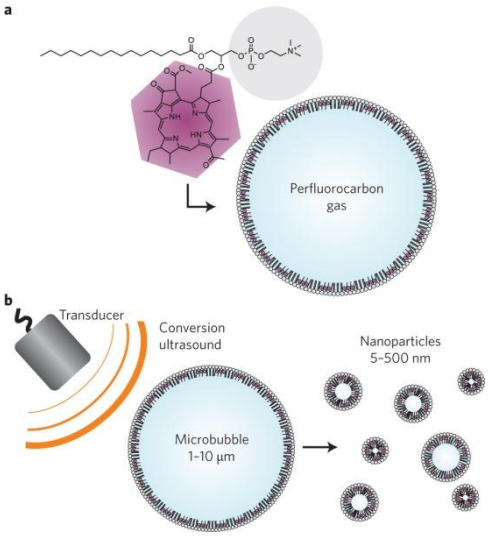
demonstrated the highest insertion potential into anionic phospholipid membranes, with complexes containing amphiphilic peptides showing the maximum insertion. However, at acidic pH, the gene complexes demonstrated maximum monolayer insertion into zwitterionic lipids, irrespective of the chemical composition of the CPP in the complexes. Our results suggest that in the neutral environment the complexes are unable to penetrate the zwitterionic lipid membranes but can penetrate through the anionic lipid membranes. However, the acidic pH mimicking the local environment in the late endosomes leads to a significant increase in adsorption of the complexes to zwitterionic lipid headgroups and decreases for anionic headgroups. These membrane–gene complex interactions may be responsible for the ability of the complexes to efficiently enter the intracellular environment through endocytosis and escape from the endosomes to effectively deliver their genetic payload.

- Photo-induced Reversible Structural Transition of Cationic Diphenylalanine Peptide Self-Assembly
  Ma, H.; Fei, J.; Li, Q.; Li, J. *Small* **2015**, *11*, 1787-1791.
  Abstract:



The photo-induced self-assembly of a cationic diphenylalanine peptide (CDP) is investigated using a photoswitchable sulfonic azobenzene as the manipulating unit. A reversible structural transition between a branched structure and a vesicle-like structure is observed by alternating between UV and visible light irradiation.

- *In situ* conversion of porphyrin microbubbles to nanoparticles for multimodality imaging
  Huynh, E.; Leung, B. Y. C.; Helfield, B. L.; Shakiba, M.; Gandier, J.-A.; Jin, C. S.; Master, E. R.; Wilson, B. C.; Goertz, D. E.; Zheng, G. *Nature Nanotech.* **2015**, *10*, 325-332.
  Abstract:

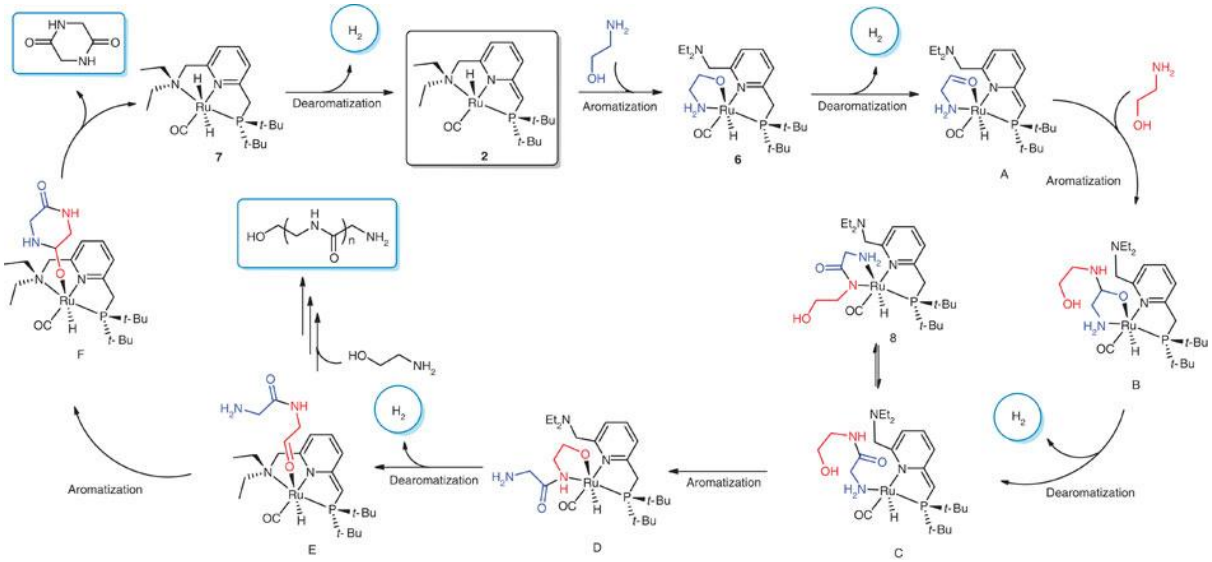


Converting nanoparticles or monomeric compounds into larger supramolecular structures by endogenous or external stimuli is increasingly popular because these materials are useful for imaging and treating diseases. However, conversion of microstructures to nanostructures is less common. Here, we show the conversion of microbubbles to nanoparticles using low-frequency ultrasound. The microbubble consists of a bacteriochlorophyll–lipid shell around a perfluoropropane gas. The encapsulated gas provides ultrasound imaging contrast and the porphyrins in the shell confer photoacoustic and fluorescent properties. On exposure to ultrasound, the microbubbles burst and form smaller nanoparticles that possess the same optical properties as the original microbubble. We show that this conversion is possible in tumour-bearing mice and could be validated using photoacoustic imaging. With this conversion, our microbubble can potentially be used to bypass the enhanced permeability and retention effect when delivering drugs to tumours.

