A mechanically interlocked molecular system programmed for the delivery of an anticancer drug

Abstract:

The development of mechanically interlocked molecular systems programmed to operate autonomously in biological environments is an emerging field of research with potential medicinal applications. Within this framework, functional rotaxane- and pseudorotaxane-based architectures are starting to attract interest for the delivery of anticancer drugs, with the ultimate goal to improve the efficiency of cancer chemotherapy. Here, we report an enzyme-sensitive [2]-rotaxane designed to release a potent anticancer drug within tumor cells. The molecular device includes a protective ring that prevents the premature liberation of the drug in plasma. However, once located inside cancer cells the [2]-rotaxane leads to the release of the drug through the controlled disassembly of the mechanically interlocked components, in response to a determined sequence of two distinct enzymatic activations. Furthermore, in vitro biological evaluations reveal that this biocompatible functional system exhibits a noticeable level of selectivity for cancer cells overexpressing β-galactosidase.

Combining a sensor and a pH-gated nanopore based on an avidin–biotin system

Abstract:

Here we propose a new approach to tailor nanopores, which combines both pH gating and sensing properties. This strategy is based on PEG like-avidin grafting in nanopores designed by atomic layer deposition (ALD). Below pH 5 the nanopore is blocked. We show that the PEG chains are at the origin of these properties.

From Bistate Molecular Switches to Self-Directed Track-Walking Nanomotors
Abstract:

Track-walking nanomotors and larger systems integrating these motors are important for wide real-world applications of nanotechnology. However, inventing these nanomotors remains difficult, a sharp contrast to the widespread success of simpler switch-like nanodevices, even though the latter already encompasses basic elements of the former such as engine-like bistate contraction/extension or leg-like controllable binding. This conspicuous gap reflects an impeding bottleneck for the nanomotor development, namely, lack of a modularized construction by which spatially and functionally separable “engines” and “legs” are flexibly assembled into a self-directed motor. Indeed, all track-walking nanomotors reported to date combine the engine and leg functions in the same molecular part, which largely underpins the device–motor gap. Here we propose a general design principle allowing the modularized nanomotor construction from disentangled engine-like and leg-like motifs, and provide an experimental proof of concept by implementing a bipedal DNA nanomotor up to a best working regime of this versatile design principle. The motor uses a light-powered contraction–extension switch to drive a coordinated hand-over-hand directional walking on a DNA track. Systematic fluorescence experiments confirm the motor’s directional motion and suggest that the motor possesses two directional biases, one for rear leg dissociation and one for forward leg binding. This study opens a viable route to develop track-walking nanomotors from numerous molecular switches and binding motifs available from nanodevice research and biology.

- **Polymeric Nanoparticles for Nonviral Gene Therapy Extend Brain Tumor Survival in Vivo**

Abstract:
we synthesize and characterize polymeric gene delivery nanoparticles and evaluate their efficacy for DNA delivery of herpes simplex virus type I thymidine kinase (HSVtk) combined with the prodrug ganciclovir (GCV) in a malignant glioma model. We investigated polymer structure for gene delivery in two rat glioma cell lines, 9L and F98, to discover nanoparticle formulations more effective than the leading commercial reagent Lipofectamine 2000. The lead polymer structure, poly(1,4-butanediol diacrylate-co-4-amino-1-butanol) end-modified with 1-(3-aminopropyl)-4-methylpiperazine, is a poly(β-amino ester) (PBAE) and formed nanoparticles with HSVtk DNA that were 138 ± 4 nm in size and 13 ± 1 mV in zeta potential. These nanoparticles containing HSVtk DNA showed 100% cancer cell killing in vitro in the two glioma cell lines when combined with GCV exposure, while control nanoparticles encoding GFP maintained robust cell viability. For in vivo evaluation, tumor-bearing rats were treated with PBAE/HSVtk infusion via convection-enhanced delivery (CED) in combination with systemic administration of GCV. These treated animals showed a significant benefit in survival (p = 0.0012 vs control). Moreover, following a single CED infusion, labeled PBAE nanoparticles spread completely throughout the tumor. This study highlights a nanomedicine approach that is highly promising for the treatment of malignant glioma.

