SYMPOSIUM M
Molecularly Imprinted Materials
April 3 – 5, 2002

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A Joint Proceedings with Symposium M/O
to be published in both book form and online
(see ONLINE PUBLICATIONS at www.mrs.org)
as Volume 723
of the Materials Research Society
Symposium Proceedings Series

*Invited paper
SESSION 1: SYNTHESIS AND CHARACTERIZATION
Chair: Mingyi Yan
Wednesday Morning, April 3, 2002
Concordia (Argent)

8:00 AM OPENING REMARKS
Past, Present and Future of Molecular Imprinting
Kenneth J. Shea

8:45 AM *M1.1
MOLECULAR IMPRINTING - A WAY TO EFFECTIVE IMITATIONS OF NATURAL ANTAGONISTS AND ENZYMES. Günter Wolff, Heinrich-Heine University, Institute of Organic and Macromolecular Chemistry, Düsseldorf, GERMANY.

In order to mimic 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 polymerization 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. Such polymers can be used for selective chromatographic resolutions, as specific detection layers in chemosensors, as artificial antibodies in radioimmuno assays, or as catalysts working in a mode similar to enzymes.

In this lecture new developments in this technique will be discussed. New 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 instead of imprinting. This type of imprinted polymers is especially suitable for the preparation of catalytically active imprinted polymers. Using different transition state analogs of alkaline ester hydrolysis and suitable catalytically active functional monomers catalysts with stronger esterolytic activity for the hydrolysis of esters, carbonates, and carbamates can be obtained. In case of stoichiometric non-covalent interaction the polymerization of catalytically active polymers can also be performed by standard suspension and miniemulsion polymerization techniques. Thus regular beads of 1.0-4.0 mm and microparticles of 100-300 nm particle diameter with narrow particle diameter distribution can be obtained. A further step directs the inorganic matrix inorganic 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.


10:00 AM M1.2
DEVELOPMENT OF IMPROVED CROSSLINKING MONOMERS FOR MOLECULARLY IMPRINTED MATERIALS. David A. Speck, Martin Sibitz-Valquez, Louisiana State University, Department of Chemistry, Baton Rouge, LA.

Currently, cross-linking monomers used for molecularly imprinted polymers (MIPs) have primarily been EGDMA or DVB, which are commonly used for polymeric interactions. However, there are benefits of using these monomers that they are inexpensive and readily available in large quantities. This is important for applications that would require large amounts of material such as industrial catalytic reactors or separations on the industrial scale. However, many future applications of imprinted polymers are envisioned in the fields of microfabricated sensors and microreactions that will only require small amounts of material. Therefore, economic price considerations of the imprinting materials is less of a concern. Instead, materials with the best performance possible are the target for microfabricated and microfabricated devices.

Most of the research in molecularly imprinted materials has focused on choice of substrate or functional monomer of the post-polymer complex. However, approximately 80-90% of the imprinted polymers are comprised of the crosslinking monomer, with the remaining 10-20% comprised of functional monomer. The large percentage of crosslinking monomer materials in imprinted polymers affords the possibility of a dramatic improvement in polymer properties. Redirecting focus on the design of crosslinking monomers for molecular imprinting, we have developed new classes of crosslinked polymers that can optimize the performance of molecularly imprinted polymers. New difunctional methacrylamide/vinylketone and methacrylamide/methacrylate hybrid crosslinking monomers have been investigated and compared with EGDMA containing formulations. The strategy for the design of new crosslinking monomers has been the development of crosslinking monomers derived from amino acids, that simultaneously serve as the functional monomer. Results for the carbonylated functionalized crosslinking monomers derived from L-malic acid and L-serine will be reported.

10:30 AM M1.3
NOVEL MONOMERS FOR NON-COVALENT MOLECULAR IMPRINTING - VORSPRUNG DURCH KREATIVITAET. Andrew J. Hall, Panagiotis Miliakos and Börje Sellergren Institut fuer Anorganische Chemie und Analytische Chemie, Johannes Gutenberg-Universität, Mainz, GERMANY.

