

Forskningsprogram <input type="checkbox"/>				<input type="checkbox"/>				
SNAP <input checked="" type="checkbox"/>		REPROSAFE <input type="checkbox"/>		FLIPP <input type="checkbox"/>		Inriktning: Ekonomiska styrmedel <input type="checkbox"/>		
				Inriktning: Informationssystem och indikatorer IPP <input type="checkbox"/>				
Projekttitel (svensk): Polycykliska aromatiska kolväten och butadien: Tillförlitlig riskuppskattning baserad på in vivo doser								
Projekttitel (engelsk): Polycyclic aromatic hydrocarbons and butadiene: Reliable cancer risk assessment based on in vivo doses								
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Miljöforskningsnämnden

Ansökan om projektbidrag inom Naturvårdsverkets forskningsprogram

Sammanfattning på svenska strukturerad enligt följande: 1) Projektets betydelse för programmet
2) Miljörelevans och förväntad betydelse för miljöpolitiken 3) Mål och hypotes 4) Metodik och genomförande
5) Kommunikationsinsatser i relation till programmet:

1. Projektets betydelse för programmet: Den högre cancerincidensen i bl.a. tätorter har antagits delvis bero på luftföroreningar som emitteras vid förbränning av olja och andra organiska bränslen. Tidigare arbeten tyder på att polycykliska aromatiska kolväten (PAH, ett stort antal ämnen som förekommer i låga koncentrationer) samt butadien härvid kan spela en relativt stor roll, genom DNA-skadande verkan av reaktiva metaboliter. På grund av komplex mekanism för den carcinogena verkan samt analytiska svårigheter är hittills gjorda uppskattningar av cancerrisker av dessa ämnen mycket osäkra. Detta projekt avser en förbättrad mekanism-baserad riskuppskattning av PAH och butadien, för tillämpning på luftföroreningar från förbränning.
2. Genom tidigare arbeten, samverkan mellan institutioner, samt nytt EU-projekt har förutsättningar skapats för arbete mot förbättrad och mer tillförlitlig riskuppskattning vid låg exponering. Detta projekt avser mekanismer och dos-respons-samband för carcinogen verkan, risker för människors hälsa och prioriteringar av riskreducerande åtgärder. Det är f.n. ej klarlagt vilken roll PAH adsorberade på partiklar spelar för den cancerriskförhöjande verkan av partiklar. På sikt kan hälsoeffekter i olika miljöer övervakas genom analys av cancerinitiatorer i blodprover.
3. Övergripande målsättning är att uppnå en tillförlitlig uppskattning av cancerrisker på grund av exponering för PAH och av butadien i omgivande luft. Eftersom den lineära "no-threshold" hypotesen (LNT) får anses gälla för cancerinitiatorer måste mätningar av doser av genotoxiska ämnen in vivo kunna göras ned till mycket låga exponeringar.
4. Doser bestäms genom analys av "addukter" till blodproteiner. Metoder framtas för mätning av doser av genotoxiska metaboliter och tillämpning i djurförsök, för studier av mekanismer (främst inom EU-projekt) och förbättrad riskuppskattning, och för butadien på exponerade personer. Hög-känsliga LC-MS metoder utvecklas i kombination med användning av selektiva material för fast fas extraktion (särskilt "molecularly imprinted polymers", (MIP) och "restricted access materials" (RAM)).
5. Resultat kommer att kommuniceras på sedvanligt sätt (vetenskapliga publikationer, konferenser etc.) samt genom deltagande i informationstillfällen relaterade till programmet.

	År 2004	År 2005
Summa sökta medel per år i kr:	857 534	850 646

Miljöforskningsnämnden
Ansökan om projektbidrag inom Naturvårdsverkets forskningsprogram

Sökta projektmedel fördelade på kostnadsslag	År 2004 (kr)	År 2005 (kr)
Personalkostnad inkl. soc. avgifter * Margareta Törnqvist, 20 % Doktorandtjänst, 100 %	128 000 328 000	128 000 328 000
Övriga omkostn exkl moms (förbrukningsmtrl, analyser, resor etc)** Förbrukningsmaterial (rör, pipettspetsar, lösningsmedel, etc.) Special kemikalier (reagens, enzymer) MS analyser (operatörskostnad, drift) LC och GC kolonner Djurförsök Dator, Fax, Porto, Språkgranskning Resor (presentation av arbetet)	30 000 30 000 50 000 30 000 10 000 5 000 15 000	30 000 30 000 50 000 20 000 15 000 5 000 15 000
Delsumma av ovanstående poster:	626 000	621 000
Förvaltningspåslag: .37..... %	231 534	229 646
Totalsumma per år: (införs sid. 1):	857 534	850 646

*) Specificera namn, tjänst **) Specificera

Samtliga övriga miljörelaterade projekt för vilka de sökande har beviljats anslag eller söker anslag för 2004-2006. OBS Även EU-finansiering.

Projekttitel	Finansiär	Tidsperiod	Sökt kr	Beviljat kr
Sökande: Cobalamin and mimics.	EU	2004	600 000	
Mekanism-baserad tillämpning för förbättrad cancer uppskattning av PAHs i omgivande luft.	EU	2004	1 200 000	
Validering och standardisering av analytiska metoder för biologisk monitorering av exponering för carcinogena substanser.	EU	2004	250 000	
Gifter bildade till följd av upphettning	EU	2004-2006	1 500 000	
Upptäckt av och cancerriskuppskattning av genotoxiska ämnen i miljön – tillämpning på akrylamid och besläktade ämnen.	Formas	2004	494 000	
Förbättrad riskuppskattning av akrylamid	Cancerfonden	2004	200 000	
Medsökande: Analys av komponenter som bildas vid pappersmassatillverkning och effekten av dessa substanser på bakterietillväxt.	MISTRA	2004-2005	1 450 000	
LC-kolonn för automatiserad membranextraktion.	Bergwalls stiftelse	2004	75 000	

Miljöforskningsnämnden
Ansökan om projektbidrag inom Naturvårdsverkets forskningsprogram

Miljörelaterade projekt för vilka sökande har beviljats anslag för 2000-2003

OBS Även EU-finansiering

Projekttitel	Finansiär	Tidsperiod	Beviljat Kr
Sökande: Cobalamin and mimics.	EC Thematic Network	2002-2003	1 000 000
Mekanism-baserad tillämpning för förbättrad cancer uppskattning av PAHs i omgivande luft.	EU	2002-2003	600 000
Validering och standardisering av analytiska metoder för biologisk monitorering av exponering för carcinogena substanser.	EU	2003	250 000
Upptäckt av och cancerriskuppskattning av genotoxiska ämnen i miljön – tillämpning på akrylamid och besläktade ämnen.	Formas	2003	494 000
Utveckling av system för kvantitativ mätning och identifiering av kemiskt reaktiva ämnen i miljön, med fisk som modell.	Formas	2002-2003	1 148 000
Förbättrad riskuppskattning av akrylamid	Cancerfonden	2003	200 000
Cancerrisker associerade med bioenergianvändning	Energimyndigheten	2001-2003	1 100 000
Medsökande: Utveckling av analytiska tekniker med MIP och RAM	Vetenskapsrådet	2002-2003	520 000