- **DNA-Templated Silver Nanoclusters for Multiplexed Fluorescent DNA Detection**
  **Abstract:**

  Novel label-free/conjugation-free molecular beacons are designed based on DNA templated-silver nanoclusters for multiplexed DNA detection. The assay is implemented in solution, which makes it easy for the in-situ and real-time analysis. This study demonstrates a new method for multiplexed detection of biological molecules by using fluorescent Ag nanocluster-based molecular beacon probes.

- **Solvent Effects on Kinetic Mechanisms of Self-Assembly by Peptide Amphiphiles via Molecular Dynamics Simulations**
  **Abstract:**
Peptide amphiphiles are known to form a variety of distinctive self-assembled nanostructures (including cylindrical nanofibers in hydrogels) dependent upon the solvent conditions. Using a novel coarse-grained model, large-scale molecular dynamics simulations are performed on a system of 800 peptide amphiphiles (sequence, palmitoyl-Val3Ala3Glu3) to elucidate kinetic mechanisms of molecular assembly as a function of the solvent conditions. The assembly process is found to occur via a multistep process with transient intermediates that ultimately leads to the stabilized nanostructures including open networks of β-sheets, cylindrical nanofibers, and elongated micelles. Different kinetics mechanisms are compared in terms of peptides secondary structures, solvent-accessible surface area, radius of gyration, relative shape anisotropy, intra/intermolecular interactions, and aggregate size dynamics to provide insightful information for the design of functional biomaterials.

- **Spin Crossover Probes Confer Multistability to Organic Conducting Polymers**
  **Abstract:**

**Switchable organic conductors** can be readily obtained by combining organic conducting polymers (CPs), with the unparalleled bistability of spin crossover (SCO) complexes. Here it is reported how CPs with embedded SCO components exhibit synergic multistability. Upon acting on the SCO probes by external stimuli (thermal activation in this case), the spin transition induces up to a 300% difference in the electrical conductivity of the CP component between the low-spin and high-spin regimes, and with a wide hysteresis at technologically
relevant temperatures. These results pave the way for the exploitation of the unique SCO switching capabilities in electronic devices.

- **Transparent, Stimuli-Responsive Films from Cellulose-Based Organogel Nanoparticles**
  **Abstract:**
  The use of bio-based nanoscaled cellulose for the construction of novel functional materials has progressed rapidly over the past years. In comparison to most of studies starting with the hydrophilic nanoscaled cellulose, surface-stearoylated cellulose nanoparticles (SS-CNPs) are used in this report for the construction of multifunctional, responsive films. SS-CNPs with an average size of 115 ± 0.5 nm are obtained after the surface-modification of cellulose under heterogeneous conditions. Crystalline cellulose core is present within SS-CNPs according to solid-state $^{13}$C nuclear magnetic resonance (NMR) spectroscopy. SS-CNPs show excellent dispersibility in nonpolar solvents and form temperature-responsive organogels in tetrahydrofuran (THF) at low temperature or after long time storage at room temperature. Moreover, transparent and self-standing films of SS-CNPs from their THF-suspension show solvent-responsive surface wettability and responsive shape-memory property. SS-CNPs can also be used for the fabrication of nanocomposite films together with nonpolar compounds, such as (2-stearoylaminoethyl) rhodamine B. Thus, these novel SS-CNPs derived from sustainable cellulose fibers are promising candidates for the construction of novel functional materials.