Molecular imprinting is a technique whereby specific recognition sites can be formed in polymer matrices via the inclusion of a template molecule during the polymerization process. With few exceptions [1], the ‘non-covalent’ technique remains rooted in the use of commodity monomers, e.g. methacrylic acid, to serve as the recognition elements. The individual interactions of such monomers with a chelate template are generally weak, thus leading to the use of a large excess of functional monomer to favour template-monomer complexation. Consequently, the polymers are characterized by a heterogeneous distribution of binding sites and exhibit significant non-specific binding of the template/matrix. In an effort to overcome such problems, we have embarked upon a programme of design and synthesis of novel polymerizable recognition elements, drawing inspiration from the field of small molecule host-guest chemistry. The use of monomers capable of strong interactions with a given template should lead to a number of benefits, e.g. a reduction in non-specific binding due to stoichiometric monomer-template complexes, and may have implications for the preparation of MIPs in more practicable formats. As targets for our novel host monomers, template molecules bearing a wide array of functionality have been chosen, all of which have relevance in the biological, medical or environmental fields (see examples below). We wish to report on the design, synthesis of these novel monomers, their binding capabilities (as determined by solution 1H NMR titrations), their incorporation into molecularly imprinted polymers and the recognition properties of the resulting polymers. Additionally, the ability of polymers such as the Freundlich and Langmuir-Freundlich, which significantly simplify the analysis so that affinity distributions can be readily generated from the corresponding experimental binding isotherms. These heterogeneous binding models also yield a quantitative measure of the heterogeneity, the total number of binding sites, and average binding affinity that allows ready comparison of different MIPs. Discussion will be the implications of the measured affinity distributions as to the mechanism of the imprinting process and for predicting their suitability in particular applications.

References:
has been used to create binding and catalytic sites for a wide variety of organic substrates. The resulting network polymers are mechanically robust materials that have been used as cationicorganic packings and selective sorbents for the separation and isolation of organic compounds. Recently, molecularly imprinted materials have been fabricated into thin films and free standing membranes for applications in membrane separation and chemical sensors. My talk will review the basic concepts of molecular imprinting and present recent developments in the area.

SESSION M2: MICROFABRICATION AND SILICA IMPRINTING
Chair: Borje Sillinger
Wednesday Afternoon, April 3, 2002
Concordia (Argent)

13:00 PM M2.2
SENSOR MATERIALS - DETECTING MOLECULES, MIXTURES AND MICROORGANISMS.
Franz L. Dickert, Wolfgang Greulich, Oliver Hayden, Peter Lieberzeit, Vienna Univ, Inst of Analytical Chemistry, Vienna, AUSTRIA.

The needle eye in chemical sensors is the coating capable of chemical recognition, analyte enrichment and selectivity are performed in this way. An optimized design with respect to the transducer used can be accomplished by molecular imprinting. Quartz wafers for SAMs fabrication can directly be coated with polystyrene/divinylbenzene copolymers imprinted with different organic solvents. These layers allow the differentiation e.g. between the xylene isomers at ambient humidity applying pattern recognition. These strategies can also be transferred to the liquid phase where even molecules without any functionality can selectively be detected. When two different print molecules are used, one as porogen and the other as template for cavity generation, two PAMs containing an equal number of aromatic rings can be distinguished by nearly two orders of magnitude in sensitivity. Printing with mixtures allows us to generate sensitive layers for the characterization both of degradation processes and quality assessment. Organic polymers and ceramics are able to extract oxidation and condensation products from engine or edible oils which are monitored by mass sensitive devices. Differential measurements between printed and non-imprinted sensors evaluate the chemical effects and the sensitivity. These proof of concepts are restricted to molecular templates, however, since we were successful to extend them to microorganisms. A stamp with microorganisms prepatterned on the surface can be used to create their image on prepolymerized materials. After hardening stable coatings with dimensions ranging from several nano- to some micrometers can be observed in these coatings. Selectivity is due to an optimized geometrical fit, but additionally the chemical surface properties are of great importance, since obviously organization processes occur between cell membranes and functional groups of the coating. Thus, the mass sensitive detection of yeast and bacteria cells, viruses and enzymes is possible.

2:15 PM M2.2
SOFT LITHOGRAPHY FOR THE FABRICATION OF MOLECULARLY IMPRINTED POLYMER MICROSTRUCTURES AND THIN FILMS.
Mingde Yan, Alika Lord, Tim Colman, Jennifer Brzisier, Portland State University, Portland, OR.

This talk outlines the application of soft lithography for the fabrication of molecularly imprinted polymer (MIP) micromolds and thin films. The technique employs crosslinked poly(dimethylsiloxane) (PDMS) that contains relief structures as an elastomeric mold to define the shape and size of the polymer. It provides an excellent tool for chemists to generate micrometer-size polymer structures without the use of the expensive microfabrication facilities. MIPs could be made either as stand-alone microstructures on silicon wafers for applications such as sensing, or be isolated as free-standing micromolds for use. MIP films could also be generated using featureless PDMS blocks. The technique has its limitation as the crosslinked PDMS swells in non-polar organic solvents that are widely used in the synthesis of many MIPs. The evaporation on the swelling of PDMS in acetonitrile and dimethylformamide will be presented.