- A novel liquid organic hydrogen carrier system based on catalytic peptide formation and hydrogenation

  Hu, P.; Fogler, E.; Diskin-Posner, Y.; Iron, M. A.; Milstein, D. *Nature Commun.* **2015**, *6*, 6859.

  Abstract:

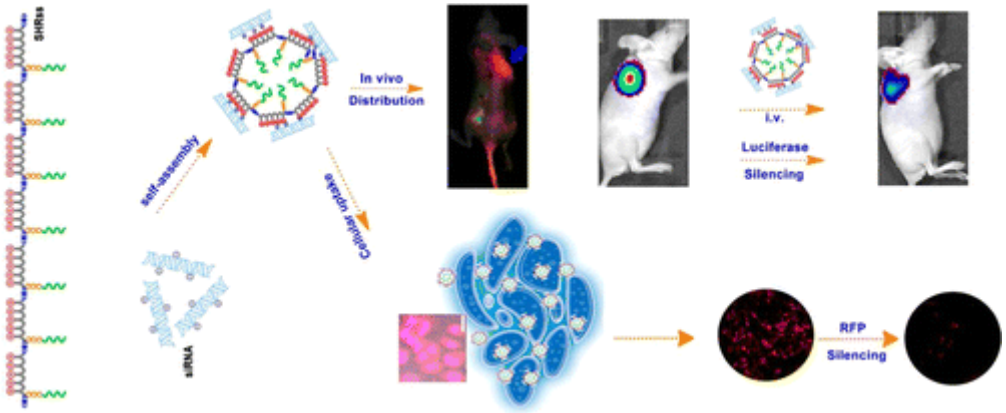


Hydrogen is an efficient green fuel, but its low energy density when stored under high pressure or cryogenically, and safety issues, presents significant disadvantages; hence finding efficient and safe hydrogen carriers is a major challenge. Of special interest are liquid organic hydrogen carriers (LOHCs), which can be readily loaded and unloaded with considerable amounts of hydrogen. However, disadvantages include high hydrogen pressure requirements, high reaction temperatures for both hydrogenation and dehydrogenation steps, which require different catalysts, and high LOHC cost. Here we present a readily reversible LOHC system based on catalytic peptide formation and hydrogenation, using an inexpensive, safe and abundant organic compound with high potential capacity to store and release hydrogen, applying the same catalyst for loading and unloading hydrogen under relatively mild conditions. Mechanistic insight of the catalytic reaction is provided. We believe that these findings may lead to the development of an inexpensive, safe and clean liquid hydrogen carrier system.

- Biodegradable Stearylated Peptide with Internal Disulfide Bonds for Efficient Delivery of siRNA In Vitro and In Vivo

Tai, Z.; Wang, X.; Tian, J.; Gao, Y.; Zhang, L.; Yao, C.; Wu, X.; Zhang, W.; Zhu, Q.; Gao, S. *Biomacromolecules* **2015**, *16*, 1119–1130.

Abstract:

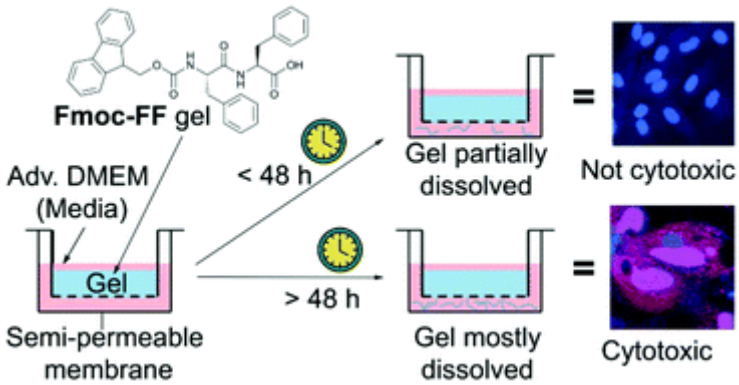


RNA-based delivery system for cancer therapy remains a challenge. In this study, a stearyl-peptide (SHR) was synthesized using arginine, histidine, cysteine, and stearyl moieties. Further, the stearyl-peptides were cross-linked by disulfide bonds to obtain cross-linked polypeptides (SHRss) with different molecular weight (SHRss1, SHRss2, SHRss3, SHRss4). The SHRss could effectively condense small interfering RNA (siRNA) into polyplexes with a hydrodynamic size of 100–300 nm and zeta potential of 20–40 mV. Flow cytometry and confocal laser scanning microscope studies revealed high cellular uptake and rapid dissociation behavior of SHRss2/siRNA complexes. Long-lasting high concentration of siRNA in cytoplasm was observed even at 24 h after SHRss2/Cy3-siRNA transfection. Compared with SHR, the SHRss showed much improved siRNA interference efficiency targeting luciferase on Luc-Hela cells. Moreover, SHRss2 exhibited higher interference efficiency and slower decay rate on Luc-Hela cells than Lipofectamine 2000 and SHR. In addition, much weaker expression of red fluorescence protein was also observed on SHRss2/simCh-treated mCherry-HEK293 cells than Lipofectamine 2000 and SHR. The SHRss did not induce cytotoxicity at siRNA concentrations of 25–200 nM under transfection. The in vivo studies demonstrated the gene interference efficiency of SHRss2/siRNA complexes. Our studies indicated that the SHRss are promising and efficient nonviral vectors for siRNA delivery.

- Dissolution and degradation of Fmoc-diphenylalanine self-assembled gels results in necrosis at high concentrations *in vitro*

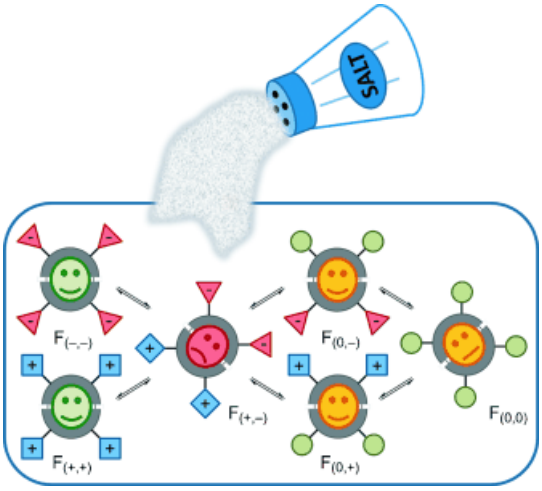
  Truong, T. W.; Su, Y.; Gloria, D.; Braet, F.; Thordarson, P. *Biomater. Sci.* **2015**, *3*, 298-307.

  Abstract:



Herein we report an approach to assess *in vitro* cellular responses to the dissolution or degradation products from Fmoc-diphenylalanine (**Fmoc-FF**) self-assembled hydrogels. Three cell lines were used in these studies and two-way ANOVA was used to assess (i) the age of gel dissolution and degradation products and (ii) exposure time on cell fate and state, using viability assays in conjunction with time-lapse fluorescence and high-resolution scanning electron microscopy investigation. The studies show that leaching time but not the exposure time affects the overall cell viability. The cytotoxic effect was only observed once the gel is completely dissolved. Further analysis revealed that the principal mechanism of cell death is necrosis. In addition, the effect of chemotherapeutics (5-fluorouracil and paclitaxel) released from the **Fmoc-FF** gel (with addition before and after gelation) on colorectal cancer cells were investigated using this methodology, demonstrating enhanced activity of these drugs compared to bulk control. This enhanced activity, however, appears to be a combination of the apoptosis caused by the cancer drugs and necrosis caused by gel dissolution and degradation products. Given that *in vivo* studies by others on Fmoc-peptides that this material is not harmful to animals, our work highlights that conventional *in vitro* cellular assays may yield conflicting messages when used for the evaluation of cytotoxicity and drug release from self-assembled gels such as **Fmoc-FF** and that better *in vitro* models, (*e.g.* 3D cell culture systems) need to be developed to evaluate these materials for biomedical applications.

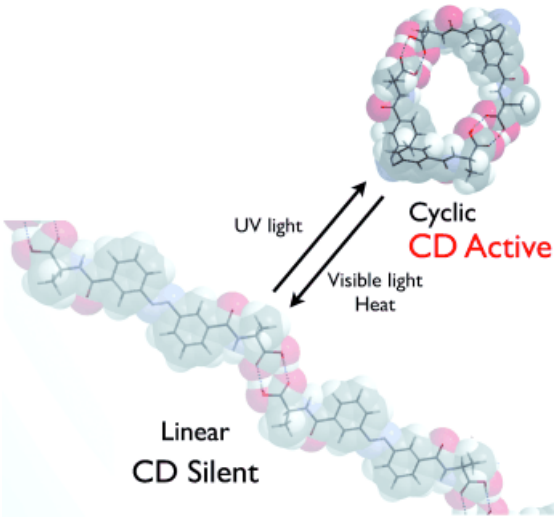
- Salt-Induced Adaptation of a Dynamic Combinatorial Library of Pseudopeptidic Macrocycles: Unraveling the Electrostatic Effects in Mixed Aqueous Media
  Atcher, J.; Moure, A.; Bujons, J.; Alfonso, I. *Chem. Eur. J.* **2015**, *21*, 6869–6878.
  Abstract:



Dynamic combinatorial libraries are powerful systems for studying adaptive behaviors and relationships, as models of more complex molecular networks. With this aim, we set up a chemically diverse dynamic library of pseudopeptidic macrocycles containing amino-acid side chains with differently charged residues (negative, positive, and neutral). The responsive ability of this complex library upon the increase of the ionic strength has been thoroughly studied. The families of the macrocyclic members concentrating charges of the same sign showed a large increase in its proportion as the ionic strength increases, whereas those with residues of opposite charges showed the reverse behavior. This observation suggested an electrostatic shielding effect of the salt within the library of macrocycles. The top-down deconvolution of the library allowed us to obtain the fundamental thermodynamic information connecting the library members (exchange equilibrium constants), as well as to parameterize the adaptation to the external stimulus. We also visualized the

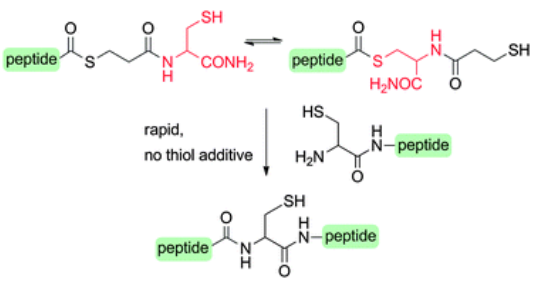
physicochemical driving forces for the process by structural analysis using NMR spectroscopy and molecular modeling. This knowledge permitted the full understanding of the whole dynamic library and also the de novo design of dynamic chemical systems with tailored co-adaptive relationships, containing competing or cooperating species. This study highlights the utility of dynamic combinatorial libraries in the emerging field of systems chemistry.

- Photoinduced Formation of an Azobenzene-Based CD-Active Supramolecular Cyclic Dimer
  Sogawa, H.; Terada, K.; Miyagi, Y.; Shiotsuki, M.; Inai, Y.; Masuda, T.; Sanda, F. *Chem. Eur. J.* **2015**, *21*, 6747–6755.
  Abstract:



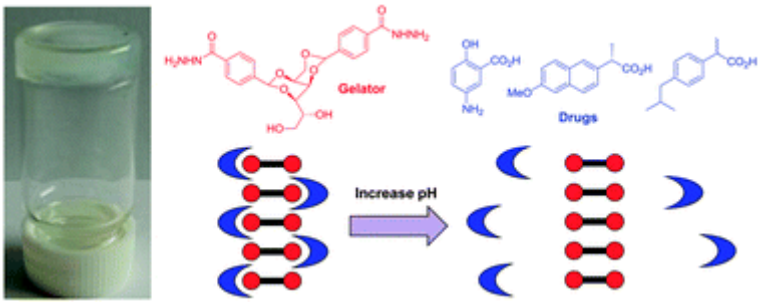
A series of new photo-responsive amino acid-derived azobenzenedicarboxylic acid derivatives (*S*)-**1 a–e** were synthesized. Compound (*S*)-**1 a** in the *trans* form exhibited no circular dichroism (CD) signal in DMF under ambient conditions, whereas intense Cotton effects were observed upon UV irradiation, indicating the formation of a chiral supramolecular structure in the *cis* form. The CD signals disappeared when trifluoroacetic acid (TFA) was added to the solution. The ester counterpart [(*S*)-**1 a'**] showed no CD signal. Hydrogen bonding between the carboxy groups seemed necessary for constructing the supramolecular structure. The kinetic studies of *cis* to *trans* isomerization of (*S*)-**1 a** demonstrated that the formation of a chiral supramolecule enhances the stability of the *cis*-azobenzene structure. The ESI mass spectrum of stilbenedicarboxylic acid (*S*)-**4**, an analogue of (*S*)-**1 b**, confirmed the formation of a dimer. A theoretical CD study revealed that (*S*)-**1 a** in the *cis* form should be present as a cyclic chiral dimer.

- Acceleration of thiol additive-free native chemical ligation by intramolecular S → S acyl transfer
  Schmalisch, J.; Seitz, O. *Chem. Commun.* **2015**, *51*, 7554-7557.
  Abstract:



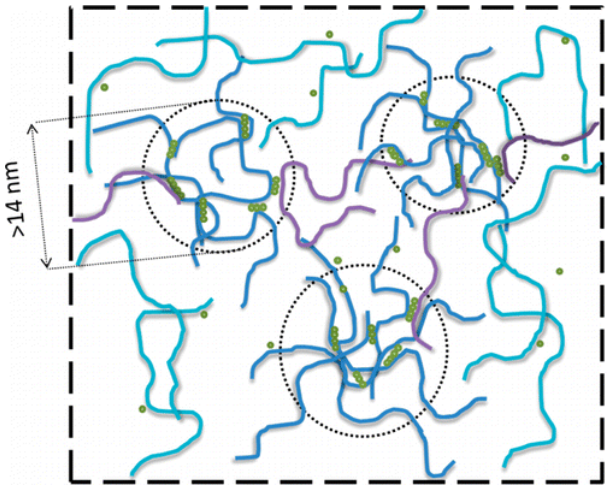
Peptide–mercaptopropionylcysteine (MPA–Cys) thioesters show a surprisingly high reactivity in native chemical ligation (NCL) and allow thiol-additive free reactions. This facilitates sequential NCL reactions and ligation–desulfurization reactions in one-pot formats. The synthetic utility is demonstrated by the synthesis of a SH3 domain.