- **A conductive liquid crystal via facile doping of an n-type benzodifurandione derivative**
  **Abstract:**
Two n-type molecular organic semiconductors (TI-BDF1 and TI-BDF2) consisting of thiophene-substituted indolin-2-one (TI) and benzodifurandione (BDF) with different branched side-chains have been synthesized to study the effect of molecular structure on molecular order, liquid crystal (LC) properties, and charge-transport. By tuning the branching point of the side-chains, TI-BDF2 shows a preferable edge-on π-face orientation and a high degree of liquid crystallinity, resulting in 4 orders of magnitude higher electron mobility than that of TI-BDF1. Subsequent n-doping of TI-BDF2 thin film with a thermally stable phosphonium salt affords a high electrical conductivity of 0.4 S cm$^{-1}$.

- **New 4,4′-Bis(9-carbazolyl)–Biphenyl Derivatives with Locked Carbazole–Biphenyl Junctions: High-Triplet State Energy Materials**

**Abstract:**

We synthesized a series of 4,4′-bis(9-carbazolyl)–biphenyl (CBP) derivatives, using methyl groups as spatially demanding groups, locking the angle between the carbazole subunit and the biphenyl backbone as potential matrix material for blue organic light-emitting diodes (OLEDs). The locked rotation was achieved by four methyl groups either in positions 1 and 8 of the carbazole subunit (1) or in positions 3, 5, 3′, and 5′ of the biphenyl subunit (2), and the fixed spatial arrangement was confirmed by X-ray analysis. The physical properties of CBP derivatives based on parent structure 2 were further tailored by electron-withdrawing CF$_3$ groups in positions 3 and 6 (3) or positions 2 and 7 of the carbazole subunits (4) or alternatively by electron-donating CH$_3$O groups in positions 2 and 7 (5) of the same building blocks. Increased triplet energies (ET) compared to that of the parent compound CBP were found for all synthesized CBP derivatives 1–5. Enhanced glass transition temperatures ranging between 129 and 202 °C further corroborate the application potential of these derivatives for matrix material in blue OLEDs.
• **Palladium-Catalyzed Glycosylation: Novel Synthetic Approach to Diverse N-Heterocyclic Glycosides**
  **Abstract:**
  An efficient and highly stereoselective method for the construction of N-heterocyclic glycosides is reported. This method is based on a palladium-catalyzed allylation which proceeded to provide N-heterocyclic glycosyl compounds in good-to-excellent yields with β- or α-selectivity. Various N-nucleophiles were examined for this reaction and selected N-glycosyl isatin substrates were further elaborated to bis-indole sugars which have potential as antiproliferative drugs.

• **Site-Specific Chemical Modification of Peptide and Protein by Thiazolidinediones**
  **Abstract:**
  A direct aldol reaction employing 2,4-thiazolidinediones as nucleophilic donors was performed to modify peptides and protein under mild conditions. Various functional groups could be readily introduced into protein without conformation change.

• **MMP-9 triggered micelle-to-fibre transitions for slow release of doxorubicin**
  **Abstract:**
  Phenylacetyl-peptide amphiphiles were designed, which upon cleavage by a disease-associated enzyme reconfigure from micellar aggregates to fibres. Upon this morphological change, a doxorubicin payload could be retained in the fibres formed, which makes them valuable carriers for localised formation of nanofibre depots for slow release of hydrophobic anticancer drugs.
**Cys\textsubscript{i}–\textit{Lys}_{i+3}–\textit{Lys}_{i+4} Triad: A General Approach for PEG-Based Stabilization of α-Helical Proteins**


Abstract:

PEGylation is an important strategy for enhancing the pharmacokinetic properties of protein drugs. Modern chemoselective reactions now enable specific placement of a single PEG at any site on a protein surface. However, few rational structure-based guidelines exist for selecting optimal PEGylation sites. Here, we explore the impact of PEGylation on the conformational stability of α-helices using an α-helical coiled coil as a model system. We find that maleimide-based PEGylation of a solvent-exposed i position Cys can stabilize coiled-coil quaternary structure when Lys residues occupy both the \(i + 3\) and \(i + 4\) positions, due to favorable interactions between the PEG-maleimide and the Lys residues. Applying this Cys\textsubscript{i}–Lys\textsubscript{i+3}–Lys\textsubscript{i+4} triad to a solvent-exposed position within the C-terminal helix of the villin headpiece domain leads to similar PEG-based increases in conformational stability, highlighting the possibility of using the Cys\textsubscript{i}–Lys\textsubscript{i+3}–Lys\textsubscript{i+4} triad as a general strategy for PEG-based stabilization of helical proteins.