3:00 PM M2.3
ON ROUTE TO THE CHIRAL IMPRINTING OF BULK SILICA.
Sanjita Inu, Jessica Deboeze, Alexander Karg, University of California at Berkeley, Dept of Chemical Engineering, Berkeley, CA.

The design, synthesis and characterization of amorphous silica with chiral pores containing functional groups immobilized therein is reported. Chirality is imprinted into the inorganic structure via condensation reactions of molecules containing a chiral center and tetramethylorthosilicate (TEOS). By removing a portion of the molecule surrounding the chiral center via chemical degradation, stereospecific pores with functional groups in their interior are synthesized within a hybrid organic-inorganic matrix. This material has been used as ceramic membranes for separations in membrane separation and chemical sensors. My talk will review the basic concepts of molecular imprinting and present recent developments in the area.
Novel imprinting approaches are presented allowing to obtain thin layers of molecularly imprinted polymers with binding sites situated at or close to the polymer surface. In a first approach, the template molecules were immobilised on a silica or gold support material. The pre-polymerisation mixtures consisting of monomer and cross-linker was then cast on these derivatised surfaces and polymerised. After polymerisation, the solid support was removed from the composite by the milder treatment. The resulting polymer layers carry surface binding sites, and were able to specifically bind the template. When a short peptide was imprinted, longer peptides having the same terminal sequence were recognised as well by the polymer. In another approach, the porous layers of imprinted polymer were formed at a solid surface by spin coating. Thereby, a linear soluble polymer was used as a porogen, which increased the viscosity of the solution and greatly facilitated spin coating. Following polymerisation, the linear polymer was extracted from the imprinted polymer leaving behind a porous structure. In a third approach, thin imprinted polymer layers were synthesised at surfaces after derivatising the latter with the polymerisation inhibitor. In this way, the polymer chains are at the same time covalently attached to the surface. These new approaches greatly increase the usefulness of molecularly imprinted polymers for immunomodulation, sensors, and affinity separation.

10:15 AM M3.3 Molecularly Imprinted Core-Shell Nanoparticles. Natalia Perez and Andrew G. Hayes, School of Chemical Sciences, University of East Anglia, Norwich, UNITED KINGDOM

Imprinted nanoparticles offer better access to ligand molecules and higher surface area than conventional ground "bulk" imprinted polymers. An easy way to control the monodispersity and final size of the polymeric nanoparticles is by using a 3D emulsion polymerisation process to produce core-shell particles. Recently, it has been shown that core-shell surface imprinted particles rebinding molecules of cholesterol in organic and aqueous solvents, based purely on hydrophilic interactions [1]. Imprinting of such particles can also be achieved using the sacrificial spacer method which combines covalent and non-covalent interactions [2]. So far they have never been tested using the more versatile non-covalent approach. Non-covalent imprinting is a simple procedure applicable to a wider range of template molecules. In order to evaluate the compatibility of core-shell particles produced in aqueous systems with non-covalent imprinting procedures, core-shell particles with a small diameter have been synthesised in the presence and absence of a porogenic solvent, and their capacity to rebinding template assessed by radioligand binding assay both in organic and aqueous media.


11:00 AM M3.4 Molecularly Imprinted Ionomers. George Murray, Johns Hopkins University Applied Physics Laboratory, Laurel, MD

Ionomers have been defined as copolymers that have a certain proportion of ionic groups. The ionic groups have a significant effect on the mechanical properties of the copolymers. This is generally due to a greater degree of crosslinking. The primary goal is to restrict chain motion and raise the glass transition temperature. These are attributes that have relevance to molecular imprinting, since restricted chain motion should help preserve the integrity of the binding site. The connection between ionomers and molecular imprinting has come from the production of metal ion imprinted resins. Metal ions are used in the production of molecularly imprinted polymer ion exchange resins and ionically permeable membranes. The polymers have ion exchange as a secondary function and as ion selective sensors. Metal ions are also being used to form imprinted polymers based on metal mediated imprint binding. We have prepared ion exchange resins, selectively permeable polymer membranes, inorganic and organic electrodes and ion selective optical sensors using a modified version of the molecular imprinting technique. The modification is a reduction in the amount of covalent crosslinking used to form the polymers. This reduction may be justified by the presence of reduced ion crosslinking and increased binding capacity of the imprinted binding site. The effects of metal ions on the thermal and mechanical properties of the polymers, as well their impact on binding selectivity, will be discussed.