Datum och sökandes underskrift, vilken samtidigt ger Naturvårdsverket tillåtelse att publicera sökandes namn på sin webbplats:	Datum och underskrift av prefekt eller motsvarande med namnförtydligande:
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Ansökan skall bestå av detta formulär jämte högst sex sidor lång projektbeskrivning på **engelska** (strukturerad som den svenska sammanfattningen samt en redovisning av kunskapsläget). Referenser till egna publikationer ges med sifferhänvisning till CV. Andra referenser ges i löpande text. Sökandes och eventuell medsökandes CV får omfatta högst två sidor. Inga bilagor kommer att beaktas vid bedömningen. Ansökan (max 10 A4-sidor, 12 punkters teckenstorlek) skall inlämnas i **original + 15 kopior samt elektroniskt** till ansok@naturvardsverket.se. Häfta ihop ansökan och använd hålat papper. Ansökan skall ha inkommit senast den 15 oktober 2003 till Naturvårdsverket, Forskningssektariatet, 106 48 STOCKHOLM.

Stockholm 2003-10-15

Ansökan till Naturvårdsverket

Forskningsprogram: Hälsoeffekter av
luftföroreningar, SNAP

**POLYCYCLIC AROMATIC HYDROCARBONS AND
BUTADIENE: RELIABLE CANCER RISK ASSESSMENT
BASED ON IN VIVO DOSES**

Sökande: Margareta Törnqvist
Institutionen för miljökemi

Medsökande: Ulrika Nilsson
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Institutionen för analytisk kemi

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POLYCYCLIC AROMATIC HYDROCARBONS AND BUTADIENE: RELIABLE CANCER RISK ASSESSMENT BASED ON IN VIVO DOSES

Contribution to the SNAP research programme

A raised cancer risk in urban areas has been partly associated with pollutants from combustion of oils and other organic fuels, with relatively large contributions from PAH and from butadiene. The cancer risk estimates for these components are, however, very uncertain.

Relevance and expected importance

Cancer risks from organic air pollutants. - During incomplete combustion of organic material several thousands of compounds are emitted, many with potential health effects, for instance increased cancer risks. Butadiene and polycyclic aromatic hydrocarbons (PAH) are, according to preliminary estimates in the beginning of the 1990-ies, important contributors to cancer risk from air pollutants (1) and from emissions from wood burning (2).

In these early estimates of cancer risks from emissions from wood burning a “worst case” scenario was modelled and no measurements of exposure levels existed. Within the frame of a project (Bioenergy-Health-Environment, BHM) from Swedish Energy Agency the pollution level in an area (Lycksele) heavily polluted by emissions from wood burning have been measured. It was shown that during the winter period the air concentrations of PAH were several-fold higher than earlier estimated as the “worst case” for wood burning and that the exposure levels of butadiene were lower than earlier estimated (3).

Based on these levels, and improved risk coefficients, it was estimated that the cancer risk from PAH is not negligible and that the risk from butadiene is lower than earlier estimated (3, 4). The cancer risk estimates are, however, still uncertain, because of uncertainties in the risk coefficients (up to a factor of 10). In order to reach a more reliable risk estimate the most active PAH have to be identified, and the relative contribution to the risk associated with exposure to those compounds has to be determined. Furthermore, it is unclear to which extent adsorbed PAH etc. on particles contribute to the cancer risk associated with exposure to particles. The uncertainty in the risk value for butadiene should be reduced.

Improved estimation of both the cancer risk and the contribution to total health risks give a basis for decisions and priority setting by authorities.

Aim

The main aim of the project is an improvement of the cancer risk estimation of the above components, based on new studies of action mechanism and dose response, and new more sensitive, analytical procedures.

Background

Cancer risk models.- An increase of the cancer risk (ΔP , probability increment of tumour development), may in principle be due to factors of two kinds. One concerns factors that lead to an increase of the mutation frequency above a ubiquitous background. In this case the cancer risk increase would be proportional to the in vivo dose of the genotoxic agent without any no-effect threshold (“LNT” hypothesis) (5). Factors of the second kind increase the cancer risk by enhancing the propensity for growth and clonal expansion, increasing the risk at doses exceeding a no-effect threshold. This means that such “promotive” factors, alone, are not expected to contribute to risk at low or very low doses.

Early models for risk estimation have been based on the increase of the fraction of animals with tumours per unit of dose in mg per kg body weight observed in experiments with rats or mice. Often linear risk coefficients have been inferred and applied directly to exposed

humans. This simplified assumption of equality of humans and rodents has been applied by WHO. In its risk-estimation procedure US EPA (6) is now assuming linearity, and allow for species differences by assuming the risk to be proportional to dose per unit body surface area.

Within a research line, now at Dept. of Environmental Chemistry at Stockholm University, a linear cancer risk model has been developed avoiding such default assumption for extrapolation between species. Differences in metabolism to ultimate genotoxic species is allowed for by measurement of in vivo doses in test animals and exposed humans. This model is already applied for cancer risks from ionising radiation (7) according to:

$$\Delta P = \beta \times D \times P^{\circ} \quad (1)$$

In this model the risk coefficient (β) is an estimate of the genotoxic potential of the carcinogen. Accordingly cancer risk increments (ΔP) at low doses will be proportional to doses (D) of the ultimate genotoxic agent in target organs and to the background incidence (P°). (P° vary between organs, strains, species, ages etc.; in the model P° for site-specific or total incidence implicitly reflect the background of “promotive”, often inherited conditions, interacting with the background mutation frequency). The in vivo dose measurement allows for differences in metabolism in the extrapolation between species. The model has been shown applicable to animal cancer test data for a few chemical carcinogens and validated for ethylene oxide (7).

Polycyclic aromatic hydrocarbons.- PAH constitute a wide class of compounds, with benzo(a)pyrene (BaP) as a well-studied indicator. A general background exposure occurs through ambient air pollution and diet. According to earlier estimates the domestic heating, particularly wood burning, is the largest emission source of PAH in Sweden (review ref. 8).

A range of individual PAH is classified as possible or probable human carcinogens. However, quantitative risk estimates are so far very uncertain. Epidemiological data on lung cancer in coke-oven workers are still the best basis for quantitative cancer risk estimates, but these results are very uncertain due to differences between PAH profiles, etc. Estimation of cancer risk from animal cancer tests with individual PAH has considerable uncertainties because PAH may provoke a cancer risk by mutagenesis or promotion or a combination of both. According to the suggested model (1), initiation (mutation) may be caused by electrophilic reactive intermediates at low doses, in a linear dose-response relationship without a threshold dose. At higher exposure levels, above a threshold, “promotion” may occur, perhaps with the non-metabolised PAH as the cause (8, 9).