**Spiropyran as a Mechanochromic Probe in Dual Cross-Linked Elastomers**


Abstract:

We study the mechanical activation of spiropyran (SP) in a doubly cross-linked polyurethane elastomer. Besides chemical cross-linking, the elastomer comprises polytetrahydrofuran as soft segments and hydrogen-bonding 2-ureido-4-pyrimidone (UPy) as hard segments. The material shows two color changes because of the ring-opening reaction of SP to merocyanine (MC) at strained state and the isomerization about the methane bridge of MC at relaxed state. Increasing tensile strain rate leads to stiffer and stronger elastomer as well as earlier activation.
of SP. The activation point of SP to MC always coincides well with strain hardening of the stress–elongation curves. We further use the two-color transitions of SP to study the fracture of the elastomer during crack propagation.

- **Probing the Interplay of Ultraviolet Cross-Linking and Non-Covalent Interactions in Supramolecular Elastomers**
  Abstract:

  Ultraviolet (UV) irradiated supramolecular polybutadienes (PBs) containing 2-ureido-4-[1H]-pyrimidone (UPy) linkages were examined as a simple model for curable supramolecular elastomers. Via precise control of UV exposure, the cure and the degradation of the vinyl groups within the PB elastomeric core were investigated. The combination of UPy binding and covalent cross-linking by UV irradiation dramatically enhanced mechanical properties of these UPy-functionalized elastomers, yielding toughness enhancement up to \( \sim 200\times \) at the 5 min UV cure. UV-initiated cross-linking dominated the curing process up to \( \sim 50 \) min exposure time. Beyond this cure time, dominant degradation of the vinyl linkages was observed. Control of this UV-initiated process yielded supramolecular elastomers with a covalently cross-linked phase induced by UV irradiation combined with a noncovalent UPy cross-linked phase induced by secondary hydrogen bonding interactions. Of particular note, it was determined that the presence of UPy hydrogen-bonded aggregates accelerated the UV cross-linking process during the initial stage of exposure. This observation was attributed to microphase-separated structure of UV-irradiated supramolecular elastomer, where UPy aggregation increased the probability of interaction between the pendant vinyls responsible for UV cross-linking. The systematic study of uniaxial tensile behavior of the UV-irradiated supramolecular elastomers offers new insight into the design and architecture of mechanically tunable supramolecular elastomers.

- **Synthesis and characterization of hexaarylbenzenes with five or six different substituents enabled by programmed synthesis**
  Abstract:
Since its discovery in 1825, benzene has served as one of the most used and indispensable building blocks of chemical compounds, ranging from pharmaceuticals and agrochemicals to plastics and those used in organic electronic devices. Benzene has six hydrogen atoms that can each be replaced by different substituents, which means that the structural diversity of benzene derivatives is intrinsically extraordinary. The number of possible substituted benzenes from n different substituents is \((2n + 2n^2 + 4n^3 + 3n^4 + n^6)/12\). However, owing to a lack of general synthetic methods for making multisubstituted benzenes, this potentially huge structural diversity has not been fully exploited. Here, we describe a programmed synthesis of hexaarylbenzenes using C–H activation, cross-coupling and [4+2] cycloaddition reactions. The present method allows for the isolation and structure–property characterization of hexaarylbenzenes with distinctive aryl substituents at all positions for the first time. Moreover, the established protocol can be applied to the synthesis of tetraarylnaphthalenes and pentaarylpypyridines.