- Self-assembled sorbitol-derived supramolecular hydrogels for the controlled encapsulation and release of active pharmaceutical ingredients
  Howe, E. J.; Okesolaa, B. O.; Smith, D. K. *Chem. Commun.* **2015**, *51*, 7451-7454.
  Abstract:



A simple supramolecular hydrogel based on 1,3:2,4-di(4-acylhydrazide)benzylidene sorbitol (DBS-$CONHNH_2$), is able to extract acid-functionalised anti-inflammatory drugs *via* directed interactions with the self-assembled gel nanofibres. Two-component hydrogel-drug hybrid materials can be easily formed by mixing and exhibit pH-controlled drug release.

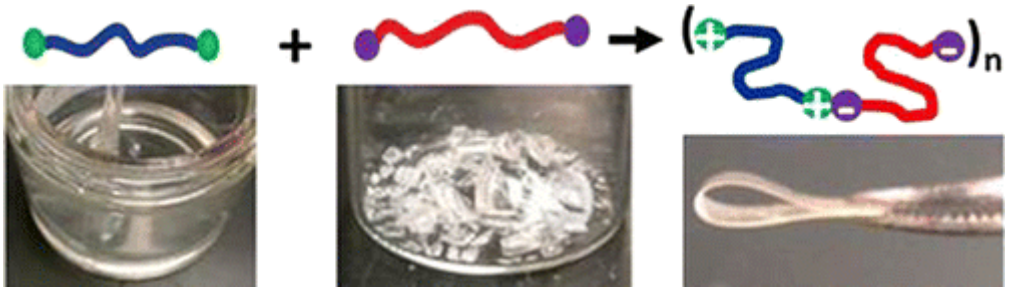
- Local Molecular Dynamics and Heterogeneity in PEO–$NiCl_2$ Supramolecular Networks
  Goldansaz, H.; van Ruymbeke, E.; Gohy, J.-F.; Fustin, C.-A.; Ries, M. E.; Bailly, C. Macromolecules **2015**, *48*, 2290—2298.
  Abstract:



The melt dynamics of poly(ethylene oxide) [PEO]–nickel chloride [$NiCl_2$] systems are analyzed by proton NMR relaxometry and rheology. A consistent picture of the corresponding microstructure is proposed based on the combined results. Rheology reveals the presence of a weak gel due to PEO–metallic salt complexation, evidenced by a low second storage modulus plateau ($<10^4$ Pa) well below the time scale of PEO terminal relaxation. NMR relaxometry shows that transverse magnetization relaxes faster with increasing salt content. Eventually a biexponential behavior is observed, manifesting the coexistence of two distinct environments, with slow and fast dynamics. The chain dynamics in the slow (hindered) domains is temperature, salt content and molecular weight

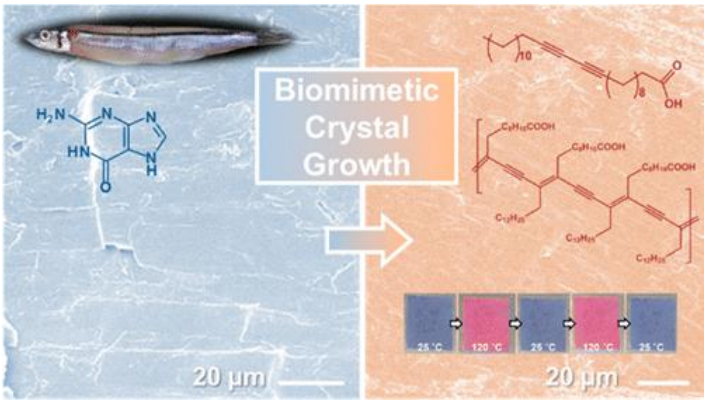
independent within experimental limits, whereas the fast (mobile) domains exhibit similar properties to that of pure PEO. The size of the hindered domains is calculated to be at least 4 times larger than that of the PEO chains, proving that hindered domains encompass many chains. The fraction of hindered domains shows an experimental upper limit of 63%. On the basis of these observations, we propose a microstructure picture for the PEO–$NiCl_2$ gels in which PEO chains are bound together via PEO–metallic salt complexes, and eventually form hindered mobility clusters. These clusters are immersed in the matrix of PEO (mobile domains). In this microstructure picture, in the linear viscoelastic regime the terminal flow of the PEO–$NiCl_2$ system is dominated by the dynamic constraint of PEO–$NiCl_2$ complexes, which arrest a fraction of PEO segments.

