SYMPOSIUM G

G: Molecularly Imprinted Materials

December 3 - 5, 2003

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* Invited paper

SESSION G1: Catalysis and Applications
Chair: Peter Kofinas
Wednesday Morning, December 3, 2003
Republic A (Sheraton)

8:30 AM *G1.1
Molecular Imprinting - Quo vadis? Boerje Sellergren, INFU, University of Dortmund, Dortmund, Germany.

Molecular imprinting refers to a technique for the synthesis of a polymer in presence of a template. The latter is most commonly a small molecule but approaches to imprint biological macromolecules or even whole cells have also been proposed. After removal of the template the formed polymer retains a functional and shape memory for the template manifested in its ability to rebind the latter or a structural analogue with high fidelity. The technique has gained and continues to gain wide spread attention due to its simplicity, robustness and the receptor like molecular recognition properties of the resulting molecularly imprinted polymers (MIPs). In this talk I will first provide an overview of the field, highlighting some recent promising contributions. In the final part I will focus on the deficiencies of MIPs, mainly with reference to biological receptors, and approaches to correct them. (1) Society of Molecular Imprinting: http://www.smi.tu-berlin.de (2) B. Sellergren (Ed) Molecularly Imprinted Polymers: Man made mimics of antibodies and their application in analytical chemistry. Elsevier Publishers, 2001.

9:15 AM *G1.2
Catalytically Active Polymers Prepared Bymolecular Imprinting. Guenter Wulff, Jun-Giu Liu and Marco Emgenbroich; Inst of Organic & Macromolecular Chemistry, Heinrich-Heine-Universitaet Duesseldorf, Dusseldorf, Germany.

In order to mimick the active site of antibodies and enzymes a molecular imprinting procedure in polymers has been introduced quite some years ago. The principle of molecular imprinting is based on the crosslinking polymerisation in the presence of binding site monomers around a molecule that acts as a template. After removal of the template, an imprint of specific shape and with functional groups capable of chemical interactions remains in the polymer.[1)] Such polymers can be used for selective solid phase extraction, for chromatographic resolutions, as specific detection layers in chemosensors, as artificial antibodies in radioimmuno assays, or as catalysts working in a mode similar to enzymes. New developments in this technique will be discussed. Special binding site monomers for non-covalent interaction are described. They show high association constants for binding to the template so that stoichiometric non-covalent interactions are possible during imprinting. This type of interaction considerably improves the mode of operation of imprinted polymers.[2)] It is especially suitable for the preparation of catalytically active imprinted polymers. Using different stable transition-state analogues of alkaline ester hydrolysis as templates and suitable catalytic functional monomers, catalysts with strong esterolytic activity for the hydrolysis of esters, carbonates, and carbamates can be obtained.[3)] By imprinting with a chiral non-racemic transition-state analogue a very active catalyst showing substrate- and enantioselectivity was obtained. The enantioselectivity observed is caused to a similar degree by selective substrate binding (thermodynamic control) and selective stabilisation of the transition-state of the reaction (kinetic control). In case of stoichiometric non-covalent interaction the polymerisation obtaining catalytically active polymers can also be performed by standard suspension and miniemulsion polymerisation techniques. Thus regular beads of 10 - 400 μm and minigels of 100 - 300 nm particle diameter can be obtained. A further step down to nanoparticles involves the intramolecular crosslinking of macromolecules by which highly crosslinked, soluble polymers with molecular weights below 200 000 and particle diameter of 5 - 10 nm can be obtained. Thus these compounds approach enzyme dimensions. 1) G. Wulff, Angew. Chem. Int. Ed. Engl. **1995**, *34*,1812 - 1832. 2) G. Wulff, C. Knorr, Bioseparation **2002**, *10*, 257 - 276. 3) G. Wulff, Chem. Rev. **2002**, *102*, 1 - 27.

10:30 AM G1.3
The Synthesis and Catalytic Application of a New Class of Imprinted Silica. John Bass and Alexander Katz; Chemical Engineering, UC Berkeley, Berkeley, California.

We have recently synthesized a new class of bulk imprinted silicates with a hydrophilic framework. This required the development of a novel synthesis stategy that uses thermolysis to affect imprint removal. Imprinted sites consisting of up to two primary amines have been synthesized within hydrophilic microporous and mesoporous inorganic-oxide frameworks. The imprinting process has been characterized by multinuclear solid-state NMR spectroscopy, thermogravimetric analysis, mass spectrometry, potentiometric titration and probe molecule binding. The latter reveal a remarkable ability to bind polar molecules that are inaccessible using materials with a hydrophobic framework. These hydrophilic imprinted silicates have been used to elucidate how the chemical environment of a silica support affects the observed activity of a synthetic heterogeneous catalyst. Due to its proximity to the active catalyst, the silica framework functions in much the same way that a solvent does in homogeneous systems. Analogous to solvent effects in homogeneous systems, we show that the framework has a strong impact on transitions occurring at the active site, governing the equilibria of adsorbed species, reaction kinetics, and turnover frequencies in model systems.

11:00 AM G1.4
Affecting Active Site Homogeneity and Effectiveness in Molecularly Imprinted Transition Metal Catalysts. Michel R Gagne, Chemistry, UNC Chapel Hill, Chapel Hill, North Carolina.

This presentation will describe recent efforts to synthesize imprinted active sites at the locus of dendritic metallomonomers. The stimulation for these experiments is the desire to maximize site-to-site homogeneity, and thereby better mimic the single site notion best exemplified by enzymes. The strategy for achieving the goal is to attach relatively small polymerizable dendritic arms to diphosphine ligands, which are in turn coordinated to a transition metal catalyst or precatalyst. Copolymerization of these arms into the matrix of a rigid but porous organic polymer provides for active sites whose chemical composition and functionality is shaped by a combination of dendrimer rigidification (imprinting) and the inherent functionality of the dendritic arms, which is also susceptible to imprinting effects. Results comparing and contrasting this dendrimer approach to a more traditional metallomonomer will be presented, the emphasis being on a description of the relative homogeneity of the resulting sites compared to non-dendritic templates. The application of these imprinted sites in the area of enantiomer-selective and shape-selective catalysis of complex organic reactions will also be presented. The emphasis will be on how the presence of an imprinted active site, and its attendant stereochemistry and shape lead to catalysts with properties unobtainable in solution analogs.

11:30 AM G1.5
Towards Practical Applications of Molecularly Imprinted Polymers (MIPs). Bernard S Green, [1]Semorex, Inc., North Brunswick, New Jersey; [2]School of Pharmacy, The Hebrew University, Jerusalem, Israel.

The technologies for producing molecularly selective, robustly stable imprinted polymers continue to expand and to impact upon many potential areas of application. The low cost and ease of synthesis of MIPs, along with the possibility of their production as beads, membranes, nanoparticles, etc. and, particularly, the nearly unlimited chemical variability that can be marshalled for interactions between the binding sites and the bound targets, promise exciting current and future applications for these materials. From the vantage points of academe plus industry a current assessment of the attraction of this "old-new" science will be critically evaluated with regard to the market potential of MIPs.

SESSION G2: Combinatorial and Computational Methods
Chair: Boerje Sellergren
Wednesday Afternoon, December 3, 2003
Republic A (Sheraton)

1:30 PM *G2.1
Molecular Simulations of Recognitive Polymer Networks Prepared by Biomimetic Configurational Imprinting as Responsive Biomaterials. Nicholas A Peppas[1,2] and David B Henthorn[1]; [1]Chemical Engineering, University of Texas, Austin, Texas; [2]Biomedical Engineering, University of Texas, Austin, Texas.