- **Self-assembling knots of controlled topology by designing the geometry of patchy templates**
  **Abstract:**

  The self-assembly of objects with a set of desired properties is a major goal of material science and physics. A particularly challenging problem is that of self-assembling structures with a target topology. Here we show by computer simulation that one may design the geometry of string-like rigid patchy templates to promote their efficient and reproducible self-assembly into a selected repertoire of non-planar closed folds including several knots. In particular, by controlling the template geometry, we can direct the assembly process so as to strongly favour the formation of constructs tied in trefoil or pentafoil, or even of more exotic torus knots. Polydisperse and racemic mixtures of helical fragments of variable composition add further tunability in the topological self-assembly we discovered. Our results should be relevant to the design of new ways to synthesize molecular knots, which may prove, for instance, to be efficient cargo-carriers due to their mechanical stability.

- **Sequence-Specific, Nanomolar Peptide Binding via Cucurbit[8]uril-Induced Folding and Inclusion of Neighboring Side Chains**
Abstract:

This paper describes the molecular recognition of the tripeptide Tyr-Leu-Ala by the synthetic receptor cucurbit[8]uril (Q8) in aqueous buffer with nanomolar affinity and exceptional specificity. This combination of characteristics, which also applies to antibodies, is desirable for applications in biochemistry and biotechnology but has eluded supramolecular chemists for decades. Building on prior knowledge that Q8 binds to peptides with N-terminal aromatic residues, a library screen of 105 peptides was designed to test the effects of residues adjacent to N-terminal Trp, Phe, or Tyr. The screen used tetramethylbenzobisimidazolium (MBBI) as a fluorescent indicator and resulted in the unexpected discovery that MBBI can serve not only as a turn-off sensor via the simultaneous inclusion of a Trp residue but also as a turn-on sensor via the competitive displacement of MBBI upon binding of Phe- or Tyr-terminated peptides. The unusual fluorescence response of the Tyr series prompted further investigation by \(^1\)H NMR spectroscopy, electrospray ionization mass spectrometry, and isothermal titration calorimetry. From these studies, a novel binding motif was discovered in which only 1 equiv of peptide binds to Q8, and the side chains of both the N-terminal Tyr residue and its immediate neighbor bind within the Q8 cavity. For the peptide Tyr-Leu-Ala, the equilibrium dissociation constant value is 7.2 nM, whereas that of its sequence isomer Tyr-Ala-Leu is 34 μM. The high stability, recyclability, and low cost of Q8 combined with the straightforward incorporation of Tyr-Leu-Ala into recombinant proteins should make this system attractive for the development of biological applications.

- **Large Area Synthesis of a Nanoporous Two-Dimensional Polymer at the Air/Water Interface**

  Abstract:

We present the synthesis of a two-dimensional polymer at the air/water interface and its nm resolution imaging. Trigonal star, amphiphilic monomers bearing three anthraceno groups on a central triptycene core are confined at the air/water interface. Compression followed by photopolymerization on the interface provides the two-dimensional polymer.
scanning tunneling microscopy suggests that the polymer is periodic with ultrahigh pore density.

- **Supramolecular Interaction of Fullerenes with a Curved π-Surface of a Monomeric Quadruply Ring-Fused Porphyrin**
  
  Abstract: Molecular binding of fullerenes, C60 and C70, with the ZnII complex of a monomeric ring-fused porphyrin derivative (2-py) as a host molecule, which has a concave π-conjugated surface, has been confirmed spectroscopically. The structures of associated complexes composed of fullerenes and 2-py were explicitly established by X-ray diffraction analysis. The fullerenes in the 2:1 complexes, which consist of two 2-py molecules and one fullerene molecule, are fully covered by the concave surfaces of the two 2-py molecules in the crystal structure. In contrast, in the crystal structure of the 1:1 complex consisting of one 2-py molecule and one C60 molecule, the C60 molecule formed a π–π stacked pair with a C60 molecule in the neighboring complex using a partial surface, which was uncovered by the 2-py molecule. Additionally, the molecular size of fullerene adopted significantly affects the 1H NMR spectral changes and the redox properties of 2-py upon the molecular binding.