In human exposure (at low levels), most probably, the genotoxicity of PAHs is the dominating mechanism in its cancer-risk-increasing action. Therefore, for a reliable risk estimate from animal cancer tests, the different action mechanisms have to be evaluated separately. In the development and evaluation of reliable risk models for PAH, measurement of doses of reactive and mutagenic metabolites is of utmost importance.

Butadiene.- 1,3-Butadiene is a component in emissions from combustion of organic material and therefore occurs as an air pollutant. It is an established rodent carcinogen, mouse being more sensitive than rat. Butadiene is classified by IARC as a probable human carcinogen, and is considered by the US EPA to be a human carcinogen (10). The human lifetime cancer risk for chronic exposure to BD has recently been re-estimated to 0.08 per ppm by US EPA, based on increased leukaemia risks observed in occupationally exposed workers (10). This coefficient is 4 times lower than the earlier value from cancer tests in mice. The cancer risk coefficient is, however, still very uncertain, being limited to one study on leukemia incidence.

Risk assessment from cancer tests of butadiene has been difficult, partly because the sensitivity of mouse and rat differs by a factor of 100-1000 (cf. 11, 12). The mechanism of this difference in butadiene-induced carcinogenicity has been suggested to be due to species-

related differences in the enzymatic production and detoxification of reactive metabolites. Diepoxybutane exhibits, because its ability to form cross-links in DNA, a very high mutagenic potential, compared to simultaneously formed monoepoxides (see Fig. 1).

Therefore knowledge about the dose (that is concentration x time) of diepoxybutane in mice and rats used in cancer tests of butadiene, and in the next step in butadiene-exposed humans, are of basic importance for improved cancer risk assessment of butadiene.

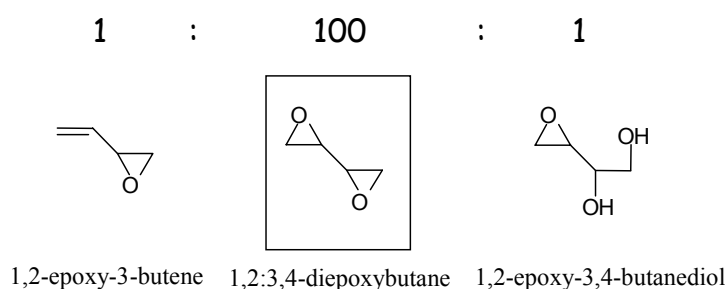


Fig. 1. Relative genotoxic potency of epoxides formed through metabolism of 1,3-butadiene.

Methods for dose measurement.- In our risk model (1) in vivo dose of the genotoxic agent is a corner-stone. In vivo doses are measured in blood through adducts to blood proteins (hemoglobin or serum albumin) in the test animal species and in humans. Methods for determination of protein adducts by mass spectrometry and their applications are recently been reviewed (13).

The N-alkyl Edman method, for measurement of adducts from electrophilically reactive compounds to N-terminal valine in Hb through gas chromatography-mass spectrometry (GC/MS) analysis, developed at SU, has been applied internationally for measurement of exposure and in vivo doses for a range of low-molecular weight compounds. With this method a high sensitivity has been achieved, permitting detection, e.g., of background exposures. This method is, however, not applicable to all electrophilic compounds. Therefore, efforts have been devoted to development of alternative methods for adduct measurement, to a large extent based on liquid chromatography-mass spectrometric analysis (LC-MS).

Methods and accomplishment

Butadiene.- For cancer risk estimation of butadiene it is a prerequisite to measure the in vivo dose of diepoxybutane. Adducts from the monofunctional epoxy-metabolites from butadiene, but not from diepoxybutane, could be measured by the above N-alkyl Edman method. A method based on analysis by LC/MS of diepoxybutane adducts to N-termini of Hb after enzymatic cleavage and enrichment of modified N-terminal heptapeptides have been developed within a Ph.D.-project. Quantitative analysis of Hb adducts in samples from diepoxybutane-treated or epoxybutene-treated mice and rats has been performed (14-16). Studies are now ongoing on Hb samples from mice and rats exposed to butadiene. Although, results indicate large species differences in metabolism (in agreement with the large difference between species in the carcinogenic action of butadiene), it is doubtful whether sufficient sensitivity is attainable with this method for measurement of diepoxybutane doses in butadiene-exposed rodents. Still more this applies to samples from butadiene-exposed humans. To attain higher sensitivity an alternative method development based on

hydrazinolysis of Hb and enrichment of the diepoxybutane adduct has been initiated (see below), for analysis by GC-MS or LC-MS. After evaluation this method will be applied to samples from butadiene-exposed rodents for a evaluation of cancer risk model and better risk assessment. In the next step the method will be tested at samples from humans occupationally exposed to butadien for evaluation of the relative doses of diepoxybutane.

PAH.- As for PAH this research group participates in an EU project (AMBIPAH, 2003-06) which studies basic problems and mechanisms involved in carcinogenesis of PAH. These are e.g. cancer promotion and simultaneous induction of bioactivating enzymes, expected to follow a thresholded dose response and with interactions with other factors. Five selected PAHs (including BaP and fluoranthene) are studied by different methods (in vivo and in vitro) with regard to promotive action (microarray for gene expression) and mutagenicity (in vitro and short-term tests in vivo in mouse). Five models of PAH are studied. The accessible material from the animal experiments with studies of promotion and mutagenic potency of 5 PAH is most valuable for clarification of mechanisms of action. Tissue samples will be collected for different doses and different time points.

This group will primarily measure doses of genotoxic diepoxides in blood through adducts to blood proteins from the in vivo studies in mice. In parallel work DNA adducts are studied. With regard protein adducts, first hand of BaP and FA, will be studied. As a first step protein adducts after treatment of animals with radio-labeled compounds, available for BaP and FA, are studied. In the next step methods for enrichment and analysis by LC-MS will be explored and developed (see below).

Within the budget frame of the ongoing EU project the resources available will only permit very limited exploration of LC/MS analysis for the analysis of diepoxides of BaP. This additional project in collaboration with Dept. of Analytical Chemistry would focus on development (with new techniques)of methods for LC-MS: a)Towards analytical methods for diepoxides of PAH with high sensitivity and for quantitative work; b) Application to several of the model PAH studied within the EU-project; c) Application to animal tests within the EU-project for studies clarification of mechanisms and dose-response relationships. d) Testing of methods for application to humans.