SESSION M4: NANOSTRUCTURE AND MOLECULAR RECOGNITION (Chair: David A. Spiwick)

1:30 PM M4.1 Approaches to Surface Confined Templated Binding Sites for Molecular Recognition and Catalysis Applications. Börje Sellergren, Chassidy Sulzky, Magdalena Türičová, Darrell Rickett, and Andrew J. Hall, Institut für Anorganische Chemie und Angewandte Chemie, Johannes Gutenberg Universität Mainz, Mainz, GERMANY

Molecularly imprinted polymers (MIPs) are presently made and used in many laboratories to achieve highly selective separations of mainly small lipophilic molecules comparable with the conventional imprinting technique. In order to widen the scope of the technique we are facing the typical challenges associated with the current imprinting procedure (i.e. to achieve recognition of very polar or nonpolar compounds or recognition of biological macromolecules in water, to reduce the nonspecific binding, to improve the mass transfer properties and to enhance the sample load capacity). Some of the problems may be overcome by the use of two new approaches to confine templated binding sites to accessible surfaces. In the first of these an optimised monomer formulation is used to graft polymers on nanoporous or welldefined particle size and shape, pore systems and pore size distributions. These are based on the use of surface immobilised initiators or initiators with the objective of confining chain propagation to the vicinity of the support surface. This offers a means of fine tuning the layer thickness for either high efficiency (analytical) or high capacity (preparative) applications. An alternative method makes use of template modified porous silica beads that after polymerisation and etching leaves behind porous polymer beads containing surface confined binding sites. In this method the polymerisation step is performed under surface bound free radical initiator conditions. Macromolecules 2001, in press.


2:15 PM M4.2 Molecularly Imprinted in Self-Assembled Materials. Jun Liu, Biomolecular and Interfaces Department, Sandia National Laboratories, Albuquerque, NM

Self-assembly of molecular building blocks, micelles and other colloidal materials have led to a wide range of 3-dimensionally organized nanostructural materials. In addition, applying self-assembled molecular monolayers in such materials provides unique opportunities to tailor the surface chemistry in the nanostructures. The objective of this presentation is to discuss the potential of combining molecular imprinting techniques and self-assembly approaches in the fabrication of new functional nanoprotective coatings. A new class of ordered monomolecular materials, containing self-assembled molecular monolayers embedded with size and shape selective microcavities, will be discussed. The formation of such materials involves co-assembly of ceramic and surfactant liquid crystalline structures, molecular imprinting, and formation of self-assembled monolayers. Compared to 3-dimensional structures and amorphous materials, the organized nanostructures are desirable platforms for molecular imprinting because of the very large specific surface area and the highly controlled geometrical environments. Besides the size and shape selectivity, other novel properties not commonly observed, such as tunable access, will also be discussed.

3:30 PM M4.3 Diasteroselective Fluorescent Sensing for Cinchona Alkaloids by Methylene Blue-Based Imprinted Polymers Co-Assembled with Methacrylic Acid. Toshifumi Takeuchi, Graduate School of Science and Technology, Kobe University, Kobe, JAPAN

A diasteroselective molecularly imprinted polymer (MIP) for (l)-cinchonidine (CD), (P)-PPM, CD), was prepared by the combined use of methacrylic acid and vinylsulfonated Za[11], polypropylene functional monomers. Compared to MIPs using only methacrylic acid
or Zn(II) porphyrin as a functional monomer, PM(CD) and PP(CD), respectively. PP(M(CD)) showed higher binding affinity for CD in chromatographic tests using the MPs-packed columns. Scatchard analysis gave a higher association constant of PPM(CD) for CD than those of PP(CD) and PM(CD). The MPs containing Zn(II) porphyrin in the binding sites, PM(CD) and PP(CD), showed the fluorescent quenching according to the binding of CD and the quenching was significant in the low concentration range, suggesting that the high affinity binding sites contain the porphyrin residue. The correlation of the relative fluorescence intensity against log of CD concentrations was linear for all MPs. These results revealed that the MPs having highly specific binding sites was assembled by the two functional monomers, vinylsubstituted Zn(II) porphyrin and metallochelate acid, and they cooperatively worked to yield the specific binding. In addition, the Zn(II) porphyrin-based MPs appeared to act as fluorescence sensor selectively responded by binding events of the template molecule. Fe(III) porphyrin based imprinted polymers will also be discussed.