- **Chemistry of Anthracene–Acetylene Oligomers XXV: On-Surface Chirality of a Self-Assembled Molecular Network of a Fan-Blade-Shaped Anthracene–Acetylene Macrocycle with a Long Alkyl Chain**
  
  Abstract: An anthracene cyclic dimer with two different linkers and a dodecyl group was synthesized by means of coupling reactions. The calculated structure had a planar macrocyclic π core and a linear alkyl chain. Scanning tunneling microscopy observations at the 1-phenyloctane/graphite interface revealed that the molecules formed a self-assembled monolayer that consisted of linear striped bright and dark bands. In each domain, the molecular network consisted of either Re or Si molecules that differed in the two-dimensional chirality about the macrocyclic faces, which led to a unique conglomerate-type self-assembly. The molecular packing mode and the conformation of the alkyl chains are discussed in terms
of the intermolecular interactions and the interactions between the molecules and the graphite surface with the aid of MM3 simulations of a model system.

- **Hedgehog-shaped \{Mo368\} cluster: unique electronic/structural properties, surfactant encapsulation and related self-assembly into vesicles and films**


  **Abstract:**

  The hedgehog-shaped \{Mo368\} cluster shows unique electronic (extremely high extinction coefficient) and structural features, especially regarding its size, the high number of delocalized electrons which allows to measure the surface enhanced Raman scattering (SERS) spectrum and the option for coordination chemistry inside the cavity. Its relative instability in aqueous solution can be overcome by embedment in a hydrophobic shell of dimethyldioctadecylammonium cations. The resulting hybrid self-assembles into spherical vesicles in acetone–water mixtures, according to a process directed by hydrophobic–hydrophilic interactions. It also forms rather stable Langmuir monolayers while a second layer evolves under higher surface pressure, in accordance with a rather low alkyl surface density.

- **Spider’s super-glue: thread anchors are composite adhesives with synergistic hierarchical organization**


  **Abstract:**

  Silk is a key innovation in spiders, fascinating both biologists and material scientists. However, to fulfil their biological function silken threads must be strongly fastened to substrates or other threads. The majority of modern spiders produce a unique and rather unexplored bio-adhesive: the two-compound pyriform secretion, which is spun into elaborate patterns (so called attachment discs) and used to anchor silken threads to substrates. Strong adhesion is achieved on a high variety of surfaces with a minimum of material consumption. Pyriform threads polymerize under ambient conditions, become functional within less than a
second and can remain stable for years. They are biodegradable, biocompatible and highly versatile – the adhesion and the overall toughness of the attachment disc can be controlled by spinneret movements on a macroscopic level (ref. 1: V. Sahni et al., Nat. Commun., 2012, 3, 1106, DOI: 10.1038/ncomms2099). We found that the pyriform thread is a silk fibre that is coated with glue-like cement consisting of aligned nanofibrils, lipid enclosures and a dense, isotropic boundary layer. The threads are spun in a meshwork pattern that promotes stress distribution and crack arresting. Our results demonstrate, that hierarchical organization and fibre embedding may explain the high adhesive strength and flaw tolerance of a structure made by the same, rather simple type of silk glands.

- Quadruple Switching of Pleated Foldamers of Tetrathiafulvalene–Bipyridinium Alternating Dynamic Covalent Polymers
  Abstract:

  Tetrathiafulvalene and bipyridinium can be oxidized and reduced, respectively, to radical cations. Depending on their redox state, a donor–acceptor interaction or a radical–cation dimerization can occur. These noncovalent forces have been used to induce two tetrathiafulvalene–bipyridinium alternating dynamic covalent polymers to fold (see picture) and unfold reversibly in four ways.

