SYMPOSIUM M
Molecularly Imprinted Materials

April 3 – 5, 2002

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*Invited paper
SESSION M1: SYNTHESIS AND CHARACTERIZATION

Chair: Mingli 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 MMICS OF NATURAL ANTAGONISTS AND ENZYMES. Günter Wulf, Heinrich-Heine University, Institute of Organic and Macromolecular Chemistry, Düsseldorf, GERMANY.

In order to mimic the active sites 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 even in imprinted. This type of imprinted polymers is especially useful for the preparation of catalytically active imprinted polymers. Using different transition state analogues of alkaline ester hydrolysis and suitable catalytic functional monomers catalysts with strong 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 microspheres of 10-3000 nm particle diameter with narrow particle diameter distribution can be obtained. A further step describes the influence of 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.


10:00 AM M1.2
DEVELOPMENT OF IMPROVED CROSSLINKING MONOMERS FOR MOLECULARLY IMPRINTED MATERIALS. David A. Speck, Martin Sibrian-Vasquez, 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 commercially available. The benefit of using these monomers is 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 microextractions that will only require small amounts of material. Therefore, economic price considerations of the imprinted materials is less of a concern. Instead, materials with the best performance is the goal for microfabricated and microextractions devices.

Most of the research in molecularly imprinted materials has focused on choice of substrate or functional monomer of the pre-polymer complex. However, approximately 80-90% of the imprinted polymers are composed 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 commensurate improvement in polymer properties. Redirecting focus on the design of crosslinking monomers for molecular imprinting, we have developed new classes of crosslinked polymers to obtain different performance of molecularly imprinted polymers. New difunctional methacrylic/vinylketone and methacrylic/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 carboxylate functionalized crosslinking monomers derived from L-aspartic acid and L-serine will be reported.

10:30 AM M1.3
NOVEL MONOMERS FOR NON-COVALENT MOLECULAR IMPRINTING - VORSPRUNG DURCH KREATIVEITÄT. Andrew J. Hall, Panagiotis Moutsios and Börje Sellergren Institut für 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 polymerisation 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 chiral 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 characterised by a heterogeneous distribution of binding sites and exhibit significant non-specific binding of the template/analyte. In an effort to overcome such problems, we have embarked upon a programme of design and synthesis of novel polymerisable 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 now wish to report on the design and 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 Lingmic-Freundlich, which significantly simplify the analysis so that affinity distributions can be readily generated from the corresponding equilibrium 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. We 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:

11:00 AM M1.4
CHARACTERIZATION OF MOLECULARLY IMPRINTED POLYMERS USING HETEROGENEOUS BINDING MODELS. Ken D. Shimasu, University of South Carolina, Department of Chemistry and Biochemistry, Columbia, SC.

MIPs are heterogeneous materials containing binding sites with a broad range of affinity constants. We have recently quantitatively measured the breadth and shape of the heterogeneity in MIPs by applying heterogeneous binding models. The measured affinity distributions give a more accurate and complete measure of the binding properties of MIPs and enable a better understanding of the mechanism of the imprinting process. More recently, we have applied specific heterogeneous binding models such as the Freundlich and Lingmic-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. Discussed 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.

11:30 AM M1.5

Molecular imprinting is a general protocol for the synthesis of cross-linked network polymers containing receptor and/or catalytic sites for small organic molecules. The imprinting process consists of a print molecule or template that is bound either covalently or noncovalently to functionalized monomers. The resulting prefabricated complex is copolymerized with an excess of crosslinking monomer in the presence of an equal volume of inert solvent (porogen) and a free radical initiator. Thermal or photochemical initiated polymerization results in a highly cross-linked insoluble polymer. Removal of the template, in most cases by extraction or hydrolysis, leaves sites in the polymer that have incorporated the functionalized monomers. These sites are complementary to the template molecule. Moreover, the functional groups are specifically positioned to converge on the template molecule in a reciprocal fashion. Molecular imprinting
has been used to create binding and catalytic sites for a wide variety of organic substrates. The resulting network polymers are mechanically robust and retain their activity on inorganic surfaces.

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

10:30 AM M2.2
SENSOR MATERIALS - DETECTING MOLECULES, MIXTURES AND MICROORGANISMS.
F. 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 molecularly-imprinted quartz wafers for SAMs. A fabrication can directly be coated with polystyrene/diarylbenzene copolymers with different organic solvents. These layers allow the differentiation between the xylene isomers at ambient humidity applying patterns of recognition. These patterns can 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 is monitored by mass sensitive devices. Differential measurements between printed and non-printed sensors evaluate the chemical effects and the sensitivity. These processes are restricted to molecular templates, however, since we were successful to extend them to microorganisms. A stamp with microorganisms prearranged on the surface can be used to create their image on prepolymerized materials. After hardening stable cavities with dimensions ranging from several nanometers 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 bacterial cells, viruses and enzymes is possible.