SESSION M5. POSTER SESSION
Chair: M. Joseph Roberts
Thursday Evening, April 4, 2002
8:00 PM
Metropolitan Ballroom (Argent)

M5.1
COMPUTATIONAL FLUID DYNAMICS MODELS OF MOLECULARLY IMPRINTED MATERIALS IN MICROFLUIDIC CHANNELS. Christian J. Wolber, M. Joseph Roberts, Polymer Science and Engineering Branch, Naval Air Systems Command, NAWCAD, China Lake, CA.

Current research will lead to rapid-prototyping of chemical sensors that utilize microfabricated molecularly imprinted (MI) materials. CD/CDF software may be used to model flow and chemical binding properties of MI materials in microfluidic channels. This type of software expedite the results when changes in properties are made. The surface concentration of bound analyte on a monolithic MIP within microfluidic channels can be modeled using its experimental binding kinetics. The time necessary to reach a detection limit is determined and optimized as a function of flow parameters.

M5.2
SELECTIVE RECOGNITION OF SMALL PEPTIDES USING NiNTA RECEPTOR SITES. Peter G. Conrad, II, Kenneth J. Shen, University of California, Irvine, Dept. of Chemistry, Irvine, CA.

Molecular recognition of small molecules involves the selection of specific functional groups through multiple interactions. Molecularly imprinted polymers (MIPs) provide a high degree of selectivity for specific analytes via the development of recognition sites during the polymerization process. Ordered interactions orient functional monomers in a pre-polymerization complex with template molecules. The monomers are incorporated into a micromolecular network polymer with cross-linking monomers. Following extraction of the template, the binding sites remain in the polymer matrix. These sites exhibit selectivity towards the template compound. The development of micromolecular receptors for small peptides using NiNTA technology has allowed both the polymerization and recognition processes to be carried out in an aqueous environment, which does not compromise the strong metal-ion interactions primarily responsible for ligand recognition. The Ni(II) centers possess strong binding affinities towards histidine and N-terminal histidine containing peptides. This presentation will focus on polymers formulated with NiNTA receptor sites and the diverse applications associated with these MIPs.

M5.3
IMPRINTING OF STEROIDS USING BIFUNCTIONAL FLUORESCENT MONOMERS. Dolly Bhatta and Kenneth J. Shen, University of California, Irvine, Department of Chemistry, Irvine, CA.

Brevetoxin B is a marine neurotoxin associated with massive kills of fish and other marine life along coastal areas around the world. We wished to explore if molecularly imprinted polymers (MIPs) can be developed for the detection of this neurotoxin in the ocean. An approach would be the use of a fluorescent sensor within the polymer that could register the characteristic change (a quenching or a fluorescence shift) upon the binding of brevetoxin within the imprinted polymer. Our strategy for the imprinting of brevetoxin, or a surrogate steroid such as cholesterol, involves the use of a bifunctional monomer such as alkenone 1, which is covalently attached to both the template and the fluorescent probe. After polymerization with a crosslinking monomer such as divinyl benzene (DVB), the resulting polymer 2 can undergo a LAH reduction to give MIP 3. With MIP 3 in hand, we hope to see a fluorescent change upon binding of the steroid due to a change in the microenvironment of the fluorescent probe. This poster will consider the synthesis of novel monomers of type 1 and subsequent fluorescent study of MIPs of type 3.

M5.4
HIERARCHICALLY IMPRINTED STATIONARY PHASES. MESOPOROUS POLYMER BEADS CONTAINING SURFACE-COMPLEMENTED BINDING SITES. Thomas R. Farmer, Andrew J. Hall, Börje Sellergren, Institut für Anorganische Chemie und Analytische Chemie, Johannes Gutenberg Universität, Mainz, GERMANY.

Immobilization of a template on the surface of a porous silica mold, polymerization in the mold followed by dissolution of the silica results in a "mirror image" pore system containing binding sites residing uniquely at the pore walls.[2] We recently reported on the application of hierarchical imprinting to produce methacrylate-based mesoporous beads useful for chromatographic applications, which featured surface confined binding sites for adenine or trimethylpyrimidine.[2] Here we report a detailed characterization of these materials based on nitrogen sorption measurements, thermogravimetric analysis, energy dispersive X-ray analysis, fluorescence microscopy, scanning electron microscopy, IR and elemental analysis. Furthermore, the chromatographic selectivity of these hierarchically imprinted polymers has been evaluated, allowing conclusions concerning the nature of the binding sites to be drawn.[1]


M5.5
DESIGN, SYNTHESIS AND APPLICATION OF NOVEL MONOMERS FOR MOLECULAR IMPRINTING TECHNOLOGY: BRINGING MOLECULES TOGETHER. Panagiotis Maniati, Andrew J. Hall, Jakob T. Moses, Börje Sellergren, Institut für Anorganische Chemie und Analytische Chemie, Johannes Gutenberg Universität, Mainz, GERMANY.