Proteins, enzymes, and antibodies have the ability to discern specific molecules out of a whole host of species and selectively bind them with remarkable affinity. Imprinting methods enable the creation of synthetic polymers with a binding ability that would be a great advance for applications in chemical sensors, single-molecule separations, and even artificial enzymes and antibodies. In our laboratories, we are studying the creation of recognitive materials whereby a controlled nanostructure consisting of distinct binding sites is created in a polymer network through a biomimetic configurational imprinting procedure. We have synthesized materials capable of selectively binding important biological compounds such as sugars, fats, peptides, and proteins using non-covalent methods. Glucose sensitive polymeric networks prepared under both aqueous and

non-aqueous conditions have shown strong selectivity and binding capacity. These materials have also been patterned on devices using lithographic techniques to produce a glucose sensing MEMS device. One difficulty in creating materials able to recognize and bind large molecules such as proteins and peptides is the limited diffusion through a polymer network. We have engineered micro- and nanoparticles with large surface to volume ratios. Studies of model proteins including bovine serum albumin (68 kDa) and chicken egg lysozyme (14kDa) have lead to particles that are fast acting and selective with possible applications as synthetic antibodies and in immunoassays. The major challenge in recognitive material design is the careful selection of reaction conditions that will lead to successful imprinting. Factors include strength of intermolecular interactions, presence of a disrupting solvent, molecular tumbling, and reaction speed. In order to elucidate what leads to favorable imprinting, we have developed theoretical models capable of simulating network formation. Using a combined quantum mechanics / molecular mechanics approach, we are able to predict the final network structure of a recognitive material. Results from these simulations have been verified using NMR and FTIR spectroscopies.

2:15 PM G2.2
Validation of the Computational Design of Imprinted Polymers. Kal Karim, IBST, Cranfield University, Silsoe, United Kingdom.

Over the last four years Cranfield University has developed a generic protocol for MIP design using a computer-aided rational design technique. The concept is to simulate a complex formation between selected monomers and template in a monomer mixture using a Silicon Graphics workstation running UNIX, with SYBYL 6.9© as the industry standard molecular modelling software. Traditionally, the choice of polymer composition is based on information available from the literature, about the behaviour of similar systems, individual experience of chemists or extensive experimental trials. Attempts have been made to develop rational generic protocols using thermodynamic calculations and combinatorial screening approaches. In practice, the application of these methods will always be limited to very specific cases and examples. Although many developed polymers perform effectively in separation and sensing, there has been no real rationality in the design and synthesis of MIPs apart from the technique now pioneered at Cranfield. The method is based on screening of a virtual library of functional monomers against target compounds in conditions mimicking the polymerisation mixture. The result of this screening permits selection of monomers, which are able to form a strong complex with the template. This approach can be used also to predict the exact stiochiometric ratio of monomers to template in a self-assembled complex existing in a given solvent and at a particular temperature. We have shown that the flexibility of modifying the modelling parameters (temperature chosen for the "annealing" procedure, dielectric constants, type of interactions) can be modified in order to simulate the real polymerisation or re-binding conditions. With our method, we have designed MIPs for a wide range of templates such as triazine herbicides, pesticides, algal and fungal toxins, explosives, peptides and a variety of drugs and have corroborated the computational results with results obtained experimentally with very good agreement. We have found clear correlations between the result of modelling and polymer properties (affinity and selectivity) for most of the polymer systems studied. There are still some problems associated with the design of MIPs. Thus the modelling of the self-assembling process ideally should be followed by modelling of the polymerisation process. This would help to understand, predict and optimise the polymer structure and, perhaps, the distribution of the functional monomers in the bulk polymer and its surface. Another challenge is to understand the role of real experimental conditions such as polymerisation temperature, solvent and dielectric constant of the monomer mixture on the polymer performance and to use them in molecular modelling. This work is a report on four years of intense study aimed at computational design of imprinted polymers performed at Cranfield and furnishes analysis of successes and problems associated with this technology.

2:45 PM G2.3
Progress in Developing Nerve Agent Sensors Using Combinatorial Techniques. John C. DiCesare, Jennifer L. Parker, Starr N. Horne, Justin M. Kita, Raghu Earni and Christopher J. Peeples; Chemistry and Biochemistry, The University of Tulsa, Tulsa, Oklahoma.

Development of a sensor capable of selective detection of specific nerve agents is imperative in today 's atmosphere of terrorism. The sensor needs to be inexpensive, portable, reliable, absent of false positives, and available to all military and first responders. By utilizing the techniques of molecular imprinting, combinatorial chemistry, silica sol-gel synthesis and lanthanide luminescence, a sensor for the detection of the hydrolysis product of the nerve agent Soman is being developed. There are many parameters that require investigation in order for the sensor to become a reality. These parameters include 1) the selection of a chelate, which can bind to the lanthanide and anchor the nerve agent simulant, during the formation of the molecularly imprinted polymer, 2) the determination of the environment best suited for this complex formation, 3) the selection of the ratio best suited for lanthanide, chelate and simulant complexation, 4) the formation, as well as modification of the silica sol-gel for molecular imprinting to take place, and 5) the proper quantity and ratio of monomers used to create the three dimensional imprint. Key to the success of optimizing these parameters is the development of a combinatorial assay that allows for the synthesis and testing of tens of thousands of combinations of parameters. The development of the combinatorial assay as well as progress on the optimization of the molecular imprints for the selective binding of nerve agent simulants will be presented.

3:30 PM G2.4
Tailoring of High-Performance MIPs for Separation and Sensing. Sergey Piletsky, IBST, Cranfield University, Silsoe, Bedfordshire, United Kingdom.

It is generally believed that the success of molecular imprinting depends on the formation of monomers-template complex and preserving its structure during the polymerization step. We have provided and additional confirmation for this by proving that this is an initial phase of polymerization reaction which determines the fundamental recognition properties of synthesized materials. The parameters which affect complex formation during polymerization phase are: (i) type and concentration of monomers; (ii) polymerization temperature; (iii) pressure; (iv) cross-linker; (v) solvent. We have developed a new computational approach which permits to model monomers-template interactions in monomer mixture. The computational approach permits: a) to select the best monomers ideally suited for a polymer formation, possessing high affinity for the template; b) to mimic the specific polymerization or binding conditions by changing the dielectric constant and atomic charges of the monomer/template models; c) to predict the relative polymer specificity and affinity. The modeling approach allows also analyzing role of other parameters such as polymerization temperature and pressure, influence of cross-linker and solvent on the complexation process and on the properties of synthesized polymer. Computational approach is very fast and reliable. The total modeling time required to identify "ideal" monomer composition is one week. The correlation between modeling and testing results is approaching 70-80%, which is very good for a predictive modeling of synthetic receptors. The polymerization temperature and pressure in monomer mixture are extremely important factors determining the properties of synthesized materials, in particular their affinity and selectivity. We have shown that the polymerization temperature strongly affects quantity and quality of monomers-template and polymer-template interactions. The direct correlation exists between polymerization temperature and pressure and the optimal experimental conditions for separation and sensing. We have shown also that the type and concentration of cross-linker and solvent can be specifically optimized to tailor polymer properties for a specific type of application and also adapt polymer performance for specific experimental conditions. The molecular modeling and rational design of imprinted polymers can improve substantially the polymer performance. Some of the best polymers synthesized recently in our laboratory by using this approach possess very high affinity (nM range), which makes them superior to polyclonal antibodies, selectivity, which is higher than this of monoclonal antibodies and natural receptors, and also very high binding capacity (50-120 mg/g). The rational analysis and predictive modeling permits to engineer new generation of synthetic receptors with superior characteristics and also tailor them for particular requirements of practical applications.