In studies of occupationally exposed humans protein adducts of diepoxides of BaP have been measured by GC/MS after cleavage through mild hydrolysis mainly of PAH tetrols esterified with carboxyl groups (see refs. in 8). Due to spontaneous hydrolysis of these esters this approach is not useful for dosimetry. Therefore, stable adducts useful for measurement in both humans and rodents have been sought (17). Method development has focused on measurement by LC/MS of adducts from diepoxide of BaP to histidine in serum albumin (SA) after hydrazinolysis of SA and enrichment by solid phase extraction (SPE) (18). This procedure has been shown to work in experiments with mice, but probably with insufficient reproducibility and sensitivity (17 and to be published). A new development, has been initiated based on cleavage of SA or Hb by alkaline or enzymatic hydrolysis and enrichment of PAH adducts, first-hand to histidine in SA, and analysis by LC-MS. Adducts to SA treated in vitro with diepoxide of BaP have been isolated and identified by LC-MS. At present samples from rats treated i.p. with BaP is isolated for analysis. New procedures for isolation of adducts will be explored (see below).

Application of new analytical methodology.- In this project, new selective materials for solid phase extraction (SPE) and liquid chromatography (HPLC) will be used together with mass spectrometry (LC-MS) in order to obtain the selectivity and sensitivity required and also to reduce the time needed for the analysis of the complex blood samples. LC-MS with electrospray ionization (ESI) or atmospheric pressure ionization (APCI) has become the

primary analytical method for several environmental and bioanalytical problems due to a very high selectivity especially when tandem mass spectrometry (MS-MS) is used. However, problems such as signal suppression due to co-eluting matrix, such as proteins, are common especially in ESI. Clean up of the sample and some kind of chromatographic separation are often required to obtain a sufficient sensitivity and to ensure correct quantitative determination of the analyte by LC-MS.

Selective removal of proteins and other large biomolecules usually involves their denaturation by addition of an organic solvent or acidifying of the sample, followed by centrifugation. The disadvantage of this technique is the inherent risk that solutes will be included and co-precipitated, leading to a loss of precision, accuracy and sensitivity. Developing rapid and sensitive analytical procedures using LC-MS, the use of selective solid-phase extraction (SPE) columns can be considered a primary choice in order to decrease the matrix effects in the LC-MS interfaces. Restricted access materials (RAM) are an example of these materials, which allow a direct and repetitive injection of untreated biofluids (e. g. hemolyzed blood, plasma, serum, milk, fermentation broth, supernatants of cell cultures and tissue homogenates) (19-27). Molecular Imprinting (MI) technology enables the preparation of materials with host sites that recognize specific guest molecules, analogous to the "lock-and-key" paradigm of antibodies and enzymes (28-42). The advantages of these materials are: (a) a degree of specificity in some cases approaching that of antibodies, (b) great temporal and thermal stability, and (c) wide applicability with complex matrices such as biological or environmental samples and in multi-component analysis.

Preparation and use of selective SPE materials such as molecularly imprinted polymers (MIPs) and restricted access material (RAM) has been the focus of our analytical research for several years. A molecularly imprinted polymer solid phase extraction (MISPE) method has been developed for extraction of a flame retardant metabolite, diphenyl phosphate (DPhP) with high recoveries and repeatability from urine samples (43-44). Compared to a commercial SPE material (a mixed-mode anion exchanger) the MIP yields similar recoveries but extracts of much higher purity. Another example is the development of an on-line SPE-LC/MS/MS method using RAM for the simultaneous determination of nine organophosphate esters in untreated human blood plasma (45). The detection limits were in the range of 0.2-1.8 ng/ml of plasma and the total analysis time was only 27 minutes.

At present a MISPE material has been synthesized for extraction of the N-terminal hydrazinolysis product of the Hb-diepoxbutane adduct. The hydrazinolysis produces a very complex mixture of cleaved peptide chains, thus selective clean-up is needed to enable MS detection of the target analyte occurring at low concentrations. The imprinted polymer was prepared in acetonitrile using methacrylic acid as the functional monomer, ethylene glycol dimethacrylate as the cross-linker and a structural analogue of the analyte as the template molecule. The polymer is now under evaluation regarding recoveries and repeatability. The preliminary results are promising and show a highly stable material and a high overall sensitivity of the MISPE-LC-ESI-MS method. The estimated limit of detection is 50 pg.

Collaboration, resources

M.T. is participant in an EU project (2003-06) concerning mechanism-based risk assessment of PAH. This project contributes to important contacts (coordinator S. Kyrtopoulos, Athens), collaboration, and with valuable material from animal experiments to be studied within this project.

Earlier work in MT's group both with regard to cancer risk model, development of methods for in vivo dosimetry through measurement of protein adducts for the studied compounds gives a solid platform for the project. The collaboration with coapplicants U.N. and C.C, with experience of new analytical techniques, is further strengthening the project.

Department of Environmental Chemistry is since 2002 located in the same building as the Department of Analytical Chemistry, in the Arrhenius Laboratory at Stockholm University. This nearness facilitates the already initiated collaboration. Furthermore, the co-operation also gives access to a large instrument park. The MS facility at the Dept. of Analytical chemistry, SU, also includes the Stockholm University Proteomic Facility. The facility at the present holds eleven mass spectrometers such as are MALDI, GC-MS, LC-MS and LC-GC-MS instruments, which includes single quadrupole, triple quadrupole, ion trap, and time of flight mass analysers. The department is experienced in bioanalytical and environmental MS applications, both on GC-MS and LC-MS.