- A Perfect Match: Fullerene Guests in Star-Shaped Oligophenylenevinylene Mesogens
  Abstract:

  Come into my arms: Stilbenoid star-shaped mesogens pack densely, in helical structures that have a short correlation length, in columnar liquid-crystal phases. Attaching a fullerene guest to the interior of the star fills the void space between the arms and considerably increases the
mesophase stability by approximately 70 °C. The stabilization is the result of the formation of a fullerene triple helix.

- **Multidimensional hierarchical self-assembly of amphiphilic cylindrical block comicelles**
  **Abstract:**

  Self-assembly of molecular and block copolymer amphiphiles represents a well-established route to micelles with a wide variety of shapes and gel-like phases. We demonstrate an analogous process, but on a longer length scale, in which amphiphilic P-H-P and H-P-H cylindrical triblock comicelles with hydrophobic (H) or polar (P) segments that are monodisperse in length are able to self-assemble side by side or end to end in nonsolvents for the central or terminal segments, respectively. This allows the formation of cylindrical supermicelles and one-dimensional (1D) or 3D superstructures that persist in both solution and the solid state. These assemblies possess multiple levels of structural hierarchy in combination with existence on a multimicrometer-length scale, features that are generally only found in natural materials.

- **Materials that couple sensing, actuation, computation, and communication**
  **Abstract:**

  Tightly integrating sensing, actuation, and computation into composites could enable a new generation of truly smart material systems that can change their appearance and shape autonomously. Applications for such materials include airfoils that change their aerodynamic profile, vehicles with camouflage abilities, bridges that detect and repair damage, or robotic skins and prosthetics with a realistic sense of touch. Although integrating sensors and actuators into composites is becoming increasingly common, the opportunities afforded by embedded computation have only been marginally explored. Here, the key challenge is the gap between the continuous physics of materials and the discrete mathematics of computation.
Bridging this gap requires a fundamental understanding of the constituents of such robotic materials and the distributed algorithms and controls that make these structures smart.

- **Imaging of β-amyloid plaques by near infrared fluorescent tracers: a new frontier for chemical neuroscience**
  Abstract:

  Brain amyloid depositions are the main hallmarks of Alzheimer's and other protein misfolding diseases. Since they are believed to precede clinical symptoms by several years, imaging of such fibrillar aggregates is particularly suitable to diagnose the onset of the disease in its early stage and monitor its progression. In this context, near infrared (NIR) imaging has been proposed as a promising and non-invasive method to visualize amyloid plaques *in vivo* because of its acceptable depth of penetration and minimal degree of tissue damage. In this tutorial review, we describe the main chemical and physicochemical features of probes associated with fluorescence emission in the NIR region. The review focuses on the recent progress and improvements in the development of small-molecule NIR fluorescent probes and their *in vivo* application in living animals. In addition, the possible therapeutic application of NIR probes to block the pathological aggregation process will be discussed, raising the fascinating possibility of their exploitation as theranostic agents.

- **The chemistry and engineering of polymeric hydrogel adhesives for wound closure: a tutorial**
  Abstract:

  The closure and repair of wounds after traumatic or surgical injury is of significant clinical and research importance. While sutures remain the common wound closure technique, they have many disadvantages. Consequently, polymeric hydrogel adhesives have emerged as essential materials for wound management and repair because of their tunable chemical and physical properties, which enable them to adhere or stick to tissues, possess sufficient mechanical strength to stay intact and be subsequently removed, provide complete wound
occlusion, and act as a barrier to bacterial infection. Moreover, these materials absorb wound exudates and keep the wound moist for faster healing. This tutorial review summarizes the key chemical features that enabled the development and use of polymeric hydrogels as wound adhesives, sealants, and hemostats, their design requirements, synthetic routes, determination of properties, and the tests needed to evaluate their performances. This tutorial review is a reference and a starting point for scientists and clinicians working or interested in the field of wound management and, importantly, for the general audience who is interested in polymers for medical applications.