2:15 PM M2.2
SOFT LITHOGRAPHY FOR THE FABRICATION OF MOLECULARLY IMPRINTED POLYMERIC MICROSTRUCTURES AND THIN FILMS.
Min-Min Yang, Aliko Lord, Tim O’Brien, Jennifer Brasier, Portland State University, Portland, OR.

This talk outlines the application of soft lithography for the fabrication of molecularly-imprinted polymer (MIPs) 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-scale 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 freestanding micromolds. MIP films could also be generated using feature-less 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 acetone and dimethylformamide will be presented.

3:00 PM M2.2
ON ROUTE TO THE CHIRAL IMPRINTING OF BULK SILICA.
Santiago Xi, Jessica Defreeze, Alexander Katz, 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 imparted into the inorganic structure via condensation reactions of molecules containing a chiral center and tetramethylthoracililcic acid (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 material that can be used as sensors and catalysts.

Applications of the imprinted silanes as specific adsorbents, in addition to catalysis, will be discussed.

3:45 PM M2.4
EXPERIMENTAL AND THEORETICAL INVESTIGATION OF THE GAS-SURFACE INTERACTION MECHANISM ON MOLECULARLY IMPRINTED SILICO USED AS GAS SENSOR MATERIAL.
Dario Narducci, Pierzio Bernardinello, Istituto Nazionale per la Fisica della Materia and Dept. Materials Science, Univ. of Milano Bicocca, Milan ITALY; Giorgio Mero, Dept. Biotechnology, Univ. of Milano Bicocca, via della Scienza, Milan, ITALY.

Over the last years a growing interest has showed up towards the study of chemical systems characterized by weak interactions between molecules. Supramolecular chemistry has quickly extended its field of action to synthetic systems in which such interactions determine modifications of the chemical and physical properties. At the same time, the development of methodologies suitable to modify as an atomic scale the structure of condensed matter have offered horizons in which devising materials whose property were thought in connection with new functionality. This paper reports the results of an investigation aimed at using supramolecularly assembled monolayers to modify the supramolecular interactions between Si surfaces and gaseous molecules. Specific goal is that of employing molecularly imprinted silicon surfaces to develop a new class of chemical sensors capable of detect species with enhanced selectivity. Single crystal (111) silicon have been modified by grafting organic molecules onto its surface by using wet chemistry synthetic methods. Silicon has been activated toward nucleophilic attack by brominating its surface using a modified version of the purely organic method. The obtained materials have been successfully tested as reactive chemical sensors toward NO₂, SO₂, CO, NH₃ and methanol. Current-voltage characteristics measured at different gas compositions showed that the mechanism of surface electron density modulation involves a modification of the junction barrier height upon gas adsorption. Quantum-mechanical simulations of the interaction mechanism, carried out using Density-Functional Theory, confirm that gas-SAM interaction leads to a change of the Si surface electron density. These results appear to open up new relevant applications of SAM techniques in the area of gas sensing.

SESSION M5: MEMBRANES AND NANOPARTICLES
Chair: Ken D. Shimizu
Thursday Morning, April 4, 2002
Concordia (Argent)

8:30 AM M5.1
MOLECULARLY IMPRINTED MATERIALS.
Klaus Mosbach, Lei Ye, Lund University, SWEDEN.

This brief abstract summarizes some recent developments from our Center for Molecular Imprinting related to the topic of this symposium. After a short presentation of the principle of molecular imprinting and its recognition [1], the use of different materials including hybrid [2] for the formation of the host will be discussed, followed by examples given of different formats used such as small beads [3,4], membranes and microcones [5] summarized in a recent review [6]. In closing, potential directions for the next generation in molecular imprinting technology will be discussed [7,9].

References:
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 covalently on solid support materials. 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 chemical treatment, resulting in imprinted 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, thin 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. Follow-up 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 initiator. 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 immunosensors, sensors, and affinity separation.