4:00 PM G2.5
Molecularly Imprinted Polymers Targeted for Penicillin G. Maria Kempe and Henrik Kempe; Department of Cell and Molecular Biology, Lund University, Biomedical Center, Lund, Sweden.

In animal husbandry, antibiotics are used in therapeutic and prophylactic treatment of mastitis and other infections and as food additives for growth promotion. Both legislative authorities and consumer groups have observed the need of restricting the use of antibiotics. The concerns relate to the development of antibiotic resistant bacterial strains and the risk of allergic reactions in hypersensitive individuals ingesting foodstuff contaminated with antibiotics. Antibiotic-free milk is required also from an industrial point of view, since starter cultures in the dairy industry are inhibited by the presence of antibiotics in the milk. To be able to control the observance of prohibitions and restrictions on the use of antibiotics, efficient methods for their detection in foodstuff are needed. Current methods include microbial inhibition tests, enzymatic assays, enzyme-linked immunoassays, and various chromatographic methods. Several of the tests used for routine screening of milk samples do not

discriminate between different β-lactam antibiotics. MIPs selective for antibiotics could potentially serve as selective recognition elements in sensors and other analytical devices. In this study, we have developed and synthesized synthetic recognition elements selective for penicillin G by molecular imprinting. The work is part of an EC-funded project aiming at developing portable instrumentation for the analysis of antibiotics in milk. Libraries of molecularly imprinted polymers (MIPs) and control polymers were synthesized using a range of functionalized monomers and cross-linkers. Chemometric methods were used to optimize the compositions of the polymers. Screening of the MIP and control polymer libraries was done by a batch-wise radioligand binding assay with ^{3}H-labelled penicillin G. MIP candidates were selected for competition studies with other β-lactams and other antibiotics. Molecular recognition studies in aqueous media were carried out chromatographically using the MIPs as stationary phases. Novel methods for the preparation of spherical beads were also developed.

4:30 PM G2.6
New Insight from Modeling Non-covalently Imprinted Polymers. David A Spivak and Hyunjung Kim; Chemistry, Lousiana State University, Baton Rouge, Louisiana.

New developments in the characterization of binding sites in molecularly imprinted polymers have allowed a more quantitative study of the distribution of sites found in these materials. By carefully choosing a series of templates, quantitive information can be obtained that allow a better model of an imprinted binding site. The objective of this study was to model a series of polymers imprinted with increasing amounts of template (S-cyclohexyl benzylamine), keeping the monomer (and initiator) concentration constant. Binding isotherms (Sb vs Cf) were fit to a Freundlich isotherm: (1) $S_b = A * Cf^v$ where A and v are the fitting parameters. The fitting parameters were then substituted into a corresponding affinity distribution equation and plotted in a ln N (Ki) versus ln K format. The affinity distributions for each of the eight different MIPs made with increasing percent of template revealed a number of interesting features. Even though only one interaction exists in solution between the functional monomer, methacrylic acid (MAA), and the template S-cyclohexyl benzylamine (which has one amine); analysis of the number of binding sites and average association constant support a model where two (or more) MAA groups in the binding site are required for optimum performance. This finding suggests that binding site structure is not determined by "locking-in" the solution phase pre-polymer complex; instead, it is determined during polymerization. Because of the difficulty in characterization the binding site structures during and after polymerization, the actual events determining the final binding site structure are still unknown. However, it is reasonable to hypothesize that phase separation phenomenon that take place during polymerization could allow for the aggregation of polar groups in binding site "pockets". This would give rise to binding sites with higher order complexes coupled with shape selectivity afforded by the binding cavity formed around the template. From this new model comes a more complete understanding of the underlying mechanisms of MIP binding site formation which could facilitate improvements in MIP process design in the future.

SESSION G3: Poster Session
Chair: Joseph Roberts
Wednesday Evening, December 3, 2003
8:00 PM
Exhibition Hall D (Hynes)

G3.1
Biomimetic recognition of viruses using molecularly imprinted polymer hydrogels. Linden DeVenecia Bolisay, John March, William E Bentley and Peter Kofinas; Chemical Engineering, University of Maryland, College Park, Maryland.

Molecular imprinting is an emerging technology which allows the synthesis of materials containing highly specific receptors sites having an affinity for a target compound. We are aiming to develop molecular imprinted polymer (MIP) sensors, for biomimetic recognition of viruses. Our experimental results indicate that hydrogels can be produced, which can recognize green fluorescent protein recombinant baculovirus. Although it is expected that imprinted cavities will be distorted due to the swelling of the hydrogel in water, our experiments show that even the swollen gels exhibit remarkable affinity toward recombinant baculovirus. The proposed methodologies for the synthesis and characterization of MIPs thus offer exciting avenues for the development of novel biosensing materials and techniques. The development of a virus imprinted MIP would apply to the identification, classification, and removal of viruses. This is currently a very difficult task, but the need is widespread in diverse sectors, including national security, human and animal health, crop protection, and biologics production. The development of general methods using MIP sensors capable of specific recognition of biological analytes would have an enormous value in medicine and bioanalytics.

G3.2
Study of Recognition of Brucine in Poison Nut with Technology of MIP. Chao Ding and Wensheng Guo; Institute of Chemical Science & Engineering, Liaoning university, Shenyang, Liaoning, China.

Molecular imprinting polymer has been a kind of attractive material as new selective sorbent for solid-phase extraction of organic compound. Molecular imprinting technique using selectively absorption, enrichment and separation to activated component can obtain pure substance from Chinese herbal medicine. In the experiment, we utilized suspension polymerization for preparing a molecular imprinting polymer using brucine as the template molecule and acrylic acid as the functional monomer. Some white and solid microspheres were obtained. After extracting the template molecule these microspheres were loaded in a separation column. Brucine was selectively separated from coarse extraction of poison nut by separation column, at the same time we got another main alkaloid: strychnine. It will be a new tool for people to study Chinese herbal medicine if applying molecular imprinting technology to separation and purification of herb.

G3.3
Optical Molecularly Imprinted Polymer Sensor Design. Yin-Chu Chen[1], Jennifer J Brazier[2], Mingdi Yan[2], Paulo B Bargo[1] and Scott A Prahl[1]; [1]BME, OHSU, Portland, Oregon; [2]Department of Chemistry, PSU, Portland, Oregon.

A theoretical model was built and validated experimentally for the fluorescence collection efficiency of a molecularly imprinted polymer (MIP) sensor on a transparent substrate. The sensing element was polyurethane imprinted with anthracene. The quantum yield of anthracene within the polymer matrix, the fluorescence property of polymer, and the absorption characteristics of anthracene and polymer were measured. The fluorescence emission at 404 nm was measured from MIP with thicknesses ranging from 100 to 2000 μm containing imprinted anthracene concentrations ranging from 60 to 600 ppm for excitation at 358 nm. These measurements showed 14% standard deviation in the model. This particular polyurethane system could only distinguish anthracene down to 15 ppm due to the self-fluorescence of polyurethane. Our model suggests that (1) thicker MIP films have higher sensitivity, (2) thin-film MIP sensor performance is relatively insensitive to background absorption, and (3) background fluorescence of polymer is the dominant factor in MIP sensor performance.