In the field of molecular imprinting the design and synthesis of novel monomers has been seen as a rather expensive and time consuming pursuit. However, the rewards outweigh the effort required. We have synthesised novel monomers for the recognition of uracil, buturuccine and carbamoyl acid, respectively, basing our designs on functional complementarity between the "host" monomer and the "guest" template, thereby "bringing the molecules together". The extent of monomer-template interaction has been studied via 1H NMR titrations and association constants have been determined. The monomers have then been incorporated into Molecularly Imprinted Polymers (MIPs), whose recognition properties have been evaluated in the chromatographic mode (HPLC) in comparison to Non-Imprinted Polymers (NIPs). Uracil is the only DNA base lacking an ecyclic amino group and is thus difficult to imprint using commodity monomers, e.g. MAA. Using our novel monomers, we have observed a direct correlation between the hydrogen bond strength determined in solution and the discrimination and binding site fidelity observed in the subsequently prepared polymers. Additionally, monomers with enhanced selectivity for buturuccine, commonly used as sedative and hypnotic drugs, could be used for isolation and purification of these drugs during their production and for the selective extraction and pre-concentration of samples containing them, simplifying any subsequent quantification process. Finally, effective targeting of carbamoyl acid moieties should lead to recognition of biologically important molecules, such as amino acids and the C-termini of peptides.

M5.6
STUDIES OF THE PROCESS OF FORMATION, NATURE AND STABILITY OF BINDING SITES OF MOLECULARLY IMPRINTED POLYMER. Francesca Lanzi, Andrew J. Hall, Börje Sellergren, Institut für Anorganische Chemie und Analytische Chemie, Johannes Gutenberg Universität, Mainz, GERMANY; Manuel Ruther, Polymer Research Unit, Physics Department, Trinity College, Dublin, IRELAND.

In Molecular Imprinting [1,2] the nature of the templated binding sites and their formation mechanism are poorly understood. For this reason our group is carrying out a series of fundamental studies concerning known imprinting protocols, with the primary aim of shedding some light on the role of the template in the different steps of the polymerisation process. In the primary chain to the build-up of the porous structure. In this paper we are
reporting on the results of two different studies performed on the MAA/EDMA/Sethylidene (3) and MAA/EDMA/ammon (4) model systems, concerning the effect of: i) the presence of Sethylidene on the kinetics of polymerisation of MAA/EDMA in different solvents (by in situ IH NMR measurements); ii) a late addition of the template (ammon) on the recognition properties (based on binding experiments on a small scale). The studies indicate that the template is playing a decisive role right from the start of the polymerisation, although the formation of the sites is a rather slow process. The results of a post-polymerisation cationic curing and the recognition properties of template polymers will also be reported as an indirect method of investigating the nature and stability of the binding sites. In this context we will present data concerning drug release from template pore size distributions for imprinted and non-imprinted polymers.

The authors would like to acknowledge the support of the European Community in the framework of the TMR Project MICA.

M5.7 BINDING STUDIES ON RESINS IMPRINTED WITH S-NAPROXEN, Yue Hu, Robert A. Orwoll, Departments of Applied Science and Chemistry, College of William and Mary, Williamsburg, VA.

Resins were prepared in a free-radical polymerization of 4-vinyl pyridine and ethylene glycol dimethacrylate in the presence of 5(S)-N-(3,4-dihydroxy-2H-1-benzopyran-2-yl)acetic acid (S-naproxen). Initially 5(S)-naproxen, the imprinted molecule, i.e. template, was assembled with the monomer 4-vinylpyridine by non-covalent interactions. After the polymerization, continuous removal of the template left binding sites that retain complementarity specificity and affinity. Calculated from the amount of template removed, the binding parameter including the number of binding sites and association constant were found to be complementary to precise and evaluated. The association constant of S-naproxen with the imprinted resin was found to be significantly higher than for the non-imprinted resin. The results indicate that the incorporation of a distribution of association constants ("affinity spectrum") was tested for this system.

M5.8 PICOMOLAR DETECTION OF POLYCLORINATED AROMATIC CONTAMINANTS IN WATER USING A QUARTZ CRYSTAL MICROBALANCE COATED WITH A MOLECULARLY IMPRINTED POLYMER THIN FILM, Janet D., Univ. of Mass. Dept. of Chemistry, Amherst, MA; Jacques Penelle, Univ. of Mass. Dept. of Polymer Science and Engineering, Amherst, MA; Vincent M. Bazzell, Univ. of Mass. Dept. of Chemistry, Amherst, MA.

