- Inter *versus* intra-molecular photoinduced charge separation in solid films of donor–acceptor molecules
  Safa, S.; Eng, M.P.; An, Z.; Zhang, X.; Barlow, S.; Marder, S.R.; Durrant, J.R. *Chem. Commun.,* **2008**, 4915 – 4917.
  Abstract:

We report on photoinduced charge separation in solid films of two perylene diimides; intramolecular charge separation and recombination is correlated with a reduction in the yield of long-lived, intermolecular charge-separated species.

- Supramolecular aptamer–thrombin linear and branched nanostructures
  Weizmann, Y.; Braunschweig, A.B.; Wilner, O.I.; Cheglakov, Z.; Willner, I. *Chem Commun.*, **2008**, 4888 – 4890.
  Abstract:

α and β conjugated bis-aptamers against thrombin act as bidentate "glue" for the self-assembly of thrombin nanowires. Mixing the bidentate aptamer with a tripodal tridentate α aptamer construct yields branched thrombin nanowire structures.

- Artificial β-barrels
  Sakai, N. ; Mareda, J. ; Matile, S. *Acc. Chem. Res.* **2008**, *41*, 1354-1365.
  Abstract:

In biology, β-barrels, cylindrically rolled-up forms of β-sheets, are ubiquitous structural motifs within various binding proteins, pores, and enzymes. This biological multifunctionality suggested that synthetic artificial β-barrels would provide access to many different functions beyond the limitations of peptide chemistry. Unlike the relative ease of formation of synthetic (de novo) α-helix bundles, the synthesis of artificial β-barrels remains a challenge. To bypass the folding problems involved, we have employed “unfoldable” rigid-rod scaffolds as privileged staves (staves are the wood strips that form the sides of macroscopic barrels); the resulting barrel-stave supramolecules exhibit their expected multifunctionality. Several “rigid rod” β-barrels that act as receptors, ion channels, pores, catalysts, and sensors have been prepared and studied. The most recent topic of interest concerns the use of artificial β-barrels as multicomponent sensors (“artificial tongues”) in complex analyte matrices. For multicomponent sensing, we have designed artificial β-barrels to form pores that can open and close in response to chemical stimulation within lipid bilayers. With use of fluorogenic vesicles, changes in pore activity are readily detectable with either the naked eye or multiwell screening formats. The varying responsiveness to substrates and products makes synthetic pores versatile detectors of chemical reactions, of the activity of the enzymes that catalyze these reactions, and of their inhibitors. In sensing applications, the “perfect” selectivity of enzymes is exploited to generate analyte-specific signals. Reactive signal amplifiers are then covalently linked to the products of enzymatic signal generation to enhance their pore blockage potency. With the help of signal generators and amplifiers, we have employed artificial β-barrel pores to sense sweet (sucrose, lactose), sour (acetate, lactate, citrate), and umami (“deliciousness”, glutamate) components in various food samples. This breakthrough naturally led us to design and synthesize refined pores for advanced sensing applications. We have developed methods to build guest-binding sites not only at internal and external barrel surfaces but also near the core or near the periphery of the pore. Further refinements include the introduction of asymmetric staves for voltage gating and anchoring of the pore at the membrane−water interface.

- Stimuli-responsive surfaces for bio-applications
  Mendes, P.M. *Chem. Soc. Rev*. **2008**, *37*, 2512-2529.
  Abstract:

The development of surfaces that have switchable properties, also known as smart surfaces, have been actively pursued in the past few years. The recent surge of interest in these switchable systems stems from the widespread number of applications to many areas in science and technology ranging from environmental cleanup to data storage, micro- and nanofluidic devices. Moreover, the ability to modulate biomolecule activity, protein immobilisation, and cell adhesion at the liquid–solid interface is important in a variety of biological and medical applications, including biofouling, chromatography, cell culture, regenerative medicine and tissue engineering. Different materials have been exploited to induce such changes in surface biological properties that are mostly based on self-assembled monolayers or polymer films. This *critical review* focuses on the recent progress in the preparation of these switchable surfaces, and highlights their applications in biological environments. The review is organized according to the external stimuli used to manipulate the properties of the substrate—chemical/biochemical, thermal, electric and optical stimuli. Current and future challenges in the field of smart biological surfaces are addressed.