- Supramolecular Multiblock Polystyrene−Polyisobutylene Copolymers via Ionic Interactions
  Zhang, L.; Kucera, L. R.; Ummadisetty, S.; Nykaza, J. R.; Elabd, Y. A.; Storey, R. F.; Cavicchi, K. A.; Weiss, R. A. *Macromolecules* **2014**, *47*, 4387–4396.
  Abstract:



A supramolecular multiblock copolymer was synthesized by mixing two telechelic oligomers, α,ω-sulfonated polystyrene, HO_3S-PS-SO_3H, derived from a polymer prepared by RAFT polymerization, and α,ω-amino-polyisobutylene, H_2N-PIB-NH_2, prepared by cationic polymerization. During solvent casting, proton transfer from the sulfonic acid to the amine formed ionic bonds that produced a multiblock copolymer that formed free-standing flexible films with a modulus of 90 MPa, a yield point at 4% strain and a strain energy density of 15 MJ/m^3. Small angle X-ray scattering characterization showed a lamellar morphology, whose domain spacing was consistent with the formation of a multiblock copolymer based on comparison to the chain dimensions. A reversible order–disorder transition occurred between 190 and 210 °C, but the sulfonic acid and amine functional groups were observed to decompose at those elevated temperatures based on companion optical microscopy and spectroscopy measurements. For high nonlinear strains, the dynamic modulus, *G*′, decreased by nearly an order of magnitude and the loss modulus, *G*″, decreased by a factor of 1.4, but both recovered to their original values once the strain was reduced to within the linear response region.

- Advanced Biomimetic Approach for Crystal Growth in Nonaqueous Media: Morphology and Orientation Control of Pentacosadiynoic Acid and Applications
  Okaniwa, M.; Oaki, Y.; Kaneko, S.; Ishida, K.; Maki, H.; Imai, H. *Chem. Mater.* **2015**, *27*, 2627-2632.
  Abstract:



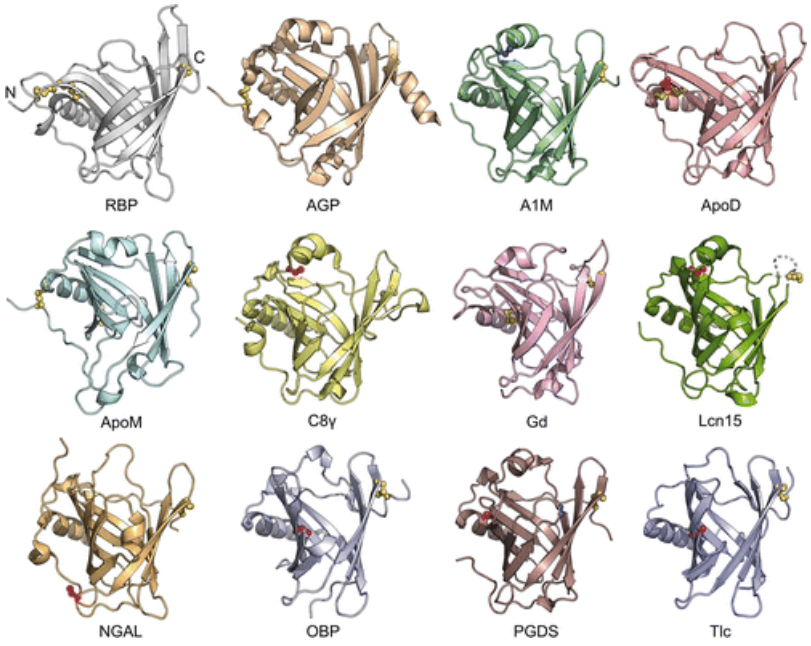
In nature, biological macromolecules control the growth of inorganic crystals under mild conditions in aqueous media. Inspired by biomineralization, biomimetic approaches have been studied for growth control of inorganic crystals in aqueous media by using organic molecules and polymers. The approaches were not applied to nonaqueous systems for the development of functional organic materials. Here, we have applied biomimetic approaches to growth control of organic crystals in nonaqueous media. Morphology and orientation of 10,12-pentacosadiynoic acid (PCDA) crystals, a diacetylene derivative, were controlled in organic media with the additive organic polymers and surface-modified substrates. The oriented PCDA ribbons were obtained by an advanced biomimetic approach. After topochemical polymerization, the resultant polydiacetylenes (PDA) ribbons were applied to the thermochromic materials with intercalation of metal ions and the semiconductor layer of an organic field-effect transistor. The present work implies that biomimetic approaches can be applied to morphology and orientation control of organic crystals.

- The Heat-Up Synthesis of Colloidal Nanocrystals
  van Embden, J.; Chesman, A. S. R.; Jasieniak, J. J. *Chem. Mater.* **2015**, *27*, 2246-2285.
  Abstract:

The successful transition of any nanocrystal-based product from the research phase to the commercial arena hinges on the ability to produce the required nanomaterial on large scales. The synthesis of colloidal nanocrystals using a heat-up (non-injection) method is a reliable means to achieve high quality nanomaterials on large scales with little or no batch-to-batch variation. In this class of synthesis precursors are heated within a reaction medium to induce a chemical reaction that yields monomer for nucleation and growth. Use of the heat-up technique circumvents the pitfalls of mixing time and poor heat management inherent to classical “hot-injection” methods. In heat-up syntheses monomer is produced in a more continuous fashion during the heating stage, making it more difficult to separate the nucleation and growth stages of the reaction, a factor that is

conventionally considered detrimental toward achieving homogeneous colloidal dispersions. However, through the judicious selection of precursors, stabilizers, and reaction heating rates, these stages can be managed to yield colloids of comparable quality to those achieved via classical hot-injection methods. In this review we provide the reader with a fundamental basis upon which to understand the reaction requirements for achieving such favorable growth conditions. Given that the most important consideration in these reactions is precursor (and stabilizer) selection, we also provide an exposition of the precursor chemistry appropriate to achieving high quality products when using heat-up techniques. These topics form the foundation for critically evaluating the field of heat-up nanocrystal synthesis to date, including the synthesis of binary, ternary, and quaternary metal chalcogenide and pnictogenide nanocrystals, as well as metallic, metal oxide, and f-block containing nanocrystals.