References

1. Törnqvist, M. and Ehrenberg, L. (1994) On cancer risk estimation of urban air pollution. *Environ. Health Perspect.* 102, Suppl. 4, 173-182.
2. Ehrenberg, L. and Törnqvist, M. Småskalig vedeldning och cancer risker. Kunskapssammanställning. SNV. Rapport 4224, 1993.
3. Biobränsle-Hälsa-Miljö, "Utsläpp och luftkvalitet" och "Småskalig Energianvändning", Prel. slutrapport till Energimyndigheten, juli 2003.
4. Biobränsle-Hälsa-Miljö, Hälsoklustret, Kapitel. Cancer risker från emissioner från förbränning av biomassa (Törnqvist, M and Fred, C., förf.). Rapport till Energimyndigheten.
5. Törnqvist, M. and Ehrenberg, L. (2001) Estimation of cancer risk due to environmental chemicals based on in vivo dose measurement. *J. Environ. Pathol. Toxicol. Oncol.* 20 (4) 263-271.
6. USEPA (1999) Guidelines for Carcinogen Risk Assessment, (NCEA-F-0644, July 1999) at www.epa.gov.
7. Granath, F., Vaca, C.E., Ehrenberg, L.G. and Törnqvist, M. Å. (1999) Cancer risk estimation of genotoxic chemicals based on target dose and a multiplicative model. *Risk Analysis* 19, 309-320.
8. Boström, C.E., Gerde, P., Hanberg, A., Jernström, B., Johansson, C., Kyrklund, T., Rannug, A., Törnqvist, M., Victorin, K. and Westerholm, R. (2002) Cancer risk assessment, indicators and guidelines for polycyclic aromatic hydrocarbons (PAH) in the ambient air. *Environ. Health Perspect.* 110, Suppl. 3, 451-489.
9. Sjögren, M., Ehrenberg, L., and Rannug, U. (1996) Relevance of different biological assays in assessing initiating and promoting properties of polycyclic aromatic hydrocarbons with respect to carcinogenic potency. *Mutat. Res.* 358, 97-112.
10. US EPA, U.S. Environmental Protection Agency (2002) Health Assessment of 1,3-Butadiene. National Center for Environmental Assessment, Office of Research and Development, Washington, DC.
11. Jackson, M.A., Stack, H.F., Rice, J.M., and Waters, M.D. (2000) A review of the genetic and related effects of 1,3-butadiene in rodents and humans. *Mutat. Res.* 462, 181-213.
12. Swenberg, J.A. et al. (2001) Using DNA and hemoglobin adducts to improve the risk assessment of butadiene. *Chem. Biol. Interact.* 135-136, 387-403.
13. Törnqvist, M., Fred, C., Haglund, J., Helleberg, H., Paulsson, B. and Rydberg, P. (2002) Protein adducts: quantitative and qualitative aspects of their formation, analysis and applications. *J. Chromatogr. B*, 778, 279-308.
14. Kautiainen, A., Fred, C., Rydberg, P. and Törnqvist, M. (2000) A liquid chromatography tandem mass spectrometric method for in vivo dose monitoring of diepoxybutane, a metabolite of butadiene. *Rapid Commun. Mass Spectrom.* 14, 1848-1853.
15. Fred, C., Kautiainen, A., Athanassiadis, I. and Törnqvist, M. (2003) Hemoglobin adduct levels in rat and mouse after treatment with 1,2,3,4-diepoxybutane. *Chem. Res. Tox.* (submitted).
16. Fred, C., Grawé J., Cantillana, T., Henderson A., Björkman, H., Golding, B. T. and Törnqvist, M. (2003) Hemoglobin adducts and micronucleus frequencies in mouse and rat after epoxybutene or isoprene monoxide treatment. (manuscript)
17. Helleberg, H. (2001) Biomarkers aiming at cancer risk estimation of polycyclic aromatic hydrocarbons. Ph.D. thesis, Stockholm University, Stockholm.
18. Helleberg, H. and Törnqvist, M. (2000) A new approach for measuring protein adducts from benzo[a]pyrene dilepoxide. *Rapid Commun. Mass Spect.* 14, 1644-1653.
19. Wagner, K., Miliotis, T., Marko-Varga, G., Bischoff, R., Unger, K.K. (2002) *Analytical Chemistry* 74(4), 809-820.
20. Chiap, P., Rbeida, O., Christiaens, B., Hubert, P., Lubda, D., Boos, K.-S. and Crommen, J. (2002) *Journal of Chromatography A*, 975(1), 145-155.
21. Petrovic, M., Tavazzi, S. and Barcelo, D. (2002) *Journal of Chromatography A*, 971(1-2), 37-45.
22. Koeber, Robert; Fleischer, Claudia; Lanza, Francesa; Boos, Karl-Siegfried; Sellergren, Boerje; Barcelo, Damia. *Analytical Chemistry* (2001), 73(11), 2437-2444.

23. Lopez de Alda, M.J., Diaz-Cruz, S., Petrovic, M. and Barcelo, D. (2003) *Journal of Chromatography A*, 1000(1-2), 503-526.
24. Poole, C.F. (2003) *Trends in Analytical Chemistry*, 22(6), 362-373.
25. Hogendoorn, E. and Van Zoonen, P. (2000) *Journal of Chromatography A* 892(1+2), 435-453.
26. Boos, K.-S. and Grimm, C.-H. (1999) *Trends in Analytical Chemistry* 18(3), 175-180.
27. Dorsey, J.G., Foley, J. P., Cooper, W.T., Barford, R. A. and Howard G. (1992) *Analytical Chemistry* 64(12), 353R-89R.
28. Bartsch, R. A., Maeda, M., Eds. *Molecular and Ionic Recognition with Imprinted Polymers*; American Chemical Society: Washington, D. C., 1998.
29. Mayes, A. G. and Mosbach, K. (1997) *Trends Anal. Chem.*, 16, 321-332.
30. Vlatakis, S. and Arnold, F. H. (1995) *Curr. Opin. Biotechnol.*, 6, 218-224.
31. Wulff, G. A. *Chem., Int. Ed. Engl.*(1995) 34, 1812-1832.
32. Mosbach, K., Yu, Y., Andersch, J. and Ye, L. (2001) *Journal of the American Chemical Society*, 123(49), 12420-12421.
33. Haginaka, J.S. (2000) *Anal. Chem.* 72(21), 5206-10.
34. Takeuchi, T., Fukuma, D. and Matsui, J. (1999) *Anal. Chem.* 71(2), 285-290.
35. Krull, I.S. edited by Reid, E., Hill, H.M. and Wilson, I.D. (1999) *Trends in Analytical Chemistry* 18(6), 439-440.
36. Owens, P. K., Karlsson, L., Lutz, E. S. M. and Andersson, L. I. (1999) *Trends in Analytical Chemistry* 18(3), 146-154.
37. Shi, H., Tsai, W. B., Garrison, M. D., Ferrari, S. and Ratner, B. D. (1999) *Nature*, 398(6728), 593-7.
38. Sellergren, B. (1997) *Trends in Analytical Chemistry*, 16(6), 310-320.
39. Kempe, M., Mosbach, K. (1995) *Journal of Chromatography A*, 694(1), 3-13.
40. Koster, E. H. M., Crescenzi, C., den Hoedt, W., Ensing, K. and de Jong, G. J. (2001) *Analytical Chemistry* 73:3140-3145.
41. Crescenzi, C., Bayouhd, S., Cormack, P. A. G., Klein, T. and Ensing, K. (2001) *Analytical Chemistry* 73:2171-2177.
42. Ellwanger, A., Karlsson, L., Owens, P. K., Berggren, C., Crescenzi, C., Ensing, K., Bayouhd, S., Cormack, P., Sherrington, D. and Sellergren, B. (2001) *Analyst* 126:784-792.
43. Möller, K., Nilsson, U. and Crescenzi, C. (2003) *Analytical and Bioanalytical Chemistry* . Original Paper ABC-00459-2003.R1 (accepted for publication).
44. Möller, K., Nilsson, U. and Crescenzi, C. (2001) *Journal of Chromatography A*, 938:121-130.
45. Amini, N., Crescenzi, C. (2003) *Journal of Chromatography B*, 795(2), 245-256.

CURRICULUM VITAE

Margareta Å. Törnqvist

Associate prof. and position as university lecturer at Dept. of Environmental Chemistry at Stockholm University.