G3.4
Molecular Imprinting of 3-Hydroxybenzoic Acid: Specific and General Binding Sites. Yue Hu and Robert A. Orwoll; Departments of Applied Science and Chemistry, College of William and Mary, Williamsburg, Virginia.

A resin, imprinted with 3-hydroxybenzoic acid (3HBA), was synthesized from acrylamide (AA, functional monomer) and ethylene glycol dimethacrylate (EGDMA, crosslinking agent). Batch analyses showed that the imprinted polymer has a specific affinity for the meta-substituted 3HBA, but not for its para-substituted isomer (4HBA) nor for benzoic acid (BA). These results are consistent with the principle that an imprinted resin's ability to recognize is dependent on the target's size, shape, and functionality. Another resin, prepared from AA and EGDMA but in the absence of a template, had similar affinities for 3HBA, 4HBA and BA, and thus it could not differentiate among the three. The results can be interpreted with a simple two-binding-site model with one site specific for 3HBA and the other being more general with similar affinities for 3HBA, 4HBA and BA. The binding of 3HBA to the imprinted resin is characterized by an association constant and the density of sites for each kind of site using a two-site Scatchard equation.

G3.5
Molecularly Imprinted Polymers Containing Polyvalent N-Acetylglucosamine Exhibit Enhanced Binding to Lysozyme. Jayant Jagannath Khandare and Mohan G. Kulkarni; Polymer Science & Engg.Unit, National Chemical Lab., Pune, MS, India.

Molecularly imprinted polymers (MIPs) have implications in biology and medicine as they can mimic the template in which they are prepared. Such polymers exhibit greater affinity and selectivity to the template molecule during rebinding. Polyvalent interactions involve simultaneous binding between multiple ligands and their substrates. Their importance in biology and medicine is being increasingly investigated. The magnitude of the binding could be further enhanced if the ligand and the substrate were favorably predesigned towards

one another. Molecular imprinting provides a means of achieving this. We report molecularly imprinted copolymers comprising polyvalent N-Acetyl glucosamine (NAG) and N-isopropylacrylamide (NIPA) synthesized using lysozyme as a template. The molecularly imprinted polymers exhibited higher binding constants (ki) and lower inhibition concentration (I50) compared to polymers prepared in the absence of lysozyme. Competitive binding experiments demonstrate that the imprinted NAG ligands displace Biebrich Scarlet from the site F of the lysozyme. This shows that when the rebinding constants are high enough molecularly imprinted polymers can exhibit enhanced substrate binding even in the absence of crosslinking.

G3.6
Fluorescent Molecularly Imprinted Polymers (MIPs) Targeting Uracils. Panagiotis Manesiotis, Andrew J. Hall and Boerje Sellergren; INFU-University of Dortmund, Dortmund, NRW, Germany.

Molecular Imprinting offers a simple method for the creation of robust materials capable of selective and specific recognition of a variety of compound classes, e.g. pharmaceuticals, environmental pollutants, peptides (and proteins). During our efforts to prepare novel, polymerisable recognition elements for use in molecular imprinting, we have become increasingly interested in finding ways to incorporate secondary functions into our monomeric receptors. For example, the preparation of binding elements which also function as cross-linking monomers should allow the incorporation of other elements into the polymer matrix with other specific purposes, such as the hydrophilisation of the polymer matrix. In this presentation we would like to report on the properties of MIPs targeted against uracils using the novel functional monomer 6-piperidino-2,4-bis(acrylamido)pyrimidine (1), and the closely related functional monomer 2,6-bis(acrylamido)pyridine (2), as the recognition elements. We have established, via 1H NMR titrations, that solution binding of (1) to the template, 1-benzyl uracil (3), is slightly lower than that of (2). However, MIPs prepared using (1) outperform those based on (2) in the chromatographic mode, with respect to retention and selectivity. We now wish to report on a further interesting property of MIPs based on (1) and (2), namely their fluorescence activity. On addition of template solutions, fluorescence quenching occurs in both polymers. The extent of this quenching has been related back to the uptake of the template by the MIPs. Control experiments, with similar, non-template molecules shows reduced or negligible quenching of the fluorescence of the polymers. Further, addition of template solutions to the control, non-imprinted polymers leads to only small uptake of analyte and little quenching of the polymers' fluorescence. We will discuss these findings and tentatively propose the use of these polymers as selective, reporter elements in chemical sensors.

G3.7
Controlling absorption in poly(acrylic acid)/poly(allylamine hydrochloride) multilayers through templating with dye molecules. Solar Olugebefola, Michael F Rubner and Anne M Mayes; Materials Science and Engineering, MIT, Cambridge, Massachusetts.

Polyelectrolyte multilayer films created from poly(acrylic acid) (PAA) and poly(allylamine hydrochloride) (PAH) at various pH assembly conditions were characterized with and without the presence of absorbed Coomassie Brilliant Blue. Subjecting the films to elevated temperatures and basic solutions was observed to affect absorption and desorption behavior of the dye as measured by ultraviolet-visible light spectroscopy. In addition, selectivity of these films for brilliant blue versus other dyes was evaluated.

G3.8
Thin Films Imprinted by Nanometer-scale Objects. M. Joseph Roberts, Scott K. Johnson, David J. Irvin, Rich Hollins, Curt E. Johnson and Thomas Groshens; NAVAIR NAWCWD, China Lake, California.

There is an ongoing worldwide effort within the field of nanotechnology which seeks to shrink the feature sizes of present devices leading to lower mass and volume and in many cases improved figures of merit. There is great interest in new processes for production of nanoscale features, for example, 'nanoimprinting' wherein, a silicon wafer bearing a pattern produced by electron-beam lithography is used to imprint the pattern into a soft polymer film. Variations on this process include imprinting of objects such as yeast cells or crystals. Our recent work explores imprinting of nanosized objects into thin films. Scanning Probe Microscopy provides evidence for the quality of the imprinting process. The effect of imprinting on device performance will also be presented.

G3.9
Atrazine Decomposing Polymers Prepared by Molecular Imprinting Method. Toshifumi Takeuchi[1,2], Takehisa Yane[1], Takashi Mukawa[1] and Masayoshi Takase[1,2]; [1]Department of Molecular Science, Graduate School of Science and Technology, Kobe University, Kobe, Japan; [2]PRESTO, Japan Science and Technology Corporation (JST), Kawaguchi, Japan.

Recently much attention has been devoted to the synthetic materials that recognize and bind to target molecules in a specific manner. Molecularly imprinting is one of the useful methodology to synthesize these materials because it does not need complicated synthetic steps and also sophisticated binding sites are naturally formed in the polymers through supramolecular assemblies. Not only to recognize and bind to the target molecule but to add further functions to the molecularly imprinted polymers, we have tried to introduce functional group conversion ability to the binding site. Here we report the strong binding of the polymers for atrazine, and specifically, demonstrate the decomposition of atrazine into non-toxic compound atraton using this polymer. Atrazine is a kind of well-known triazine herbicide and has toxicity, so atrazine decomposing materials are of critical importance in the environment. Methacrylic acid and 2-sulfoethyl methacrylate were used as functional monomers, since atrazine is known to be decomposed under acidic condition. Combind use of them produced the decomposition of atrazine and the imprinting effects enhanced their binding affinity and catalytic activity. Analogues of atrazine compounds, simazine, propazine, and terbutylazine, which are also known as a triazine herbicide, were decomposed using this polymer as well. In the presentation, we will discuss these results in detail.