- **Surface-Based Supramolecular Chemistry Using Hydrogen Bonds**
  
  Abstract:

  The arrangement of molecular species into extended structures remains the focus of much current chemical science. The organization of molecules on surfaces using intermolecular interactions has been studied to a lesser degree than solution or solid-state systems, and unanticipated observations still lie in store. Intermolecular hydrogen bonds are an attractive tool that can be used to facilitate the self-assembly of an extended structure through the careful design of target building blocks. Our studies have focused on the use of 3,4,9,10-perylene tetracarboxylic acid diimides (PTCDIs), and related functionalized analogues, to prepare extended arrays on surfaces. These molecules are ideal for such studies because they are specifically designed to interact with appropriate diaminopyridine-functionalized molecules, and related species, through complementary hydrogen bonds. Additionally, PTCDI species can be functionalized in the bay region of the molecule, facilitating modification of the self-assembled structures that can be prepared. Through a combination of PTCDI derivatives, sometimes in combination with melamine, porous two-dimensional arrays can be formed that can entrap guest molecules. The factors that govern the self-assembly processes of PTCDI derivatives are discussed, and the ability to construct suitable target arrays and host-specific molecular species, including fullerenes and transition metal clusters, is demonstrated.

- **Fluorinated Proteins: From Design and Synthesis to Structure and Stability**
  
  Abstract:
Fluorine is all but absent from biology; however, it has proved to be a remarkably useful element with which to modulate the activity of biological molecules and to study their mechanism of action. Our laboratory's interest in incorporating fluorine into proteins was stimulated by the unusual physicochemical properties exhibited by perfluorinated small molecules. These include extreme chemical inertness and thermal stability, properties that have made them valuable as nonstick coatings and fire retardants. Fluorocarbons also exhibit an unusual propensity to phase segregation. This phenomenon, which has been termed the “fluorous effect”, has been effectively exploited in organic synthesis to purify compounds from reaction mixtures by extracting fluorocarbon-tagged molecules into fluorocarbon solvents. As biochemists, we were curious to explore whether the unusual physicochemical properties of perfluorocarbons could be engineered into proteins. To do this, we developed a synthesis of a highly fluorinated amino acid, hexafluoroleucine, and designed a model 4-helix bundle protein, α4H, in which the hydrophobic core was packed exclusively with leucine. We then investigated the effects of repacking the hydrophobic core of α4H with various combinations of leucine and hexafluoroleucine. These initial studies demonstrated that fluorination is a general and effective strategy for enhancing the stability of proteins against chemical and thermal denaturation and proteolytic degradation. We had originally envisaged that the “fluorous interactions”, postulated from the self-segregating properties of fluorous solvents, might be used to mediate specific protein–protein interactions orthogonal to those of natural proteins. However, various lines of evidence indicate that no special, favorable fluorine–fluorine interactions occur in the core of the fluorinated α4protein. This makes it unlikely that fluorinated amino acids can be used to direct protein–protein interactions. More recent detailed thermodynamic and structural studies in our laboratory have uncovered the basis for the remarkably general ability of fluorinated side chains to stabilize protein structure. Crystal structures of α4H and its fluorinated analogues show that the fluorinated residues fit into the hydrophobic core with remarkably little perturbation to the structure. This is explained by the fact that fluorinated side chains, although larger, very closely preserve the shape of the hydrophobic amino acids they replace. Thus, an increase in buried hydrophobic surface area in the folded state is responsible for the additional thermodynamic stability of the fluorinated protein. Measurements of $\Delta G^\circ$, $\Delta H^\circ$, $\Delta S^\circ$, and $\Delta C_p^\circ$ for unfolding demonstrate that the “fluorous” stabilization of these protein arises from the hydrophobic effect in the same way that hydrophobic partitioning stabilizes natural proteins.

- Advances in Chemical Protein Modification
  Abstract:
Everything you want to know about how to chemically modify proteins. Great review.