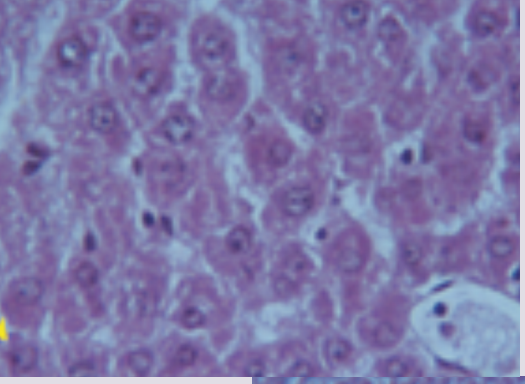
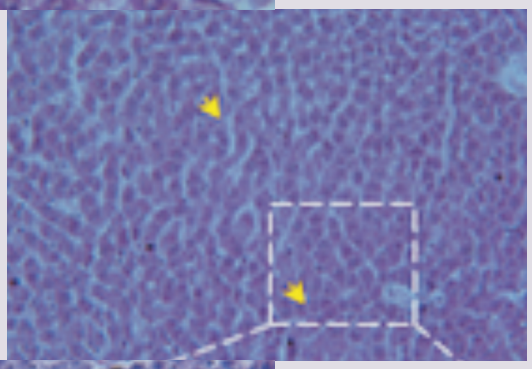
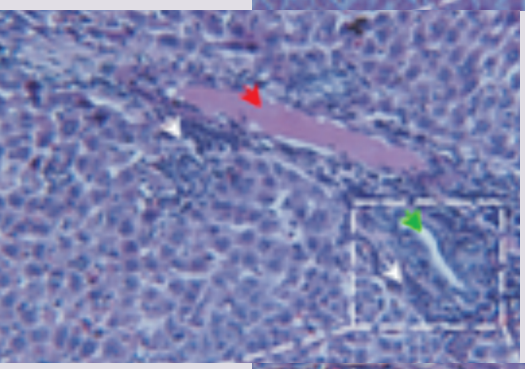
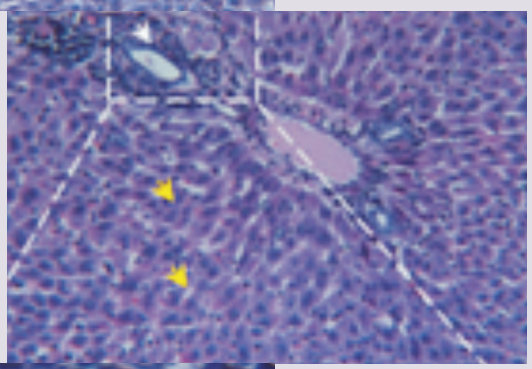
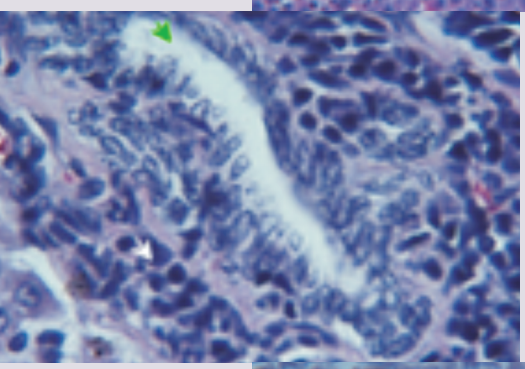


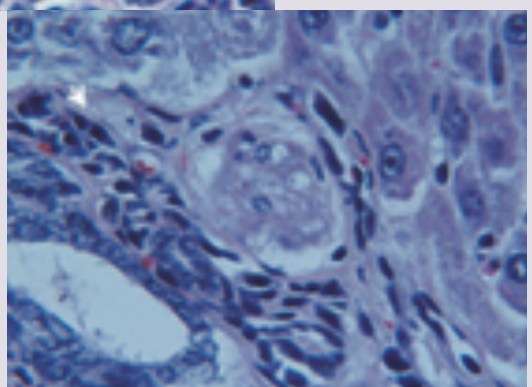




Regulatory Toxicology







Predicting acute aquatic toxicity of structurally diverse chemicals in fish using artificial intelligence approaches