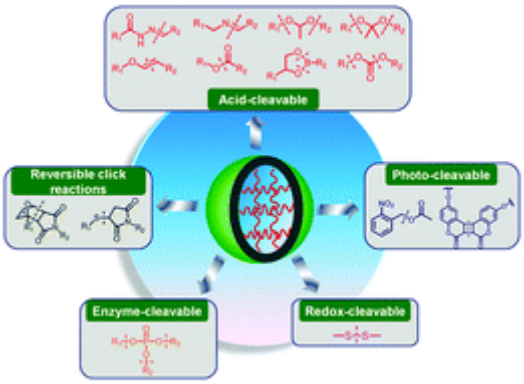
- The Menagerie of Human Lipocalins: A Natural Protein Scaffold for Molecular Recognition of Physiological Compounds
  Schiefner, A; Skerra, A. *Acc. Chem. Res.* **2015**, *48,* 976-985.
  Abstract:



While immunoglobulins are well-known for their characteristic ability to bind macromolecular antigens (i.e., as antibodies during an immune response), the lipocalins constitute a family of proteins whose role is the complexation of small molecules for various physiological processes. In fact, a number of low-molecular-weight substances in multicellular organisms show poor solubility, are prone to chemical decomposition, or play a pathophysiological role and thus require specific binding proteins for transport through body fluids, storage, or sequestration. In many cases, lipocalins are involved in such tasks. Lipocalins are small, usually monomeric proteins with 150−180 residues and diameters of approximately 40 Å, adopting a compact fold that is dominated by a central eight-stranded up-and-down β-barrel. At the amino-terminal end, this core is flanked by a coiled polypeptide segment, while its carboxy-terminal end is followed by an α-helix that leans against the β-barrel as well as an amino acid stretch in a more-or-less extended conformation, which finally is fixed by a disulfide bond. Within the β-barrel, the antiparallel strands (designated A to H) are arranged in a (+1)7 topology and wind around a central axis in a right-handed manner such that

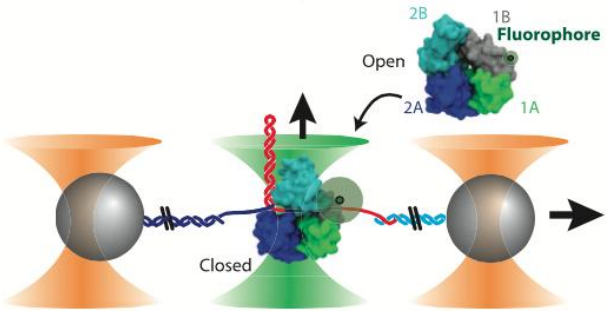
part of strand A is hydrogen-bonded to strand H again. Whereas the lower region of the β-barrel is closed by short loops and densely packed hydrophobic side chains, including many aromatic residues, the upper end is usually open to solvent. There, four long loops, each connecting one pair of β-strands, together form the entrance to a cupshaped cavity. Depending on the individual structure of a lipocalin, and especially on the lengths and amino acid sequences of its four loops, this pocket can accommodate chemical ligands of various sizes and shapes, including lipids, steroids, and other chemical hormones as well as secondary metabolites such as vitamins, cofactors, or odorants. While lipocalins are ubiquitous in all higher organisms, physiologically important members of this family have long been known in the human body, for example with the plasma retinol-binding protein that serves for the transport of vitamin A. This prototypic human lipocalin was the first for which a crystal structure was solved. Notably, several other lipocalins were discovered and assigned to this protein class before the term itself became familiar, which explains their diverse names in the scientific literature. To date, up to 15 distinct members of the lipocalin family have been characterized in humans, and during the last two decades the three-dimensional structures of a dozen major subtypes have been elucidated. This Account presents a comprehensive overview of the human lipocalins, revealing common structural principles but also deviations that explain individual functional features. Taking advantage of modern methods for combinatorial protein design, lipocalins have also been employed as scaffolds for the construction of artifical binding proteins with novel ligand specificities, so-called Anticalins, hence opening perspectives as a new class of biopharmaceuticals for medical therapy.