- Saccharide-Linked Ethynylpyridine Oligomers: Primary Structures Encode Chiral Helices
  Abe, H.; Murayama, D.; Kayamori, F.; Inouye, M. *Macromolecules* **2008**, *41*, 6903-6909.
  Abstract:

A series of glycoside-linked oligomeric 2,6-pyridylene-ethynylene (*m*-ethynylpyridine) compounds were prepared and studied for their intramolecular chiral induction. The primary structure of the oligomers, such as the lengths of ethynylpyridine moieties and linkers and the types of terminal groups and linked glycosides, was varied. From circular dichroism (CD) and 1H NMR analyses, it was found that the intramolecular hydrogen bonds between the glycoside and ethynylpyridine moieties induced the formation of higher-order, chiral helices of the oligomers. The sign and strength of CD signals for the helices were found to depend strongly on the length of ethynylpyridines and the types of terminal groups and glycosides. These results showed that the oligomers encode their higher-order structures in their primary structures.

- Porphyrin-Dithienothiophene π-Conjugated Copolymers: Synthesis and Their Applications in Field-Effect Transistors and Solar Cells
  Huang, X.; Zhu, C.; Zhang, S.; Li, W.; Guo, Y.; Zhan, X.; Liu, Y.; Bo, Z. *Macromolecules* **2008**, *41*, 6895-6902.
  Abstract:

Soluble conjugated alternating porphyrin−dithienothiophene copolymers—single-bond linked (**I**) and triple-bond linked (**IIa** and **IIb**)—were synthesized by palladium(0)-catalyzed Stille and Sonagashira coupling reactions, respectively. The thermal, electrochemical, optical, charge transport, and photovoltaic properties of these copolymers were examined; the effect of the triple bond was studied. **I** exhibits onset decomposition temperature (T_d) of 410 °C and glass-transition temperature (T_g) of 180 °C, higher than those of **IIb** (T_d, 330 °C; T_g, 130 °C). The absorption spectrum of **I** in thin film exhibits a sharp Soret band at 450 nm and two weak Q-bands at 563−619 nm, while **IIb** exhibits a sharp Soret band at 491 nm and a strong Q-band at 760 nm. The emission maxima of **I** and **IIb** in solution are located at 642 and 722 nm respectively. **IIb** is electrochemically active in both the

oxidation and reduction regions, while **I** shows only oxidation peak. The field-effect hole mobilities as high as 2.1×10^{-4} cm^2 V^{-1} s^{-1} were obtained for these copolymers. Polymer solar cells (PSCs) were fabricated based on the blend of the polymers and methanofullerene [6,6]-phenyl C61-butyric acid methyl ester (PCBM). The power conversion efficiency (PCE) of 0.3% was achieved under AM 1.5, 100 mW/cm^2 for the PSC using **IIb**:PCBM (1:3, w/w) as active layer. The PCE of the PSC based on **IIb**:PCBM (1:3, w/w) is double that based on **I**:PCBM (1:2, w/w), consistent with that **IIb** exhibits stronger Q-band absorption and higher mobility at room temperature.

- Folding a Conjugated Chain: Oligo(*o*-phenyleneethynylene-*alt*-*p*-phenyleneethynylene)
  Zhu, N.; Hu, W.; Han, S.; Wang, Q.; Zhao, D. *Org. Lett.* **2008**, *10*, 4283-4286.
  Abstract:

An oligo(*o*-phenyleneethynylene-*alt*-*p*-phenyleneethynylene) was synthesized to create a conjugated molecule capable of adopting a helical secondary structure. A special feature of such a folded molecule is that the effective directions of energy/charge transport via covalent conjugation and through π−π stacking are converged to be along the helix axis. The transition from random conformations to the helix, driven by solvophobic and aromatic stacking interactions, was controlled by solvent properties. UV−vis and fluorescence spectroscopies gave supportive evidence for the folding process.

- Toward an Artificial Aldolase
  Font, D. ; Sayalero, S. ; Bastero, A. ; Jimeno, C. ; Pericàs, M. A. *Org. Lett.* **2008**, *10*, 337-340.
  Abstract:

A new functional polymer where proline is bonded to polystyrene through a 1,2,3-triazole linker depicts characteristics targeted for an artificial aldolase. In spite of the hydrophobicity of the polymer backbone, the resin swells in water with building of an aqueous microenvironment. This property, arising from the formation of a hydrogen-bond network connecting the proline and 1,2,3-triazole fragments, is translated into a very high catalytic activity and enantioselectivity toward direct aldol reactions in water.