10:15 AM #M3.3
MOLECULARLY IMPRINTING OF POLYMERIC CORE-SHELL NANO PARTICLES. Natalia Perea 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 age emulsion polymerisation process to produce core-shell particles. Recently, it has been shown that core-shell surface imprinted particles retain molecules of cholesterol in organic and aqueous solvents, based purely on hydrophobic interactions. Imprinting of such particles can be achieved using a sacrificial spacer method which combines covalent and non-covalent interactions. 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 present and absence of a porogenic solvent, and their capability to bind 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 the aggregation of ions in a low dielectric medium. The primary objective is to restrict chain motion and raise the glass transition temperature. These are attributes that 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 imbibition as selectivity, ion exclusion as selectivity, and as ion selective sensors. Metal ions are also being used to form imprinted polymers based on metal mediated imprinting. We have prepared ion exchange resins, selectively permeable polymer membranes, and selective electrodes as well as ion selective electrodes 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 reducing groups. The ion in crosslinking 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. Spivak
Thursday Afternoon, April 4, 2002
Concordia (Argent)

1:30 PM #M4.1
APPROACHES TO SURFACE CONFINED TEMPLATED BINDING SITES FOR MOLECULAR RECOGNITION AND CATALYSIS APPLICATIONS. Bjoerg Sellergren, Chudita Sulitzyk, Magdalena Tuciri, Barbel Rücker, and Andrew J. Hall, Institut für Anorganische Chemie und Analytische 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 compatible 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 in-porous or well-defined particle size and shape, porous systems and pore size distributions. This broadens the use of surface immobilised iminitors 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 technique makes use of template modified porous silica beads that after polymerisation and etching leaves behind porous polymer beads containing surface confined binding sites.


2:15 PM #M4.2
MOLECULARLY IMPRINTING IN SELF-ASSEMBLED MATERIALS. Jun Liu, Biomolecular and Interface 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 nanostructured 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 novel functional nanoscale materials. A new class of ordered monolayer materials, containing self-assembled molecular monolayers embedded with size-and-shape selective microcavities, will be discussed. The formation of such materials involves co-assembling of nanoparticles and self-assembled monolayers by means of molecular imprinting, and formation of self-assembled monolayers. Compared to 2-dimensionally structured and monomeric materials, the organized nanostructures are desirable platforms for molecular imprinting because of the very large specific surface area and the precisely controlled geometrical environments (pore dimension, curvature, etc.). 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
DIASTEREOTOPIC FLUORESCENT SENSING FOR CINCHONA ALKALOIDS BY MOLECULARLY IMPRINTED POLYMERS CO-ASSEMBLED WITH METHACRYLIC ACID. Yoshiharu Takeuchi, Graduate School of Science and Technology, Kobe University, Kobe, JAPAN

A diastereoselective molecularly imprinted polymer (MP) for (A)-cinchonine (CD), PPM(CD), was prepared by the combined use of methacrylic acid and vinylsubstituted Zn(II) porphyrin as functional monomers. Compared to MP's using only methacrylic acid and acrylamide, the imprinted polymer shows a high selectivity in the recognition of (A)-cinchonine. The role of porphyrin in this imprinted polymer is to make the recognition site more sensitive to chirality in the solvent. This is a new example of the use of a porphyrin in a molecularly imprinted polymer. The selectivity of the porphyrin-MP system is higher than those of the corresponding systems based on classical chemosensors. The recognition ability of the polymer was examined using a fluorescence polarimetry. The fluorescence intensity of the (A)-cinchonine-PPM(CD) complex is highly increased in the binding site of the polymer. The diastereoselectivity of the recognition event is revealed by the fluorescence anisotropy of the (A)-cinchonine-PPM(CD) complex.
or Zn(II) porphyrin as a functional monomer, PM(CD) and PP(CD), respectively, PM(CD) showed higher binding ability for CD in chromatographic tests using the MP-packed columns. Sarsharuddin analysis gave a higher association constant of PM(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 fluorescence 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 concentration was linear. These results revealed that the MP having highly specific binding sites was assembled by the two functional monomers, vinylsubstituted Zn(II) porphyrin and methacrylic 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 responding by binding events of the template molecule. Fe(III) porphyrin based implanted polymers will also be discussed.


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


Current research will lead to rapid-prototyping of chemical sensors that utilize microfabricated molecularly imprinted (MIP) materials. CDFA software may be used to model flow and chemical binding properties of MIP materials in microfluidic channels. Use of this type of software expedits 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 Ni-NTA RECEPTOR SITES. P. G. Conrad, H. 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. Molecules 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. Monomers are incorporated into a micromolecule 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 Ni-NTA technology has allowed both the polymerization and recognition processes to be carried out in an aqueous environment, which does not compromise the strong metal interactions primarily responsible for ligand recognition. The Ni(II) centers possess strong binding affinities towards histidine and N-terminus histidine containing peptides. This presentation will focus on polymers formulated with Ni-NTA receptor sites and the diverse applications associated with these MIPs.