SESSION G4: New Monomers and Recognition Strategies
Chair: David Spivak
Thursday Morning, December 4, 2003
Republic A (Sheraton)

8:30 AM *G4.1
Molecularly Imprinted Polymers with Post-imprinting Conversion of the Binding Sites. Toshifumi Takeuchi, [1]Graduate School of Science and Technology, Kobe University, Kobe, Japan; [2]PRESTO, JST, Kawaguchi, Japan.

We have developed a new method of disulfide-based molecular imprinting for basic compounds, in which thiol residues that are generated by removing the disulfide-based template from the polymer matrix by reduction are converted to sulfo groups by oxidation of the polymers in order to achieve higher recognition ability [1,2]. In this presentation, dopamine imprinting will be given as an example. The imprinting strategy, the characterization of the Post-imprinting treated imprinted polymers and the effectiveness of the post-imprinted process will be discussed. [1] Mukawa, T., Goto, T., Nariai, H., Aoki, Y., Imamura, A., Takeuchi, T. Novel Strategy for Molecular Imprinting of Phenolic Compounds Utilizing Disulfide Templates, J. Pharm. Biomed. Anal. 2002,30, 1943-1947. [2] Mukawa, T., Goto, T., Takeuchi, T. Post-Oxidative Conversion of Thiol Residue to Sulfonic Acid in the Binding Sites of Molecularly Imprinted Polymers: Disulfide Based Covalent Molecular Imprinting for Basic Compounds, Analyst 2002, 127, 1407-1409.

9:15 AM G4.2
The Synthesis and Use of New Binding Elements for Molecularly Imprinted Polymers (MIPs). Andrew J Hall, Marco Emgenbroich, Panagiotis Manesiotis, Filipe M.L. Vilela and Boerje Sellergren; INFU, University of Dortmund, Dortmund, Nordrhein Westfalia, Germany.

Molecular Imprinting (MI) is a technology whereby molecular memory may be imparted to a polymer matrix. This is achieved by the polymerisation of a template and suitable binding monomers with an excess of cross-linking agent, leading to a three-dimensional network polymer possessing cavities which are complementary to the template in terms of size, shape and functionality. While a variety of methods exist for achieving this goal, by far the most commonly employed is the non-covalent approach, where it is envisaged that the template and functional monomer(s) form non-covalent complexes in solution prior to polymerisation, which are then locked in during the polymerisation process. To date, the use of specifically designed functional monomers for use in non-covalent MI has received scant attention. Indeed, the impressive performance of MIPs prepared against a wide variety of template molecules has, perhaps, mitigated against the need for specifically tailored recognition elements. However, a range of drawbacks with MIPs must still be overcome, e.g. increasing binding site fidelity, reduction of non-specific binding and the use of MIPs in competitive (aqueous) environments. Thus, we feel that there are many benefits to be gained from the use of designed functional monomers. By designing polymerisable binding elements capable of strong solution binding, it should be possible to address the issue of binding site fidelity and, to some extent, that of

non-specific binding. Further, as the strength of template-monomer binding increases, so does the ability to perform non-covalent imprinting in more polar environments. Another benefit is that functional monomers with secondary properties may be designed. In this presentation we will present some examples of our work on the design and use of novel binding monomers in the creation of MIPs against a selection of templates. The increased template affinity which may be obtained using such monomers will be highlighted, as will the building in of secondary functions, such as cross-linking ability and optical properties (UV and/or fluorescence activity). This latter development may aid in the future use of MIPs in sensory applications, with the functional monomer units acting as both binding agent and reporter group.

10:15 AM G4.3
Molecularly Imprinted Polymers for the Recognition of Riboflavin in Aqueous Media. Panagiotis Manesiotis, Andrew J. Hall and Boerje Sellergren; INFU-University of Dortmund, Dortmund, NRW, Germany.

Riboflavin (vitamin B2) is a water-soluble vitamin which is essential in the human diet. It is a major component of FAD and FMN, the co-enzymes responsible for redox reactions in biological systems. Riboflavin is relatively stable to heat and acidic pH but it decomposes to lumiflavin at alkaline pH and in the presence of UV-light. The breakdown products of riboflavin are considered to be responsible for the initiation of a chain of free radical reactions leading to the "sun-struck" flavour of milk, beer and white wine. Thus, such products are preferably stored in containers which are non-transparent to light, e.g. paper/plastic cartons in the case of milk. Therefore, the synthesis of materials that can selectively remove riboflavin from such complex matrices, without affecting the composition of the matrix in any other way, is of great interest. However, riboflavin, being a water-soluble vitamin, is not soluble in any of the solvents that are commonly used in imprinting. In order to overcome this obstacle, we have synthesised different alkyl flavins and riboflavin tetraesters, keeping the basic flavin structure unchanged and "tuning" the size and shape of the pendant chain. MIPs were then prepared using each of these templates. The recognition characteristics of the synthesised MIPs have been tested using HPLC. All the polymers exhibit enhanced recognition of their respective templates over the control NIP in organic media, with size exclusion effects also observed. Further, the size and nature of the template is shown to have a strong bearing on the retention of riboflavin itself in aqueous media.

10:45 AM G4.4
Shape-Selective Covalent Binding in Bulk Imprinted Silica. Jessica Defreese and Alexander Katz; Chemical Engineering, University of California at Berkeley, Berkeley, California.

Templated binding pockets have been synthesized via imprinting within a microporous silica framework. The synthetic approach uses a sol-gel process to co-condense a carbamate-based imprint with tetraethyl orthosilicate to produce a hybrid organic-inorganic material. Cleavage of the carbamate linkage generates a primary amine within a templated pocket that is complementary to the size and shape of the imprint. Three imprints differing only in the side-chain functionality (methyl, ethyl, and propyl homologues) have been used to synthesize the templated silicates. The materials exhibit shape-selective binding of α-methylbenzyl isocyanate versus 1-(1-naphthyl)ethyl isocyanate in batch experiments. We unequivocally show that the selectivity of the isocyanate binding arises due to the size of the templated pocket. These results demonstrate the first shape-selective covalent binding in bulk imprinted silica, and repercussions to other systems will be discussed.

11:15 AM G4.5
Discriminate Surface Molecular Recognition Sites on a Microporous Substrate: A New Approach. Ananthakrishnan Sethuraman[1], Brian Meierdiercks[1], Mina Han[1], Ravindra Kane[1], Masahiro Goto[2] and Georges Belfort[1]; [1]Department of Chemical Engineering, Rensselaer Polytechnic Institute, Troy, New York; [2]Department of Chemical Systems and Engineering, Kyushu University, Hakozaki, Fukuoka, Japan.

A novel two-dimensional surface molecular imprinting method using water-in-oil emulsion photopolymerization on a microporous polypropylene substrate was developed and used to separate the bronchodilator, theophylline, from the mild stimulant, caffeine, both of similar chemical structure. Surface molecular recognition sites were generated that could discriminate between these two molecules with a concentration-dependent separation factor of 4.9 $\pm$ 0.8 for theophylline over caffeine at 0.2 mM (1:1 v/v) solution mixture. New results that discriminate between the ions Cesium (Cs+) and Na+/K+ and also between different small biomolecules are presented. Besides demonstrating its proof of concept, the attractive features of this new imprinting method are the following: less imprint molecules are needed, it can be used to imprint from aqueous environments, post-crushing of the solid matrix is not needed, recognition sites are all near or at the surface reducing mass transfer limitations, and imprinting on synthetic microporous membranes (with convection and diffusion) instead of beads (with only diffusion) speeds up the process.