- Determination of the Electrophilicity Parameters of Diethyl Benzylidenemalonates in Dimethyl Sulfoxide: Reference Electrophiles for Characterizing Strong Nucleophiles
  Kaumanns, O.; Lucius, R.; Mayr, H. *Chem. Eur. J.* **2008**, *14*, 9675-9682.
  Abstract:

The second-order rate constants of the reactions of nine substituted diethyl benzylidenemalonates **1 a**-**i** with the carbanions **2 a**-**e** have been determined spectrophotometrically in dimethyl sulfoxide (DMSO). Product studies show that the nucleophiles attack regioselectively at the electrophilic C=C double bond of the Michael acceptors to form the carbanionic adducts **4**. The correlation log *k*(20 °C)=*s*(*N*+*E*) allows the determination of the electrophilicity parameters *E* for the electrophiles **1 a**-**i** from the rate constants determined in this work and the previously published *N* and *s* parameters for the nucleophiles **2 a**-**e**. The electrophilicities *E* for compounds **1 a**-**i** cover a range of six units (-17.7>*E*>-23.8) and correlate excellently with Hammett's substituent constants σ_p. The title compounds are roughly ten orders of magnitude less reactive than analogously substituted benzylidene Meldrum's acids, their cyclic analogues. Due to their low reactivities, compounds **1 a**-**i** are suitable reference electrophiles for determining the reactivities of highly reactive nucleophiles, such as carbanions with 16<*N*<30.

- Designed Folding of Pseudopeptides: The Transformation of a Configurationally Driven Preorganization into a Stereoselective Multicomponent Macrocyclization Reaction
  Alfonso, I.; Bolte, M.; Bru, M.; Burguete, M. I.; Luis, S. V. *Chem. Eur. J.* **2008**, *14*, 8879-8891.
  Abstract:

The efficient synthesis of large-ring pseudopeptidic macrocycles through a multicomponent [2+2] reductive amination reaction is described. The reaction was entirely governed by the structural information contained in the corresponding open-chain pseudopeptidic bis(amidoamine) precursors, which have a rigid (*R*,*R*)-cyclohexane-1,2-diamine moiety. A remarkable match/mismatch relationship between the configurations of the chiral centers of the cyclic diamine and those of the peptidic frame was observed. The macrocyclic tetraimine intermediates have been studied in detail by NMR spectroscopy, circular dichroism (CD), and molecular modeling, and the results support the appropriate preorganization induced by the match combination of the chiral centers. We have also synthesized the corresponding open-chain bis(imine) model compounds. The structural studies (NMR spectroscopy, CD, modeling) of these systems showed an intrinsically lower reactivity of the mismatch combination, even when the product of the reaction was acyclic. In addition, a synergistic effect between the two chiral substructures for the correct folding of the molecules was observed. Finally, X-ray analysis of the HCl salt of one of the macrocycles showed an interesting pattern; the macrocyclic rings stack in columnar aggregates leaving large interstitial channels filled with water-solvated chloride anions.

- Entropy- and Hydrolytic-Driven Positional Switching of Macrocycle between Imine- and Hydrogen-Bonding Stations in Rotaxane-Based Molecular Shuttles
  Umehara, T.; Kawai, H.; Fujiwara, K.; Suzuki, T. *J. Am. Chem. Soc.* **2008**, *130*, 13981–13988.
  Abstract:

The construction and switching properties of a novel class of molecular shuttles **1** with imine-bonding stations for macrocyclic diamine parts are reported. Studies on dithioacetalized [2]rotaxane **4** with two hydrogen-bonding stations and a masked imine-bonding station showed that protonation of a macrocycle increases the shuttling barrier due to hydrogen-bond formation between NH_3^+ groups and the TEG-stations. Hydrolysis of the imine-bonds of the imine-bridged molecular shuttles **1b**,**c** with TEG-stations could exclusively give the [2]rotaxane **2b**,**c**·$2H^{2+}$, with the macrocycle hydrogen-bonded with the TEG-station. In contrast, **1a** without TEG-stations gave an equilibrated mixture of **1a**, monoimine **3a**·H^+, and **2a**·$2H^{2+}$ under similar acidic hydrolytic conditions. The equilibrium between **1b**,**c** and **2b**,**c**·$2H^{2+}$ to control the position of the macrocycle could be successfully switched to either side by applying acidic hydrolytic or dehydrating conditions. Furthermore, the equilibrium was largely biased to [2]rotaxane **2b**,**c**·$2H^{2+}$ under acidic hydrolytic conditions and could be reversed in favor of bis-imine **1b**,**c** just by heating. This is a successful example of a molecular shuttle exhibiting entropy-driven translational isomerism with remarkable positional discrimination. An examination of thermodynamic parameters showed that imine-bond hydrolyses and the formation of hydrogen bonds between the macrocycle and the station are thermodynamically matched processes, because both processes are enthalpically favored and accompanied by a loss of entropy. The combination of imine-bonding and hydrogen-bonding station in a rotaxane system is the key to realizing the clear entropy-driven positional switching of the macrocycle observed.