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

Brevetoxin B is a marine neurotoxin associated with massive killings 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 would register a 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 alleneone 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 an LAH reduction to give MP 3. With MP 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 provide an overview of novel monomers of type 1 and subsequent fluorescent study of MIPs of type 3.

M5.4 HIERARCHICAL IMPRINTED STATIONARY PHASES: MESOPOROUS POLYMER BEADS CONTAINING SURFACE-ATTACHED BINDING SITES. Barbara J. Hall, Birge Sellergren, Institut für Anorganische Chemie und Analytische Chemie, Johannes Gutenberg Universität, Mainz, GERMANY.

Immobilization of a template on the surface of a porous silicate soil, polymerization in the mold followed by dissolution of the silicate results in a "mirror image" pore system containing binding sites residing uniquely at the pore walls. 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 adenosine or trimethoprim. Here, we present 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] E. Yilmaz, K. Haupt and K. Mostbach, Angew. Chem., Int. Ed., 2000, 39, 2015-2018. [2] M.M. Titirici, A.J. Hall and B. Sellergren, Chem. Mat. [in press].

M5.5 DESIGN, SYNTHESIS AND APPLICATION OF NOVEL MONOMERS FOR MOLECULAR IMPRINTING TECHNOLOGY: BRINGING MOLECULES TOGETHER. Panagiotis Masouros, Andrew J. Hall, Jakob T. Messing, Birge 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 a rather expensive and time consuming pursuit. However, the rewards far outweigh the effort required. We have synthesised novel monomers for the recognition of uracil, 2,3-butadiene, and carboxylic acids, 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 RNA 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, materials with enhanced selectivity for butadiene, commonly used as sedative and hypnotic drugs, could be used for isolation and purification of these drugs during their preparation and for the selective extraction and pre-concentration of samples containing them, simplifying any subsequent quantification process. Finally, effective targeting of carboxylic 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 POLYMERS. Francesca Laurenzi, Andrew J. Hall, Birge Sellergren Institut für Anorganische Chemie und Analytische Chemie, Johannes Gutenberg Universität, Mainz, GERMANY, Manuel Rutther, 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. More specifically, the primary chains to the build-up of the porous structure. In this paper we are
reporting on the results of two different studies performed on the MA/EDMA/Spherulite [3] and MA/EDMA/amyl (4) model systems, concerning the effect of: (i) the presence of Spherulite on the kinetics of polymerisation of MA/EDMA in different solvents [by in situ NMR measurements]; (ii) a late addition of the template (amylo) on the recognition properties [by rebinding experiment 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 curing on the porosity and the recognition properties of template-polymer 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 studies at discrete 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 (1).


(2) F. Luanz, B. Sellegren, Chromatographia 2001, 53.


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

Resins were prepared in a free-radical polymerisation of 4-vinylpyridine and ethylene glycol dimethacrylate in the presence of (S)-(-)-naproxen (S)-naproksen and vinyl-2-glycidyl ether (VG). Initially [S]-inaproxen, the imprinted molecule, i.e. template, was assembled with the monomer 4-vinylpyridine by non-covalent interactions. After the polymerisation, continuous removal of the template and binding sites that retain complementary specificity and affinity. Calculated from the amount of template removed, the binding parameters including the number of binding sites and association constant were studied using a modified version of the Scatchard equation. The binding of (S)-naproxen to the imprinted resin was investigated by in vitro dissolution testing using a chiral HPLC. The influence of drug/polymer ratio and medium pH on the selectivity of S-Imprinted resin was explored. The release of the enantiomers of racemic Naproxen and racemic ketoprofen from the resin containing two MPs, S-Imprinted MP and Sketophen MP, was also examined. The release profiles of both S-Naproxen MP granule and R-propranolol MP granule exhibited differential release of enantiomers. Also, the finding indicated the stereoselective retardation of those controlled delivery granules as well as the influence of MP formulation and environmental factors on enantioselective release mechanism. The enantiomeric release of S-Naproxen MP granule and R-propranolol MP granule appeared to depend on polymer loading and medium pH. In this case, the drug/polymer ratio of 1:2 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 MP granule was higher than its corresponding single MP granules, as a result of the cross-selectivities of the MPs. In this study, controlled delivery granules based on MPs demonstrated significant enantioselective release for several chiral drugs, and thus they 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 HYDROPOLY and HYDROPHOBIC CHROMATOGRAPHIC SUPPORT MATERIALS. B. Rückert, C. Schöckl, B. Sellegren 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 chiral stationary phases (CSPs) that exhibit selectivity against one of the enantiomers and thereby allow enantiomer separation with high resolution and lead capacity. The objective of our work is the synthesis of enantioselective molecularly imprinted chiral stationary phases (MICSPs) possessing high load capacities and improved mass transfer properties. We have focussed on the ‘grafting from’ technique, using dithiocarbamate linker moieties covalently bound to the surface of various support materials, e.g. hydrophilic poly(styrene) based and hydrophobic silica-based particles. As these surfaces modification offers the possibility to immobilise modified layers differently imprinted using several successive polymerisation steps we concentrated on this opportunity for the targeted optimisation of the CSPs for specific applications as 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.
SESSION M6: COVALENT AND NON-COVALENT IMPRINTING
Chair: Kirsten Haupt
Friday Morning, April 5, 2002
Concordia (Argent)