SESSION G5: Sensors
Chair: Michel Gagne
Thursday Afternoon, December 4, 2003
Republic A (Sheraton)

1:30 PM *G5.1
Optical Transduction Schemes for Molecularly Imprinted Polymer Sensors. George M. Murray and Glen E. Southard; Johns Hopkins University Applied Physics Laboratory, Laurel, Maryland.

Molecular imprinting is a useful technique for making a chemically selective binding site. The method involves building a synthetic polymeric scaffold of molecular compliments containing the target molecule with subsequent removal of the target to leave a cavity with a structural "memory" of the target. Molecularly imprinted polymers can be employed as selective adsorbents of specific molecules or molecular functional groups. By incorporating molecules or metal ions with useful optical properties in the binding sites of imprinted polymers, spectroscopic sensors for the imprinted molecule may be made. Sensors for specific molecules can be made using optical transduction through chromophores residing in the imprinted site. The combination of molecular imprinting and spectroscopic selectivity has resulted in sensors that are highly sensitive and nearly immune to interferences.

2:15 PM G5.2
Sensors and sensor arrays based on molecularly imprinted polymers. Ken Shimizu, Department of Chemistry and Biochemistry, University of South Carolina, Columbia, South Carolina.

Molecularly imprinted polymers (MIPs) are well suited to be use as recognition elements in molecular sensors. MIPs can be readily and inexpensively prepared, demonstrate a high degree of thermal, chemical and mechanical stability and finally can be tailored with selectivity for wide range of analytes. Presented will be some recent examples in our laboratories of the utility of MIPs as chemical sensors. The success of these systems is due in large part to a fundamental understanding of the non-linear adsorption behavior that leads to the highly concentration dependent binding properties of MIPs. This non-linear behavior both limits and also opens up new sensing applications for MIPs. In particular, to circumvent the generally poor selectivity of MIPs, sensor arrays were prepared and the differential signal between the various imprinted polymers yielded higher levels of accuracy in discriminating between structurally similar analytes.

3:15 PM G5.3
The Use of Spin Coating and Novel Porogens for the Preparation of Molecularly Imprinted Polymer Films. Ronald Schmidt[1], Klaus Mosbach[1] and Karsten Haupt[2,1]; [1]Pure and Applied Biochemistry, Lund University, Lund, Sweden; [2]University of Technology of Compiegne, Compiegne, France.

Molecularly imprinted polymers (MIPs) are synthetic materials that mimic the behavior of natural antibodies while exhibiting far greater stability than their natural counterparts. Since MIPs can withstand harsh chemical environments, one of their most important applications is in imparting high specificity to chemical sensors. However, the ability of a transducer to effectively interrogate a MIP-based recognition element often requires a MIP that has been prepared in a thin film format. We will present a novel technique for preparing MIP films that uses spin coating to spread the monomers into a thin and uniform film that is subsequently polymerized using UV irradiation. MIP films were imprinted with the chiral drug S-propranolol and evaluated in competitive binding studies using autoradiography. The preparation of films with high binding capacities required us to use novel, non-volatile porogens that do not evaporate during the spin coating process. Atomic Force Microscopy (AFM) was used to characterize the morphology of the surfaces (e.g., RMS roughness and pore structure), which was correlated with the capacities of the films. Advantages of this technique over other approaches (e.g., surface initiated polymerization) are that it is quicker, more robust and reproducible, and that it enables one to prepare films over a wide range of thickness by varying the appropriate parameters (e.g., spin rate, porogen composition, and the porogen/monomer ratio).

3:45 PM *G5.4
Imprinting with Chemical Sensors - Challenges in Molecular Recognition and Universal Application. Franz Ludwig Dickert,

Oliver Hayden and Peter Lieberzeit; Analytical Chemistry, Vienna University, Vienna, Austria.

Selective coatings for chemical sensors were developed according to the strategies of molecular imprinting and were preferably combined with mass sensitive and optical transducers. Possibilities were explored in selectivity and sensitivity whether minor changes in molecules can be chemically recognized. Thus, highly crosslinked polystyrenes were optimized for the enrichment of aromatic hydrocarbons and e.g. benzene, toluene and xylenes could be distinguished. Cavities generated by toluene imprinting preferably include the template, but xylene is nearly excluded. Thus, the influence of methyl-groups is detectable by mass-sensitive devices. Similar effects are to be found in analyzing polycyclic aromatic hydrocarbons in water, again QCM and SAW devices but also fluorescence detection is applicable. Double imprinting is a straightforward procedure for moulding suitable interaction sites and diffusion channels in polymers. Thus, problems can be overcome by the fact that the building blocks of the polymers and the templates show nearly the same sizes. Varying the ratio of two template molecules the slope of the sensor characteristics can be tuned from a pure linear relationship to a Langmuir isotherm with a plateau indicating the occupation of all cavities in the coatings. Surface imprinting techniques were used for patterning the surfaces of polymers to generate pits for the reinclusion of biopolymers. This task was realized by stamping procedures for yeast, Hela or bacteria cells whereas for smaller biogenous analytes, such as viruses and enzymes a polymerization in ultrathin layers using an aqueous phase is preferred. In this way e.g. native enzymes can be distinguished from denatured ones and it can be tested whether cells are alive. Unusual frequency enhancements by adhesion of bioanalytes on the sensor coatings indicate surface movements and that they do not behave as rigid solids.

4:30 PM G5.5
Molecular Imprinting in the Gas Phase. Dmitry Pestov, Natalia Levit and Gary Tepper; Chemical Engineering, Virginia Commonwealth University, Richmond, Virginia.

A new gas-phase molecular imprinting technique is introduced. Normally, Molecularly Imprinted Polymers (MIPs) are produced using liquid-phase polymerization reactions in the presence of a template to form synthetic, template-specific recognition sites. We have developed a new method of creating recognition sites by introducing the template from the vapor phase and performing the polymerization reaction in the solid state. In the present study we used highly crystalline diolefinic monomers with solid-state reactivity, such as 2,5-distyrylpyrazine (DSP), diethyl p-phenylenediacrylate (EPA), and dimethyl p-phenylenediacrylate (MPA). Diolefinic compounds are known to polymerize in the solid-state under UV irradiation to yield linear polymers with cyclobutane rings in the main chain. For molecular imprinting, nanoparticles of the diolefinic monomers were precipitated from a rapidly expanding supercritical solution and deposited onto the surface of a microfabricated Surface Acoustic Wave (SAW) resonator. The solid monomer particles were polymerized at room temperature directly on the surface of the SAW device in the presence of a template vapor by UV irradiation and the template was extracted from the polymer particles by purging with dry nitrogen. The resulting chemical sensor was tested upon exposure to a range of analyte vapors and exhibited preferential affinity to analytes at or below the size of the template molecule. Because the nanoscale particles are imprinted in the gas phase directly on a surface, this new imprinting technology offers certain advantages such as the ability to directly interface MIPs with a wide range of microscale devices. Thus, the imprinted nanoparticles can be used, for example, as a component in chemical sensors as well as in solid phase extraction.