- Three State Redox-Active Molecular Shuttle That Switches in Solution and on a Surface

Fioravanti, G.; Haraszkiewicz, N.; Kay, E. R.; Mendoza, S. M.; Bruno, C.; Marcaccio, M.; Wiering, P. G.; Paolucci, F.; Rudolf, P.; Brouwer, A. M.; Leigh, D. A. *J. Am. Chem. Soc.* **2008**, *130*, 2591-2601.

Abstract:

Although the desirability of developing synthetic molecular machine systems that can function on surfaces is widely recognized, to date the only well-characterized examples of electrochemically switchable rotaxane-based molecular shuttles which can do so are based on the tetracationic viologen macrocycle pioneered by Stoddart. Here, we report on a [2]rotaxane which features succinamide and naphthalene diimide hydrogen-bonding stations for a benzylic amide macrocycle that can shuttle and switch its net position both in solution and in a monolayer. Three oxidation states of the naphthalene diimide unit can be accessed electrochemically in solution, each one with a different binding affinity for the macrocycle and, hence, corresponding to a different distribution of the rings between the two stations in the molecular shuttle. Cyclic voltammetry experiments show the switching to be both reversible and cyclable and allow quantification of the translational isomer ratios (thermodynamics) and shuttling dynamics (kinetics) for their interconversion in each state. Overall, the binding affinity of the naphthalene diimide station can be changed by 6 orders of magnitude over the three states. Unlike previous electrochemically active amide-based molecular shuttles, the reduction potential of the naphthalene diimide unit is sufficiently positive (-0.68 V) for the process to be compatible with operation in self-assembled monolayers on gold. Incorporating pyridine units into the macrocycle allowed attachment of the shuttles to an acid-terminated self-assembled monolayer of alkane thiols on gold. The molecular shuttle monolayers were characterized by X-ray photoelectron spectroscopy and their electrochemical behavior probed by electrochemical impedance spectroscopy and double-potential step chronoamperometry, which demonstrated that the redox-switched shuttling was maintained in this environment, occurring on the millisecond time scale.

- Protein−Protein Interactions in Reversibly Assembled Nanopatterns
  Rakickas, T.; Gavutis, M.; Reichel,A.; Piehler,J.; Liedberg,B.; Valiokas, R. *Nano Lett.* **2008**, *8*, 3369-3375.

Abstract:

We describe herein a platform to study protein−protein interactions and to form functional protein complexes in nanoscopic surface domains. For this purpose, we employed multivalent chelator (MCh) templates, which were fabricated in a stepwise procedure combining dip-pen nanolithography (DPN) and molecular recognition-directed assembly. First, we demonstrated that an atomic force microscope (AFM) tip inked with an oligo(ethylene glycol) (OEG) disulfide compound bearing terminal biotin groups can be used to generate biotin patterns on gold achieving line widths below 100 nm, a generic platform for fabrication of functional nanostructures via the highly specific biotin−streptavidin recognition. Subsequently, we converted such biotin/streptavidin patterns into functional MCh patterns for reversible assembly of histidine-tagged (His-tagged) proteins via the attachment of a tris-nitriloacetic acid (trisNTA) biotin derivative. Fluorescence microscopy confirmed reversible immobilization of the receptor subunit ifnar2-His_{10} and its interaction with interferon-α2 labeled with fluorescent quantum dots in a 7 × 7 dot array consisting of trisNTA spots with a diameter of ~230 nm. Moreover, we carried out characterization of the specificity, stability, and reversibility as well as quantitative real-time analysis of protein−protein interactions at the fabricated

nanopatterns by imaging surface plasmon resonance. Our work offers a route for construction and analysis of functional protein-based nanoarchitectures.