8:30 AM M6.1
CHEMICAL APPROACHES TO IMPRINTING.
Michael J. Whitcombe, Inst of Food Research, Norwich, UNITED KINGDOM

The application of various “semi-covalent” protocols to the imprinting of small molecules will be described, including recent results utilizing the dimethylglycol as a sacrificial spacer. The synthesis of specialist monomers and templates for noncovalent imprinting will also be presented, along with their application to the imprinting of templates as diverse as inorganic crystals, antibodies and steroids. In the latter case, a novel surfactant approach was used to create imprinted sites at the surface of submicron particles. The use of covalently imprinted polymers in the regiospecific synthesis of polypeptides will also be described.

References:

9:15 AM M6.2
REQUIREMENTS FOR MOLECULAR RECOGNITION BY IMPRINTED POLYMERS: Elena Oral, Nicholas A. Peppas 1, 2, NSF Program on Therapeutic and Diagnostic Devices, 1 School of Chemical Engineering, 2 Department of Biomedical Engineering, Purdue University, West Lafayette, IN.

Biological molecules such as enzymes and antibodies have exceptional recognition capabilities. We investigated the properties that enable synthetic materials to recognize and bind specific compounds mimicking these biological molecules. We prepared crosslinked synthetic materials that show similar high molecular recognition capabilities for microfabrication and biosensor applications. We prepared and characterized molecularly imprinted polymers with the aim of identifying important material properties that render these materials specific. Polymer films and particles of 3-hydroxyethyl methacrylate and poly(ethylene glycol) dimethacrylate (PEGDMA) of various lengths were prepared by UV and thermally initiated free-radical polymerization, respectively. The effect of the type of crosslinking agent was also investigated by using 1,6-hexanediol dimethacrylate (HDDMA) and zinc dimethacrylate (ZDMA). Poly(ethylene glycol)-star polymer networks (31 arms) were prepared by methacrylation of chain ends and crosslinking with PEGDMA by UV-initiated free-radical polymerization to investigate the effect of functional site density. Molecular imprinting was achieved by crosslinking polymerization in the presence of biologically important templates such as glucose and cholesterol. The ratio of binding of glucose-imprinted films compared to non-imprinted films was 1.3 ± 0.7. Moreover, selectivity of these polymers towards glucose was four-fold compared to galactose and methylglucopyranoside. The difference between imprinted and non-imprinted polymers increased as the crosslinking agent was increased from 5 mol% of polymer to 80 mol%. This, together with studies of HDDMA and ZDMA, proved that the crosslinking agent was an integral part of the imprinting process, as much as the monomers. Increased functional site density of the imprint polymers showed promising behavior in decreasing non-specific binding. Modeling of binding behavior showed faster binding of template to imprinted networks. IR studies showed a decrease in rate of polymerization as a function of template concentration, which was an indication of complexation during polymerization.

10:15 AM M6.3
Barbara Windmeyer.

10:45 AM M6.4
MOLECULARLY IMPRINTED POLYMER HYDROGELS DISPLAYING HIV SUGAR BIORECOGNITION.
Paraskevi Piempi, 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 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 M6.5
MOLECULARLY IMPRINTED POLYMERS USED AS OPTICAL WAVEGUIDES FOR THE DETECTION OF FLUORESCENT ANALYTES: Jennifer Brainer, Dr. Mingdi Yang, 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 operational sensors. Filaments were comprised of polyurethane monomers, cross-linkers, and appropriate solvents to create a porous polymer matrix. Fluorescent polyaromatic hydrocarbons served as template molecules capable of interacting with the monomers through noncovalent, pi-pi forces. Fabrication of these filaments utilized the soft lithography technique of micro-molding in capillaries, MIMC. In this process, a soft elastomeric stamp of poly(dimethyldichlorosilane) 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 films will be discussed.