Born 1953 at Roslagsbro, Stockholm county, Sweden.

Graduated (Master of Engineering) from the Royal Institute of Technology, Stockholm, in chemistry – biochemistry. Since then worked at Stockholm University; presented the Ph.D. thesis in physical biology, at Dept. of Radiobiology 1989. Appointed as university lecturer at this Dept. and Dept. of Environmental Chemistry since 1988. Associate Professor at Dept. of Environmental Chemistry since 1992.

At present research leader for the cross-scientific “Risk group” (with about ten participants) at the Dept. of Environmental Chemistry at Stockholm University. Main supervisor for five and co-supervisor for one graduated Ph.D. and two graduated Ph.Lic. At present supervisor for two Ph.D students.

More than 100 scientific publications, mainly on methods for measurement of *in vivo* doses of carcinogens (as hemoglobin adducts), procedures for cancer risk estimation and their applications to urban air pollution, occupational exposures on identification and quantification of background carcinogens.

Member (since 1996) of the Swedish Toxicological Advisory Board, Stockholm; Member (since 2000) of the National Committee for Radiological Protection Research of the Royal Academy of Sciences; Member (since 2002) in the Royal Academy of Engineering Science (IVA). Earlier member of several committees and of several national working groups *e.g.* on urban air pollutants and on accidental release of harmful chemicals. (Co)organiser of several national seminars and a few international conferences (*e.g.* on mass spectrometry).

Invited speaker at about 40 international conferences and symposia, organized by among others the UN organizations the International Agency for Research on Cancer and the International Atomic Energy Agency, to the International Conference on Environmental Mutagens, and to the Institute of Food Technologists.

Awarded (1997) the Adolph A. Kammer Merit in Authorship Award by the American College of Occupational and Environmental Medicine. Received the “Environmental awards” of the Swedish Association for Graduate Engineers, 1997 and 2000. Received the “Environmental Medicine” award from the Cancer and Allergy Foundation 2003.

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Personal

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11346 Stockholm, Sweden

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Education and Qualifications:

1994-97 University of Rome "La Sapienza", Italy

Ph.D. in Analytical Chemistry.

Thesis: *"Multiresidue Method (MRM) and Selective Multiresidue Methods (SMRMs) for analyzing Pesticides Traces in Environmental Water by HPLC-MS"*.

1993 University of Rome "La Sapienza", Italy

Degree in Chemistry, (five years).

Thesis: *"Solid Phase Extraction of Polar Pesticides and HPLC determination"*.

Specialties:

HPLC/MS and MS/MS specialist. Analytical method development.

Traces analysis of drugs, pesticides, surfactants and related compounds in environmental waters (surface, ground, sea), soil and vegetables.

Traces analysis of drugs in biological matrices, matrix solid phase dispersion.

Solid Phase Extraction (SPE) with non-selective and selective materials, Molecularly Imprinted Polymers (MIPs), Analysis of Sulfonated Polymers.

Accelerated solvent and sub-critical water extraction.

HPLC with MS, UV, FL, electrochemical detector.

Computer skills:

Operating system: UNIX, MS-DOS, Macintosh, Windows NT/95/98.

Networking: TCP/IP, Microsoft, Internet servers.

Good knowledge of word processor, data sheet, data base and DAQ.

Work Experience:

2000-05 University of Stockholm, Sweden,
Department of Analytical Chemistry,
Assistant Professor

1999-00 University of Groningen, The Netherlands,
University centre for Pharmacy,
Visiting Researcher

MICA EU project, Molecular Imprinting techniques for efficient methods in Chemical Analysis

1998-99 University of Venice, Italy.

ANACAD EU project, Analysis and fate of concrete admixtures in wastewater: sulfonated naphthalene-formaldehyde-condensates (SNFC), sulfonated melamine-formaldehyde-condensates (SMFC), ligninesulfonates (LS). Collaboration contract.

1994-95 University of Venice, Italy, Dept. of Environmental Science, Analysis of surfactant and biointermediates in environmental water by HPLC-MS. Collaboration contract.

Grants and Awards:

- Ph.D. grant in chemical science 1994-1997
- Vieweg Publishing, Wiesbaden, travel grant for Ph.D. students to attend the XXI International Symposium on Chromatography (ISC), September, 15-20 1996, Stuttgart, Germany.

Selected Papers

- 31 N. Amini, C. Crescenzi 2003. *Feasibility of an on-line restricted access material/liquid chromatography/tandem mass spectrometry method in the rapid and sensitive determination of organophosphorus triesters in human blood plasma*. **Journal of Chromatography, B** accepted 16 July 2003
- 30 C. Sánchez, H. C., A. Colmsjö, C. Crescenzi, R. Batlle. 2003. *Determination of nitroaromatic compounds in air samples at femtogram level using C18 membrane sampling and on-line extraction with LC-MS*. **Analytical Chemistry ACS ASAP**.
- 29 Batlle, R., H. Carlsson, P. Tollbaeck, A. Colmsjoe, and C. Crescenzi. 2003. *Enhanced Detection of Nitroaromatic Explosive Vapors Combining Solid-Phase Extraction-Air Sampling, Supercritical Fluid Extraction, and Large-Volume Injection-GC*. **Analytical Chemistry**: 75:3137-3144.
- 28 Pojana, G., C. Carrer, F. Cammarata, A. Marcomini, and C. Crescenzi. 2002. *HPLC Determination of Sulphonated Melamines-Formaldehyde Condensates (SMFC) and Lignosulphonates (LS) in Drinking and Ground Waters*. **International Journal of Environmental Analytical Chemistry** 83:51-63.
- 27 Batlle, R., H. Carlsson, E. Holmgren, A. Colmsjo, and C. Crescenzi. 2002. *On-line coupling of supercritical fluid extraction with high-performance liquid chromatography for the determination of explosives in vapor phases*. **Journal of Chromatography, A** 963:73-82.
- 26 Moller, K., U. Nilsson, and C. Crescenzi. 2001. *Synthesis and evaluation of molecularly imprinted polymers for extracting hydrolysis products of organophosphate flame retardants*. **Journal of Chromatography, A** 938:121-130.
- 25 Koster, E. H. M., C. Crescenzi, W. den Hoedt, K. Ensing, and G. J. de Jong. 2001. *Fibers coated with molecularly imprinted polymers for solid-phase microextraction*. **Analytical Chemistry** 73:3140-3145.
- 24 Crescenzi, C., S. Bayouhd, P. A. G. Cormack, T. Klein, and K. Ensing. 2001. *Determination of Clenbuterol in Bovine Liver by Combining Matrix Solid-Phase Dispersion and Molecularly Imprinted Solid-Phase Extraction Followed by Liquid Chromatography/Electrospray Ion Trap Multiple-Stage Mass Spectrometry*. **Analytical Chemistry** 73:2171-2177.
- 23 Ellwanger, A., L. Karlsson, P. K. Owens, C. Berggren, C. Crescenzi, K. Ensing, S. Bayouhd, P. Cormack, D. Sherrington, and B. Sellergren. 2001. *Evaluation of methods aimed at complete removal of template from molecularly imprinted polymers*. **Analyst** 126:784-792.
- 22 Crescenzi, C., A. Di Corcia, A. Marcomini, G. Pojana, and R. Samperi. 2001. *Method development for trace determination of poly(naphthalenesulfonate)-type pollutants in water by liquid chromatography-electrospray mass spectrometry*. **Journal of Chromatography, A** 923:97-105.
- 21 Carunchio, F., C. Crescenzi, A. M. Girelli, A. Messina, and A. M. Tarola. 2001. *Oxidation of ferulic acid by laccase: identification of the products and inhibitory effects of some dipeptides*. **Talanta** 55:189-200.
- 20 Caracciolo, A. B., G. Giuliano, A. Di Corcia, C. Crescenzi, and C. Silvestri. 2001. *Microbial degradation of terbuthylazine in surface soil and subsoil at two different temperatures*. **Bulletin of Environmental Contamination and Toxicology** 67:815-820.
- 19 Crescenzi, C. 2000. *Analysis of s-Triazine Herbicides and Their Transformation Products*. in R. A. Meyers, editor. **Encyclopedia of Analytical Chemistry: Instrumentation and Applications**. John Wiley & Sons Ltd, Baffins Lane, Chichester, West Sussex, PO19 1UD, England.