- Reversible Photo-Switching of Single Azobenzene Molecules in Controlled Nanoscale Environments
  Kumar, A. S.; Ye, T.; Takami, T.; Yu, B.-C.; Flatt, A. K.; Tour, J. M.; Weiss, P. S. *Nano Lett.* **2008**, *8*, 1644-1648.
  Abstract:

We drive reversible photoinduced switching of single azobenzene-functionalized molecules isolated in tailored alkanethiolate monolayer matrices on Au{111}. We designed molecular tethers to suppress excited-state quenching from the metal substrate and formed rigid assemblies of single tethered azobenezene molecules in the domains of monolayer to limit steric constraints and tip-induced and stochastic switching effects. Single molecules were reversibly photoisomerized between *trans* and *cis* conformations by cycling exposure to visible and UV light. Trans and cis conformations were imaged as high (2.1 ±0.3 Å) and low (0.7 ±0.2 Å) protrusions in STM images and were assigned to the on and off states of the molecule, respectively.

- Total Synthesis of the Originally Assigned Structure of Vannusal B
  Nicolaou, K. C. ; Zhang, H. ; Ortiz, A. ; Dagneau, P. *Angew. Chem. Int. Ed.* **2008**, *47*, 8605 – 8610.
  Abstract:

The truth is out there: The chase for the originally assigned structure of vannusal B (see structural formula) by total synthesis ended successfully, but created a new puzzle, that of the true structure of this intriguing marine natural product.

- Fluorinating Cleavage of Solid Phase Linkers for Combinatorial Synthesis
  Wiehn, M. S.; Lindell, S. D.; Bräse, S. *Angew. Chem. Int. Ed.* **2008**, *47*, 8120 – 8122.
  Abstract:

Multitasking: A new preparative route to fluorine-containing compounds combines the advantages of solid-phase synthesis with the incorporation of fluorine at the end of the synthetic route. A sulfur linker enables simultaneous fluorination of the target structures in the cleavage step. As it is stable under different reaction conditions, the linker has potential in the combinatorial synthesis of fluorinated drug structures.

- Frustrated Phases of Block Copolymers in Nanoparticles
  Higuchi, T.; Tajima, A.; Motoyoshi, K.; Yabu, H.; Shimomura, M. *Angew. Chem. Int. Ed.* **2008**, *47*, 8044 – 8046.
  Abstract:

3D confinement effect: Block copolymers form novel phase separation structures in the nanoparticles owing to frustration of the nanosized confinement effect. Whereas films of the block copolymers form lamellar structures, the nanoparticles formed unique structures (Janus-type, tennis-ball-, mushroom-, wheel-, and screwlike structures) depending on the ratio between particle diameter and molecular weight.

- Merging Photoredox Catalysis with Organocatalysis: The Direct Asymmetric Alkylation of Aldehydes
  Nicewicz, D. A.; MacMillan, D. W. C. *Science* **2008**, *322*, 77 – 80.

Abstract:

Photoredox catalysis and organocatalysis represent two powerful fields of molecule activation that have found widespread application in the areas of inorganic and organic chemistry, respectively. We merged these two catalysis fields to solve problems in asymmetric chemical synthesis. Specifically, the enantioselective intermolecular α-alkylation of aldehydes has been accomplished using an interwoven activation pathway that combines both the photoredox catalyst $Ru(bpy)_3Cl_2$ (where bpy is 2,2'-bipyridine) and an imidazolidinone organocatalyst. This broadly applicable, yet previously elusive, alkylation reaction is now highly enantioselective and operationally trivial.

- Practical Synthesis of Prostratin, DPP, and Their Analogs, Adjuvant Leads Against Latent HIV
  Wender, P. A.; Kee, J.-M.; Warrington, J. M. *Science* **2008**, *320*, 649 – 652.

Abstract:

Although antiretroviral therapies have been effective in decreasing active viral loads in AIDS patients, the persistence of latent viral reservoirs prevents eradication of the virus. Prostratin and DPP (12-deoxyphorbol-13-phenylacetate) activate the latent virus and thus represent promising adjuvants for antiviral therapy. Their limited supply and the challenges of accessing related structures have, however, impeded therapeutic development and the search for clinically superior analogs. Here we report a practical synthesis of prostratin and DPP starting from phorbol or crotophorbolone, agents readily available from renewable sources, including a biodiesel candidate. This synthesis reliably supplies gram quantities of the therapeutically promising natural products, hitherto available only in low and variable amounts from natural sources, and opens access to a variety of new analogs.