SESSION G6: Drug Discovery and Therapy
Chair: Mingdi Yan
Friday Morning, December 5, 2003
Republic A (Sheraton)

8:30 AM *G6.1
Two Approaches towards Shaping New Drugs: By Assembly within Plastic Imprints or Using Biomolecules. Klaus Mosbach, Yihua Yu and Lei Ye; Pure and Applied Biochemistry, Lund University, Lund, Sweden.

Since the last presentation at the MRS meeting in San Francisco, 2001 [1], our focus at the center has been towards drug discovery using molecular imprinting technology. Apart from more obvious applications like screening of combinatorial libraries using "plastic" receptors [2], or more recently in the purification by removal of succinyl tyrosine from fermentation broth containing the widely used penicillinase inhibitor clavulanic acid [3], our efforts to obtain drugs (mainly enzyme inhibitors) have continued. Following one line of approach that we call anti-idiotypic imprinting ("imprinting the imprints"), a mould of a molecular object such as a drug acting as inhibitor to the protease kallikrein, is first allowed to be formed [4]. In the nanocavity obtained, not only a replica of the original compound can be formed by assembly of the necessary building stones, but also new structures with potentially superior properties. Following the other approach, we directly used the enzyme itself as biological mould and assembled in its cavity, the active center of the enzyme, building stones leading to a chiral inhibitor [5] (see also write-ups ref. [6] and [7]). More results from our studies on the subject will be discussed, and relevant new patent information will be given. References [1] L. Ye, K. Mosbach. In: K.J. Shea, M.J. Roberts, M. Yan, eds. Molecularly Imprinted Materials, MRS Proceedings Volume 723, Materials Research Society (2002). [2] L. Ye, Y. Yu, Klaus Mosbach. Analyst 126, 760-765 (2001). [3] Y. Yu, L. Ye, V. de Biasi, K. Mosbach. Biotech. Bioeng. 79, 23-28 (2002). [4] K. Mosbach, Y. Yu, J. Andersch, L, Ye. J. Am. Chem. Soc. 123, 12420-12421 (2001). [5] Y. Yu, L. Ye, K. Haupt, K. Mosbach. Angew. Chem. Int. Ed. 41, 4459-4463 (2002). [6] S. Borman. C&EN, Jan. 13 (2003). [7] P. Ball. Nature Materials Update, Nov. 28 (2002).

9:15 AM G6.2
Isomeric Glucose Recognition Using Molecularly Imprinted Polymer Hydrogels. Peter Kofinas, Paraskevi Parmpi and Linden De Venecia Bolisay; Chemical Engineering, University of Maryland, College Park, Maryland.

Non-covalent, aqueous, molecular imprinting of poly(allylaminehydrochloride), with D-glucose 6-phosphate monobarium salt (GPS-Ba) produced molecularly imprinted polymer hydrogels (MIP) having an affinity to glucose over fructose. The hydrogels were formed by ionic association of the template molecule, GPS-Ba, to the polymer, prior to covalent crosslinking using epichlorohydrin (EPI). The template was removed by an aqueous base wash. Batch equilibration studies using MIP hydrogels and non-molecularly imprinted polymers (NIPs) wereperformed in aqueous and buffered media to determine the binding capacities and isomeric selectivities with respect to glucose and fructose. MIP glucose hydrogels exhibited binding capacities in excess of 0.6 grams of glucose per gram of dry gel in a DI water glucose solution, and in a 50-50 glucose-fructose solution mixture. Equilibrium binding capacities of fructose were lower than those observed with respect to glucose, indicating an isomeric preference for the binding of glucose over fructose.The MIP hydrogels demonstrated specificity and selectivity for glucose while in their swollen state in environments mimicking physiological conditions.

10:15 AM G6.3
Molecularly Imprinted Bile Acid Sequestrants: Synthesis and Biological Studies. Pradeep K Dhal, Chad C. Huval, S. Randall Holmes-Farley, W. Harry Mandeville and Steven C. Polomoscanik; Drug Discovery and Development, Genzyme Corporation, Waltham, Massachusetts.

Novel bile acid sequestrants based on a polyammonium backbone were obtained by using molecular imprinting. These imprinted polymer networks were prepared by crosslinking different polyamines with various crosslinking agents in the presence of sodium cholate as the template. The template molecules were completely removed from the polymer matrices by repeated washings. The bile acid sequestration properties of these polymeric resins were evaluated under both *invitro* and *invivo* conditions. Adsorption isotherms performed in physiologically relevant media revealed that molecular imprinting leads to improvement in bile acid sequestration with about a two-fold increase in the K_a (association constant). More importantly hamsters fed with imprinted polymers in their diet excreted more bile acids than the non-imprinted control polymer. From these results it appears that molecular imprinting is a interesting approach to prepare novel polymer therapeutics.

10:45 AM G6.4
Engineering membranes for molecular recognition.
Gianluca Ciardelli[1], Caterina Cristallini[2], Niccoletta Barbani[1], Beatrice Cioni[1], Davide Silvestri[1] and Paolo Giusti[1,2]; [1]Chemical Engineering, University of Pisa, Pisa, Italy; [2]IMCB-Pisa, CNR, Pisa, Italy.

Modern therapeutic approaches in the biomedical field are increasingly requiring advanced polymeric devices for intelligent drug release and recognition of molecules of clinical interest (such as drugs, toxins, molecules involved in pathologic or inflammatory processes). The technology of molecular imprinting permits recognition sites to be inserted into a polymeric material through the polymerization of a monomer in the presence of a template, or through the dissolution of a preformed polymer in a solution containing the template and crosslinking or phase inversion so as to obtain the matrix-template complex. This paper will focus on the application of both techniques

in the realisation of polymeric membranes with molecular recognition properties. Imprint matrices are obtained by the phase inversion precipitation technique. The coagulation of the cast solution of a suitable polymeric material is carried out in the presence of a template specie, and recognition sites are formed due to the interactions between functional groups in the membrane forming polymer and the template. In this way porous membranes containing specific sites for molecules of clinical interest or proteins were prepared. Molecular imprinted membranes of acrylonitrile acrylic acid copolymer imprinted with uric acid showed satisfactory recognition capacity and selectivity towards the template (rebinding of uric acid resulted 2.4 times higher than that of theophylline, a molecule of similar structure). Porous supports of ethylene-co-vinyl alcohol-dextran blends were obtained using α-amylase as template. After extraction, properties of imprinted membranes were confirmed by comparison of rebinding and selectivity results (rebinding of imprinting enzymes 1.96 times higher than that of albumin). This approach showed not to be successful for all materials used to realise the membranes. Membranes prepared from methylmethacrylate-co-acrylic acid (a material considered more suitable for in vivo applications) imprinted with theophylline showed poor recognition properties. To overcome this problem imprinted cross-linked methylmethacrylate-methacrylic acid nanospheres were synthesized in the presence of theophylline. Methylmethacrylate-co-acrylic acid membranes containing the nanoparticles on the surface and/or inside the membrane body showed interesting release (up to 5 mg template/g of membrane) and recognition properties (0.24 mg template/ g of membrane). Nanospheres immobilised in the membrane showed a 2.5 times higher capacity to rebind the template than free, suspended nanospheres (2.5 mg template/ g of nanospheres). The different systems realised are promising solutions for ex-vivo (dyalisis, blood filtration) or in-vivo applications in the biomedical field.