- 18 Di Corcia, A., R. Cavallo, C. Crescenzi, and M. Nazzari. 2000. *Occurrence and Abundance of Dicarboxylated Metabolites of Nonylphenol Polyethoxylate Surfactants in Treated Sewages*. **Environmental Science and Technology** 34:3914-3919.
- 17 Crescenzi, C., A. Di Corcia, M. Nazzari, and R. Samperi. 2000. *Hot Phosphate-Buffered Water Extraction Coupled On-Line with Liquid Chromatography/Mass Spectrometry for Analyzing Contaminants in Soil*. **Analytical Chemistry** 72:3050-3055.
- 16 Di Corcia, A., A. B. Caracciolo, C. Crescenzi, G. Giuliano, S. Murtas, and R. Samperi. 1999. *Subcritical Water Extraction Followed by Liquid Chromatography Mass Spectrometry for Determining Terbutylazine and Its Metabolites in Aged and Incubated Soils*. **Environmental Science and Technology** 33:3271-3277.
- 15 Di Corcia, A., A. Costantino, C. Crescenzi, and R. Samperi. 1999. *Quantification of phenylurea herbicides and their free and humic acid-associated metabolites in natural waters*. **Journal of Chromatography, A** 852:465-474.
- 14 Di Corcia, A., F. Casassa, C. Crescenzi, A. Marcomini, and R. Samperi. 1999. *Investigation of the Fate of Linear Alkyl Benzenesulfonates and Coproducts in a Laboratory Biodegradation Test by Using Liquid Chromatography/Mass Spectrometry*. **Environmental Science and Technology** 33:4112-4118.
- 13 Crescenzi, C., G. D'Ascenzo, A. Di Corcia, M. Nazzari, S. Marchese, and R. Samperi. 1999. *Multiresidue herbicide analysis in soil: subcritical water extraction with an online sorbent trap*. **Analytical Chemistry** 71:2157-2163.
- 12 Di Corcia, A., C. Crescenzi, A. Marcomini, and R. Samperi. 1998. *Liquid Chromatography-Electrospray-Mass Spectrometry as a Valuable Tool for Characterizing Biodegradation Intermediates of Branched Alcohol Ethoxylate Surfactants*. **Environmental Science and Technology** 32:711-718.
- 11 Di Corcia, A., A. Costantino, C. Crescenzi, E. Marinoni, and R. Samperi. 1998. *Characterization of Recalcitrant Intermediates from Biotransformation of the Branched Alkyl Side Chain of Nonylphenol Ethoxylate Surfactants*. **Environmental Science and Technology** 32:2401-2409.
- 10 Di Corcia, A., C. Crescenzi, E. Guerriero, and R. Samperi. 1997. *Ultratrace Determination of Atrazine and Its Six Major Degradation Products in Water by Solid-Phase Extraction and Liquid Chromatography-Electrospray/Mass Spectrometry*. **Environmental Science and Technology** 31:1658-1663.
- 9 Di Corcia, A., C. Crescenzi, R. Samperi, and L. Scappaticcio. 1997. *Trace Analysis of Sulfonylurea Herbicides in Water: Extraction and Purification by a Carbograph 4 Cartridge, Followed by Liquid Chromatography with UV Detection, and Confirmatory Analysis by an Electrospray/Mass Detector*. **Analytical Chemistry** 69:2819-2826.
- 8 Crescenzi, C., A. Di Corcia, and R. Samperi. 1997. *Development of a Multiresidue Method for Analyzing Pesticide Traces in Water Based on Solid-Phase Extraction and Electrospray Liquid Chromatography Mass Spectrometry*. **Environmental Science and Technology** 31:479-488.
- 7 Crescenzi, C., A. Di Corcia, A. Marcomini, and R. Samperi. 1997. *Detection of Poly(Ethylene Glycols) and Related Acidic Forms in Environmental Waters By Liquid Chromatography/Electrospray/Mass Spectrometry*. **Environmental Science and Technology** 31:2679-2685.
- 6 Di Corcia, A., C. Crescenzi, A. Lagana, and E. Sebastiani. 1996. *Evaluation of a Method Based on Liquid Chromatography/Electrospray/Mass Spectrometry for Analyzing Carbamate Insecticides in*

Fruits and Vegetables. **Journal of Agricultural and Food Chemistry** 44:1930-1938.

- 5 Crescenzi, C., A. Di Corcia, E. Marchiori, R. Samperi, and A. Marcomini. 1996. *Simultaneous determination of alkylbenzenesulfonates and dialkyltetralinsulfonates in water by liquid chromatography*. **Water Research** 30:722-730.
- 4 Crescenzi, C., A. Di Corcia, G. Passariello, R. Samperi, and M. I. Turnes Carou. 1996. *Evaluation of two new examples of graphitized carbon blacks for use in solid-phase extraction cartridges*. **Journal of Chromatography, A** 733:41-55.
- 3 Crescenzi, C., A. Di Corcia, R. Samperi, and A. Marcomini. 1995. *Determination of Nonionic Polyethoxylate Surfactants in Environmental Waters by Liquid Chromatography/Electrospray Mass Spectrometry*. **Analytical Chemistry** 67:1797-1804.
- 2 Crescenzi, C., A. Di Corcia, S. Marchese, and R. Samperi. 1995. *Determination of Acidic Pesticides in Water by a Benchtop Electrospray Liquid Chromatography Mass Spectrometer*. **Analytical Chemistry** 67:1968-1975.
- 1 Crescenzi, C., A. Di Corcia, M. D. Madbouly, and R. Samperi. 1995. *Pesticide stability studies upon storage in a graphitized carbon black extraction cartridge*. **Environmental Science and Technology** 29:2185-2190.