Hexachlorobenzene in aqueous solutions can be selectively and rapidly detected at picomolar concentrations using a quartz crystal microbalance (QCM) and a sensor. The sensor is functionalized by robustly coating a molecularly-imprinted polymer (MIP) thin film onto the surface of a QCM chip. Obtained results indicate that a robust unit can be built able to measure the concentration of highly toxic, organochlorine pollutants in water at extremely low, environmentally significant levels. The use of a thin film coated to the surface of the QCM chip and the design of target specific electron-rich monomers results in real-time detection and appreciable sensor selectivity compared to a set of non-specific organic pollutants with varying size and electronic properties. In addition, a quantitative assessment and molecular understanding of the specific attributes arising from the imprinting process can be obtained by a Quantitative Structure Activity Relationship (QSAR) based methodology allowing us to distinguish specific and non-specific binding events. This is accomplished by comparing the partition coefficient of each target to the sensor response, which results in a linear relationship. A deviation from the linearity indicates selectivity that is due to the imprinted molecule.

M5.9 AN EXAMINATION OF THE VARIABLES IN THE MOLECULAR IMPRINTING PROCESS WITH RESPECT TO THE HETEROGENEOUS DISTRIBUTION OF BINDING SITES. Robert J. Ugleh, H. Ken D. Shintani, Univ. of South Carolina, Dept of Chemistry and Biochemistry, Columbia, SC.

Variables in the molecular imprinting process were systematically examined for their effects on the heterogeneous distribution of binding sites in MIPs. A finite distribution analysis enabled a more complete study of the effects of each variable on the shape of the distribution and percentages of high- and low-affinity sites in comparison to previous studies which applied homogeneous model to heterogeneous MIPs. Variables examined were concentration of template, polymerization initiation (UV vs thermal) and apparent crosslinking density in a methacrylic acid/ethylene dimethacrylate matrix imprinted with ethyl adipate-8-nectane. All the polymers were found to have binding properties consistent with an equilibrium distribution of binding sites, and were analyzed by fitting the binding data with a Freundlich isotherm and calculating an affinity distribution using a newly derived distribution equation. In general, the quality of the MIPs improved with higher concentrations of template, lower temperatures, and higher apparent crosslinking densities.

M5.10 ENANTIOSELECTIVE RELEASE OF CONTROLLED DELIVERY GRANULES BASED ON MOLECULARLY IMPRINTED POLYMERS. Roongnapa Srichan, Teerapol Srichan, Triut Rattanamont, Dept. of Pharmaceutical Sciences, Prince of Songkla University, Hatyai, Songkhla, THAILAND.

The objectives of our study were to examine enantioselective release of controlled delivery granules based on molecularly imprinted polymers (MIPs) for various racemic drugs, including Naproxen and Ketoprofen (NSAIDs) and propranolol (β-blockers), and to evaluate the use of controlled delivery granule containing a combination of different MIPs for the multiple simultaneous enantioselective controlled delivery of mixed racemic drugs. In this work, the MIP beads selected to S-Naproxen, S-Ketoprofen as well as R-Propranolol were prepared using multi-step swelling and thermal polymerization method. Afterward, the MIP beads were formulated with racemate of the chiral drugs and a binder followed by granulation. Then, the enantioselective release of racemic drugs from the prepared MIP granules was investigated by in vitro dissolution test using a chiral HPLC for assays of enantiomer concentrations. The influence of drug/polymer ratio and medium pH on the enantioselective release of MIP granules were explored. The release of the enantiomers of racemic Naproxen and racemic Ketoprofen from the granule containing two MIPs, S-Naproxen MIP and S-Ketoprofen MIP was also examined. The release profiles of both S-Naproxen MIP granule and R-Propranolol MIP granule exhibited different release of enantiomers. Also, the finding indicated the stereoselective retardation of those controlled delivery granules as well as the influence of MIP formulation on enantioselective release mechanism. The enantioselective release profiles of S-Naproxen MIP granule and R-Propranolol MIP granule appeared to depend on polymer loading and medium pH. In this case, the drug/polymer ratio of 1:26 showed the best enantioselective release with initial enantiomeric excess of 100%. On the other hand, the enantioselectivity of both granules was the greatest in buffer pH 7.4. Furthermore, the efficiency in enantioselective release of the combined MIP granule was higher than its corresponding single MIP granules, as a result of the cross-selectivities of the MIPs. In this study, controlled delivery granules based on MIPs demonstrated significant enantioselective release for several chiral drugs, and thus may be developed to utilize as a tool for administration of a chiral pharmaceutical as single enantiomer.