11:15 AM G6.5
Abstract Withdrawn

SESSION G7: New Molecular Imprinting Formats
Chair: Ken Shimizu
Friday Afternoon, December 5, 2003
Republic A (Sheraton)

1:30 PM *G7.1
Recent Advances in Molecular Imprinting. Kenneth Shea, Department of Chemistry, University of California-Irvine, Irvine, California.

Molecular imprinting is a general protocol for creating receptor and/or catalytic sites in cross-linked network polymers. Imprinted polymers (MIPs) are mechanically and chemically robust functional thermosets that can be used as chromatographic packings and sorbents for the separation and isolation of targeted organic compounds. The talk will focus on recent developments in molecular imprinting and will include the fabrication of imprinted thin films that mediate the selective transport of complex organic molecules and biological markers and the micro fabrication of imprinted polymers.

2:15 PM G7.2
Ultrathin Molecularly Imprinted Polymer Films. Mingdi Yan, Reeta Joshi and Anu Raman; Chemistry, Portland State University, Portland, Oregon.

Molecularly imprinted polymer thin films are important in separation and sensor applications. Currently MIP preparation methods often yield films that are non-uniform, irregular and fragile. We are developing new imprinting chemistry and procedures that gave rise to ultrathin MIP films (<1 mm). The films were prepared by spin coating and were therefore uniform and the thickness could be well controlled. The imprinting chemistry is versatile and the functional element can be tailored for various templates. This talk will focus on the imprinting chemistry, synthetic strategies and binding characteristics. Procedures leading to the fabrication of patterned MIP thin films and arrays will also be discussed.

2:45 PM G7.3
Molecularly Imprinted Micro- and Nano-Particles by Precipitation Polymerization. Lei Ye and Klaus Mosbach; Pure and Applied Biochemistry, Lund University, Lund, Sweden.

Molecular imprinting is one of the most efficient methods for preparing synthetic materials that possess user defined recognition properties. Instead of building molecular receptors using complicated organic synthesis, molecular imprinting delivers robust binding materials straight forward from simple building blocks, and most often in a predictable manner. The ever increasing interest in molecular imprinting research in the past decade has brought new technical developments and applications. We have developed a precipitation polymerization method for preparing molecularly imprinted polymer micro- and nano-particles. The imprinted materials displayed favorable binding characteristics towards targeted analyte molecules. By introducing a novel photon-harvesting reporter close by the imprinted binding sites, we could directly translate analyte binding into an optical signal. In this contribution we will discuss engineering of imprinted micro- and nano-particles into a core-shell structure, as well as improved function of the new materials.

3:30 PM G7.4
One-Stage Synthesis of Molecularly Imprinted Polymer Nanospheres. Guenter E. M. Tovar[1,2], C. Gruber[1], M. Dettling[1], S. Sezgin[1], M. Lehmann[1], M. Herold[1], A. Weber[2] and H. Brunner[1,2]; [1]Institute for Interfacial Engineering (IGVT), University of Stuttgart, Stuttgart, Germany; [2]Fraunhofer Institute for Interfacial Engineering and Biotechnology (IGB), University of Stuttgart, Stuttgart, Germany.

Molecular imprinting is a template polymerization which produces artificial binding sites in polymers. Their specific cavities can be used for molecular recognition reactions mimicking the antibody-antigen interaction, but now with a completely synthetic system. A major drawback for a broad exploitation of the imprinting technology as specific polymer material is the preparation method. Molecularly imprinted polymers (MIP's) are synthesized as polymer monoliths, ground, sieved and a portion of about 20% of useful particles is selected for further use. These particles are intrinsically irregularly shaped and have typical dimensions in the range 10 - 20 μm. MIP's prepared this way, however, proofed to be highly effective and selective as stationary phase in HPLC. MIP's with a more defined morphology and of smaller size would open new application fields by using them as selectors in a liquid or an ultrathin coating. In a new approach, we synthesized therefore MIP's as nanoscopic spheres. A variety of highly crosslinked copolymer networks, e.g. poly(methacrylic acid)-co-(ethylene glycol dimethacrylate) nanoparticles were prepared by miniemulsion polymerization in presence of various amino acid derivatives (e.g. L- and D-boc-phenylalaninanilid) as molecular templates with a yield of 98 $\pm$ 2.[1] Coagulate-free and stable latexes were obtained. The prepared polymer colloids are in the size range of 50 - 300 nm. The efficiency of the imprinting process was quantified by ligand binding experiments using UV/Vis and HPLC. The nanoscopic molecularly imprinted polymers (MIP's) allowed for the first time for an examination of the non-covalent interaction between the synthetic receptor and various ligands by microcalorimetry.[2] The preparation and the use of the colloidal MIP's, e.g. as the surface coating of an optical waveguide sensor, and as the specifier in a selective composite membrane are presented.[3] [1] D. Vaihinger, K. Landfester, I. Kräuter, H. Brunner, G. E. M. Tovar, *Macromol.Chem.Phys.* **2002**, 203, 1965. [2] A. Weber, M. Dettling, H. Brunner, G. E. M. Tovar, *Macromol.RapidCommun.* **2002**, 23, 824. [3] M. Lehmann, H. Brunner, G. E. M. Tovar, *Desalination* **2002**, 149, 315

4:00 PM G7.5
Phase Inversion Inprinted Approaches To Moleculer Imprinted Membranes Having Scaffolding Interaction Sites To Target Molecuole. Kobayashi Takaomi, S. Manisone, X.S. Ling, . Onodera and J. Miura; Chemistry, Nagaoka University of Tecnonology, Nagaoka, Japan.

Polymers having scaffolding functional sites for interacting with target molecule were important strategy to molecular imprinting membrane assembly. To fabricate recognition imprint sites in the membrane assembly, phase inversion processes of liquid polymer solution to coagulated solid polymer in water could form porous membrane support. The original technique was extended to several polymers having carboxylic acid, sulfone, amine-carbonyl groups and amphiphilic quaternized ammonium ion as scaffolding sites to fix target molecules into the assembly. Characteristics of membrane adsorbents and fluorescence emission behavior would discuss in addition to its morphological properties of imprinted membranes.

4:30 PM G7.6
Development of a Novel Methodology for Surface Molecular Imprinting. Raluca Voicu[1], Abdiaziz A Farah[1], Raluca Barjovanu[1], Pascal L'Ecuyer[2], Farid Bensebaa[2] and Karim Faid[1]; [1]IMS - NRC, Ottawa, Ontario, Canada; [2]ICPET - NRC, Ottawa, Ontario, Canada.

A novel concept of molecular imprinting using surface characterization techniques in conjunction with a nanotemplating methodology will be presented. A stamp bearing a surface-attached moiety is contacted with a variety of functional monomers. Following their polymerization and the selective removal of the stamps, recognition cavities are created on a substrate surface and are found to be selective towards the moiety of interest. A carboxylic derivative of theophylline is

attached on an amino-modified substrate, through carbodiimide chemistry for the formation of amide bonds. Monomers bearing carboxylic groups are polymerized on top of the theophylline-containing substrate. After the selective removal of the stamping material, a nanotemplated surface is obtained, bearing cavities capable of recognizing the theophylline molecules. Surface characterization techniques are used as tools for assessing the recognition and selectivity characteristics of these new nanotemplated substrates: XPS (X-ray Photoelectron Spectroscopy), SPM (Scanning Probe Microscopy), contact angle and fluorescence confocal microscopy. The use of such printing-like techniques will provide a versatile and highly desirable tool for the controlled modulation of surface properties, in a large scale, which is highly sought in separation, environment and food sciences or pharmaceutical and biotech industries.