Developed global modeling tools capable of categorizing structurally diverse chemicals in various toxicity classes according to the EEC and European Community directives and to predict their acute toxicity in fathead minnow using set of selected molecular descriptors. Accordingly, artificial intelligence approach based classification and regression models, such as probabilistic neural networks (PNN), generalized regression neural networks (GRNN), multilayer perceptron neural network (MLPN), radial basis function neural network (RBFN), support vector machines (SVM), gene expression programming (GEP), and decision tree (DT) were constructed using the experimental toxicity data. Diversity and non-linearity in the chemicals' data were tested using the Tanimoto similarity index and Brock-Dechert-Scheinkman statistics. Predictive and generalization abilities of various models constructed here were compared using several statistical parameters. PNN and GRNN models performed relatively better than MLPN, RBFN, SVM, GEP, and DT. Both in two and four category classifications, PNN yielded a considerably high accuracy of classification in training (95.85% and 90.07 %) and validation data (91.30% and 86.96 %), respectively. GRNN rendered a high correlation between the measured and model predicted -log LC_{50} values both for the training (0.929) and validation (0.910) data and low prediction errors (RMSE) of 0.52 and 0.49 for two sets. Efficiency of the selected PNN and GRNN models in predicting acute toxicity of new chemicals was adequately validated using external datasets of different fish species (fathead minnow, bluegill, trout and guppy). The PNN and GRNN models showed good predictive and generalization abilities and can be used as tools for predicting toxicities of structurally diverse chemical compounds.

Singh et al.; Ecotoxicology Environmental Safety; 2013; 95; 221-233

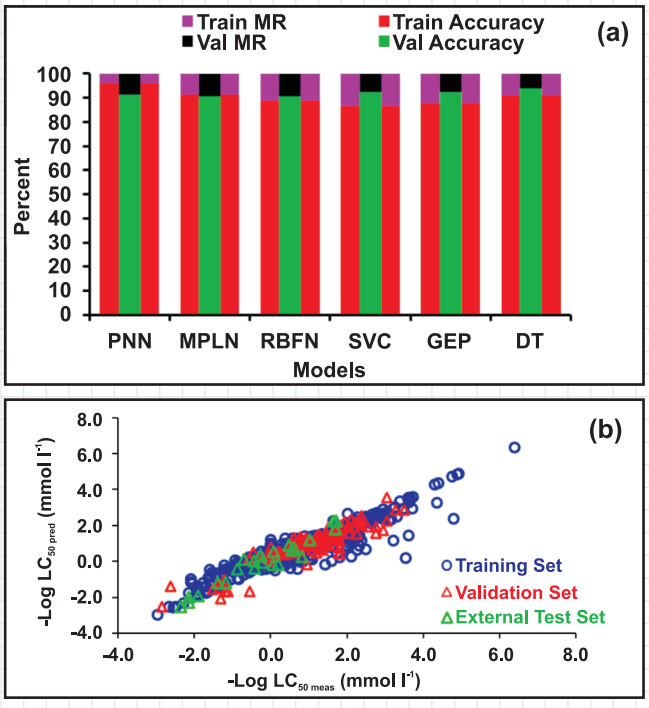


Figure (a) Misclassification rates (MR) and accuracies yielded by different models, (b) shows generalization and predictive abilities of the GRNN model to predict the acute aquatic toxicity of diverse chemicals in fathead minnow.

Predicting carcinogenicity of diverse chemicals using probabilistic neural network modeling approaches

Developed robust global models capable of discriminating positive and non-positive carcinogens; and predicting carcinogenic potency of chemicals in rodents. The dataset of 834 structurally diverse chemicals extracted from Carcinogenic Potency Database (CPDB) was used which contained 466 positive and 368 non-positive carcinogens. Twelve non-quantum mechanical molecular descriptors were derived. Structural diversity of the chemicals and nonlinearity in the data were evaluated using Tanimoto similarity index and Brock-Dechert-Scheinkman statistics. Probabilistic neural network (PNN) and generalized regression neural network (GRNN) models were constructed for classification and function optimization problems using the carcinogenicity end point in rat. Validation of the models was performed using the internal and external procedures employing a wide series of statistical checks. PNN constructed using five descriptors rendered classification accuracy of 92.09 % in complete rat data. The PNN model rendered classification accuracies of 91.77%, 80.70% and 92.08% in mouse, hamster and pesticide data, respectively. The GRNN constructed with nine descriptors yielded correlation coefficient of 0.896 between the measured and predicted carcinogenic potency with mean squared error (MSE) of 0.44 in complete rat data. The rat carcinogenicity model (GRNN) applied to the mouse and hamster data yielded correlation coefficient and MSE of 0.758, 0.71 and 0.760, 0.46, respectively. The results suggest for wide applicability of the inter-species models in predicting carcinogenic potency of chemicals. Both the PNN and GRNN (inter-species) models constructed here can be