M5.11 ATTEMPTS TO GRAFT ‘LIVING’ MOLECULARLY IMPRINTED POLYMERS FROM HYDROPHILIC AND HYDROPHOBIC CHROMATOGRAPHIC SUPPORT MATERIALS. B. Rücker, C. Schaltzky, B. Sellergren Institut für Angewandte Chemie und Analytische Chemie, Johannes Gutenberg-University, Mainz, GERMANY.

Due to the increasing demand for drugs in enantioselectively pure form, chiral technologies are becoming increasingly important in the pharmaceutical industry. Therefore, the use of chromatographic preparative methods is becoming more widespread. These are based on chromatographic stationary phases (CSPs) that exhibit selectivity against one of the enantiomers and thereby allow enantiomer separation with high resolution and load capacity. The objective of our work is the synthesis of enantioselective molecularly imprinted chiral stationary phases (MIP-CSPs) possessing high load capacities and improved mass transfer properties. We have focused on the grafting from technique, using dithiocarbamate initiator molecules covalently bound to the surface of various support materials, e.g. hydrophilic polysiloxane, based and hydrophobic silica-based particles. As this surface modification offers the possibility to obtain molecularly imprinted layers differently imprinted via several successive polymerization steps we concentrated on this option for the targeted optimisation of the CSPs for specific applications in pharmaceutical industry. The quality of the grafted copolymeric films has been investigated using a variety of techniques (IR spectroscopy, elemental analysis, nitrogen adsorption, SEM, TEM and HPLC) as we will present here.
produce molecular imprinted polymer (MIP) hydrogels which selectively bind glucose over fructose even while in their water-swollen state. This synthetic methodology for MIPs might offer exciting avenues for novel biorecognition techniques. Glucose selective MIPs could lead to the development of a pharmaceutical, which would aid in the treatment of type II diabetes, and to the development of a glucose sensor. While methods of template function vary among research groups, the majority of studies to date have concentrated on synthesizing imprinted polymers from monomer, rather than crosslinking an existing polymer with functionality conducive to a biorecognizable imprint. This research employs molecular imprinting starting from a readily available polymer, which greatly simplifies the synthesis of the MIPs and may bring the technology closer to commercialization. The effect of polymer hydrogel synthesis parameters on glucose binding capacity and specificity will be presented, as well as experimental results demonstrating isomeric glucose biorecognition in aqueous and phosphate buffered solutions from mixed sugar media.

11:15 AM M05
MOLECULARLY IMPRINTED POLYMERS USED AS OPTICAL WAVEGUIDES FOR THE DETECTION OF FLUORESCENT ANALYTES. Jennifer Brassier, Dr. Mingdi Yan, Portland State University, Dept of Chemistry, Portland, OR.

Molecularly imprinted polymers have found a niche in many sensor applications. The host-guest theory responsible for the sensitive and selective detection of imprint molecules has been applied to a combination of analytes and polymer systems. Furthermore, diverse fabrication techniques have created imprinted polymers ranging in design from bulk species to thin films. This project demonstrates the novel approach of fabricating imprinted polymers as fiber optic filaments in 50 micron dimension and incorporating these filaments into optical sensors. Filaments were comprised of polystyrene monomers, cross-linkers, and appropriate solvents to create a porous polymer matrix. Fluorescent polymeric hydrocarbons served as template molecules capable of interacting with the monomers through noncovalent, π-π forces. Fabrication of these filaments utilized the soft lithography technique of micro-molding in capillaries, MMIC. In this process, a soft elastomeric stamp of poly(dimethylsiloxane) was used to create microchannels, which were filled with an imprinted solution by capillary action. Polymerization and stamp removal leave behind filaments used as optical waveguides. Binding characteristics of the fiber optic elements were measured and compared to those previously determined for 20 micron particles and films of the same imprinting system. The application of these filaments will be discussed.

10:15 AM M03
Abnormal Wound.

10:45 AM M06
MOLEULARLY IMPRINTED POLYMER HYDROGELS DISPLAYING IMMUNE-SUGAR BIORECOGNITION. Paraskevi Papi, University of Maryland, College Park, Department of Materials and Nuclear Engineering, College Park, MD; Peter Kofman, University of Maryland College Park, Department of Chemical Engineering, College Park, MD.

Molecular imprinting is an emerging technology which allows the synthesis of materials containing highly specific receptors sites, with an affinity for target compounds. We have developed methods to