- Micro- and nanogels with labile crosslinks – from synthesis to biomedical applications
  Zhang, X.; Malhotra, S.; Molina, M.; Haag, R. *Chem. Soc. Rev.* **2015**, *44*, 1948-1973.
  Abstract:



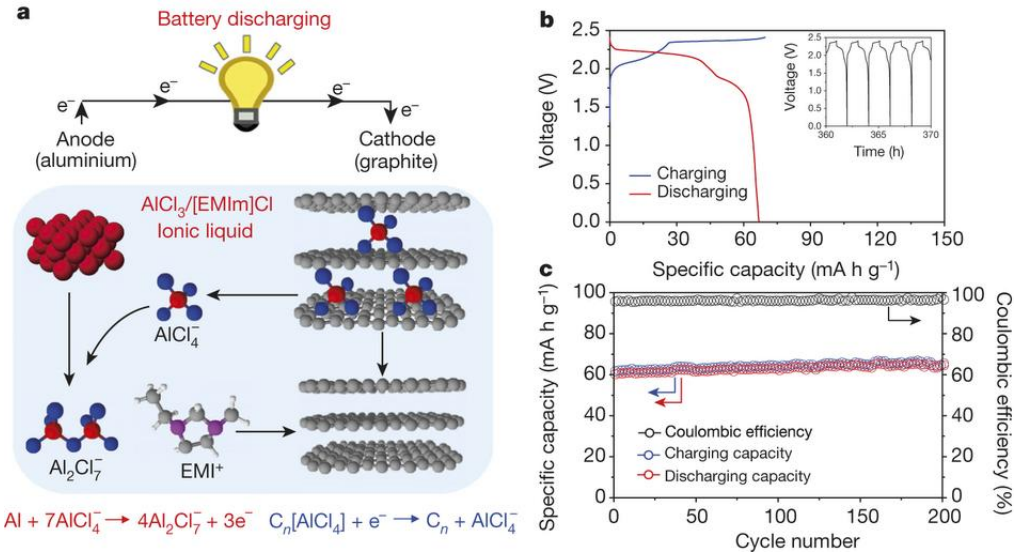
Micro- or nanosized three-dimensional crosslinked polymeric networks have been designed and described for various biomedical applications, including living cell encapsulation, tissue engineering, and stimuli responsive controlled delivery of bioactive molecules. For most of these applications, it is necessary to disintegrate the artificial scaffold into nontoxic residues with smaller dimensions to ensure renal clearance for better biocompatibility of the functional materials. This can be achieved by introducing stimuli-cleavable linkages into the scaffold structures. pH, enzyme, and redox potential are the most frequently used biological stimuli. Moreover, some external stimuli, for example light and additives, are also used to trigger the disintegration of the carriers or their assembly. In this review, we highlight the recent progress in various chemical and physical methods for synthesizing and crosslinking micro- and nanogels, as well as their development for incorporation of cleavable linkages into the network of micro- and nanogels.

- Direct observation of structure-function relationship in a nucleic acid–processing enzyme
  Comstock, M. J.; Whitley, K. D.; Jia, H.; Sokoloski, J.; Lohman, T. M.; Ha, T.; Chemla, Y. R. *Science* **2015**, *348*, 352-354.
  Abstract:



The relationship between protein three-dimensional structure and function is essential for mechanism determination. Unfortunately, most techniques do not provide a direct measurement of this relationship. Structural data are typically limited to static pictures, and function must be inferred. Conversely, functional assays usually provide little information on structural conformation. We developed a single-molecule technique combining optical tweezers and fluorescence microscopy that allows for both measurements simultaneously. Here we present measurements of UvrD, a DNA repair helicase, that directly and unambiguously reveal the connection between its structure and function. Our data reveal that UvrD exhibits two distinct types of unwinding activity regulated by its stoichiometry. Furthermore, two UvrD conformational states, termed closed and open, correlate with movement toward or away from the DNA fork.

- An ultrafast rechargeable aluminium-ion battery
  Lin, M.-C.; Gong, M.; Lu, B.; Wu, Y.; Wang, D.-Y.; Guan, M.; Angell, M.; Chen, C.; Yang, J.; Hwang, B.-J.; Dai, H. *Nature* **2015**, *520*, 324–328.
  Abstract:



The development of new rechargeable battery systems could fuel various energy applications, from personal electronics to grid storage. Rechargeable aluminium-based batteries offer the possibilities of low cost and low flammability, together with three-electron-redox properties leading to high capacity. However, research efforts over the past 30 years have encountered numerous problems,

such as cathode material disintegration, low cell discharge voltage (about 0.55 volts), capacitive behaviour without discharge voltage plateaus (1.1–0.2 volts or 1.8–0.8 volts) and insufficient cycle life (less than 100 cycles) with rapid capacity decay (by 26–85 per cent over 100 cycles). Here we present a rechargeable aluminium battery with high-rate capability that uses an aluminium metal anode and a three-dimensional graphitic-foam cathode. The battery operates through the electrochemical deposition and dissolution of aluminium at the anode, and intercalation/de-intercalation of chloroaluminate anions in the graphite, using a non-flammable ionic liquid electrolyte. The cell exhibits well-defined discharge voltage plateaus near 2 volts, a specific capacity of about 70 mA h g^{-1} and a Coulombic efficiency of approximately 98 per cent. The cathode was found to enable fast anion diffusion and intercalation, affording charging times of around one minute with a current density of ~4,000 mA g^{-1} (equivalent to ~3,000 W kg^{-1}), and to withstand more than 7,500 cycles without capacity decay.