Kortfattad CV för Ulrika Nilsson, medsökande.

Namn: Ulrika Nilsson
Adress: Kungshög, 179 96 Svartsjö
Personnummer: 581226-7861
Akademisk titel: Fil. dr.
Anställning: Forskare
Arbetsplats: Institutionen för Analytisk Kemi, Stockholms Universitet.

Disputerade 1992 vid Institutionen Analytisk kemi, Stockholms universitet med avhandlingen "Properties of some chlorinated polycyclic aromatic hydrocarbons with respect to chemical analysis". Fick sedan anställning som forskare vid Arbetslivsinstitutet (ALI), dåvarande Arbetsmiljöinstitutet, vid Enheten för Toxikologi och Kemi där jag under ett antal år arbetade bl.a. med isolering och MS-identifiering av kontaktallergena ämnen i samarbete med professor A-T Karlbergs forskargrupp. Dessutom har jag arbetat med identifiering av och provtagningsmetoder för nya typer av luftburna flamskyddsmedel, organiska trifosfater. Huvudansvarig för masspektrometriavdelningen vid ALI. Började 1997 vid Institutionen för Analytisk Kemi, där jag fick anställning som forskare. Jag bedriver forskning rörande bl. a. mätmetoder för kemiska hälsorisker i arbetsmiljön. För närvarande arbetar jag huvudsakligen med att utveckla bättre luftprovtagningsmetoder för flamskyddsmedel i inomhusmiljön och för isocyanater, samt med utveckling av snabba analysmetoder för biologiska prover. Det sistnämnda rör främst molekylavtrycksteknik och miniatyriserade membranextraktioner för flamskyddsmedel, metaboliter, läkemedel i urin och blodplasma. Jag har handlett 1 doktorand, Ove Jonsson, fram till doktorsexamen. Han disputerade i juni-03 inom området membranextraktion. Jag handleder för närvarande totalt 4 doktorander vid institutionen. Förutom detta är jag huvudansvarig för masspektrometriavdelningen vid institutionen.

Jag är medförfattare till ett 30-tal vetenskapliga publikationer och forskningsrapporter och har presenterat vetenskapliga arbeten vid en rad nationella, nordiska och internationella konferenser. Jag har deltagit som medarbetare i organisationskommitten för en europeisk konferens, 6th European Meeting on Mass spectrometry in Occupational and Environmental Health, som hölls i Stockholm i september 1999 samt för en annan internationell konferens, 1st International Symposium on Isocyanates in Occupational Environments, Stockholm 19-21 juni, 2000.

Undervisning:

Har handlett ca 20 examensarbeten sedan 1997 och deltar vid undervisning på grundkurs, 2 påbyggnadskurser samt en doktorandkurs vid institutionen. Har startat och har ansvaret för en påbyggnadskurs i masspektrometri vid institutionen. Har i samarbete med forskare vid andra institutioner vid Stockholms universitet även startat en doktorandkurs i organisk masspektrometri, där jag även medverkar som föreläsare. Har år 2002 även startat en vidareutbildningskurs i masspektrometri för industrianställda.

Vetenskapliga publikationer i internationella tidskrifter sedan 2000:

Carlsson H, Nilsson U, Östman C. Video Display Units: An Emission Source of the Contact Allergenic Flame Retardant Triphenyl Phosphate in the Indoor Environment. *Environmental Science & Technology*, 34 (2000) 3885-3889

Jonsson O, Dyremark E, Nilsson U. Development of a membrane-assisted liquid-liquid extractor (MLLE) for organophosphate esters at trace levels in human blood plasma. Identification of triphenyl phosphate and octyl diphenyl phosphate. *Journal of Chromatography B* 755 (2001) 157-164.

Battle R, Colmsjö A, Nilsson U. Determination of Gaseous Toluene Diisocyanate Using Solid-Phase Microextraction with On-Fiber Derivatization. *Fresenius Journal of Analytical Chemistry* 369 (2001) 524-529.

Nordqvist Y, Johansson R, Nilsson U, Colmsjö A. Development of a denuder sampler for determination of gaseous 2,4-toluene diisocyanate. *Fresenius J Anal Chem* 371 (2001) 39.

Battle R, Colmsjö A, Nilsson U. Development of a personal isocyanate sampler based on DBA derivatization on solid-phase microextraction fibers. *Fresenius J Anal Chem* 371 (2001) 514.

Möller K, Crescenzi C, Nilsson U. Synthesis and evaluation of molecularly imprinted polymers for extracting hydrolysis products of organophosphate flame retardants. *Journal of Chromatography A* 938 (2001) 121.

Möller K, Crescenzi C, Nilsson U. Determination of a Flame Retardant Hydrolysis Product in Human Urine by SPE and LC-MS. A Comparison of Molecular Imprinted Solid Phase Extraction with a Mixed Mode Anion Exchanger. *Analytical and Bioanalytical Chemistry* (2003) In press.

Isetun S, Nilsson U, Colmsjö A, Johansson R. Air sampling of organophosphate triesters using SPME at non-equilibrium conditions. Submitted to *Analytical and Bioanalytical Chemistry* 2003.

Jonsson O, Nilsson U. Miniaturized dynamic liquid-liquid extraction of organophosphate triesters from blood plasma using the hollow fibre-based XT-tube extractor. *Analytical and Bioanalytical Chemistry* 377 (2003) 182-188.

Nordqvist Y, Nilsson U, Colmsjö A. Evaluation of denuder sampling for a mixture of three common gaseous diisocyanates. *Analytical and Bioanalytical Chemistry* 375 (2003) 786-791.

Nordqvist Y, Nilsson U, Colmsjö A, Dahl A, Gudmundsson A. Evaluation of a cylindrical denuder for sampling aerosols of methylene diphenyl diisocyanate. Submitted to *Journal of Separation Science* 2003.

Jonsson O, Nilsson U. Determination of organophosphate ester plasticisers in blood donor plasma using a new stir-bar assisted microporous membrane liquid-liquid extractor. *Journal of Separation Science* 26 (2003) 886-892.

Jonsson O, Nordlöf U, Nilsson U. The XT-Tube Extractor: A Hollow Fiber-Based Supported Liquid Membrane Extractor for Bioanalytical Sample Preparation. *Analytical Chemistry* 75 (2003) 3506-3511.

Jonsson O, Nilsson U. Simultaneous determination of acidic and basic drugs in urine and blood plasma using two supported liquid membrane extractors connected in series and liquid chromatography-mass spectrometry. Submitted to *Analytical Chemistry* 2003.