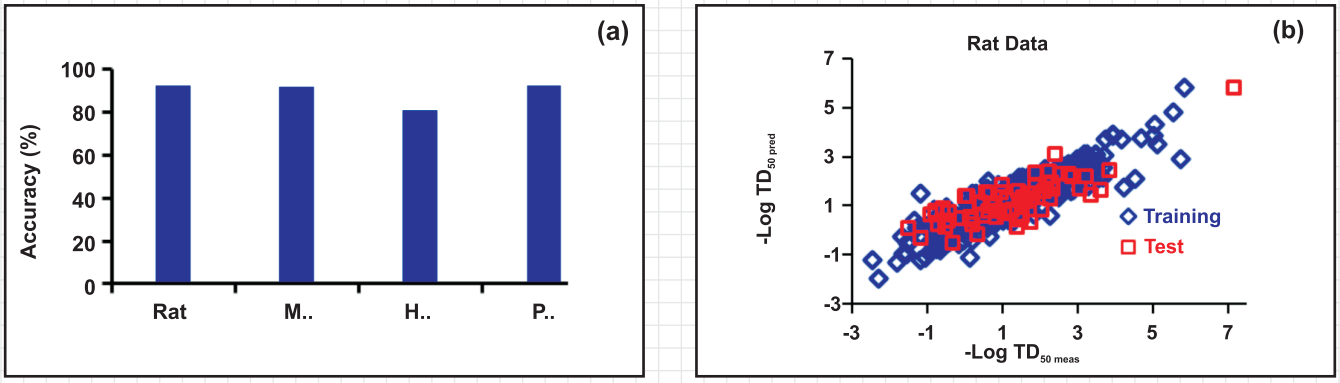


Figure (a) Classification accuracies (positive and non-positive carcinogens) in rat, mouse, hamster, and pesticide data yielded by optimal PNN model (b) shows generalization and predictive abilities of the interspecies GRNN model to predict the carcinogenic potency of diverse chemicals.

useful tools in predicting the carcinogenicity of new chemicals for regulatory purposes.
Singh et al., Toxicology and Applied Pharmacology doi: http://dx.doi.org/10.1016/jtaap.2013.06.029

Analysis of imidacloprid residues in fruits, vegetables, cereals, fruit juices, and baby foods and daily intake estimation in and around Lucknow, India

A total of 250 samples-including fruits, fruit juices, and baby foods (50 samples each), vegetables (70 samples), and cereals (30 samples)-were collected from Lucknow, India, and analyzed for the presence of Imidacloprid residues. The QuEChERS (quick, easy, cheap, effective, rugged, and safe) method of extraction coupled with high-performance liquid chromatographic analysis were carried out, and Imidacloprid residues were qualitatively confirmed by liquid chromatography-mass spectrometry. Imidacloprid was not detected in samples of fruit juices and baby foods. It was, however, detected in 38 samples of fruits, vegetables, and cereals, which is about 15.20% of the total samples. Of samples of fruits, 22% showed the presence of Imidacloprid, and 2% of samples showed residues above the maximal residue limit. Although Imidacloprid was detected in 24% of vegetable samples, only 5.71% showed the presence of Imidacloprid above the maximal residue limit. However, 33% of cereal samples showed the presence of Imidacloprid, and about 3% of samples were above the maximal residue limit. The calculated estimated daily intake ranged between 0.004 and 0.131mg/kg body weight, and the hazard indices ranged from 0.007 to 0.218 for these food commodities. It is therefore indicated that lifetime consumption of vegetables, fruits, fruit juices, baby foods, wheat, rice, and pulses may not pose a health hazard for the population of Lucknow because the hazard indices for Imidacloprid residues were below one.
Kapoor et al.; Environmental Toxicology and Chemistry; 2013; 32; 723-727

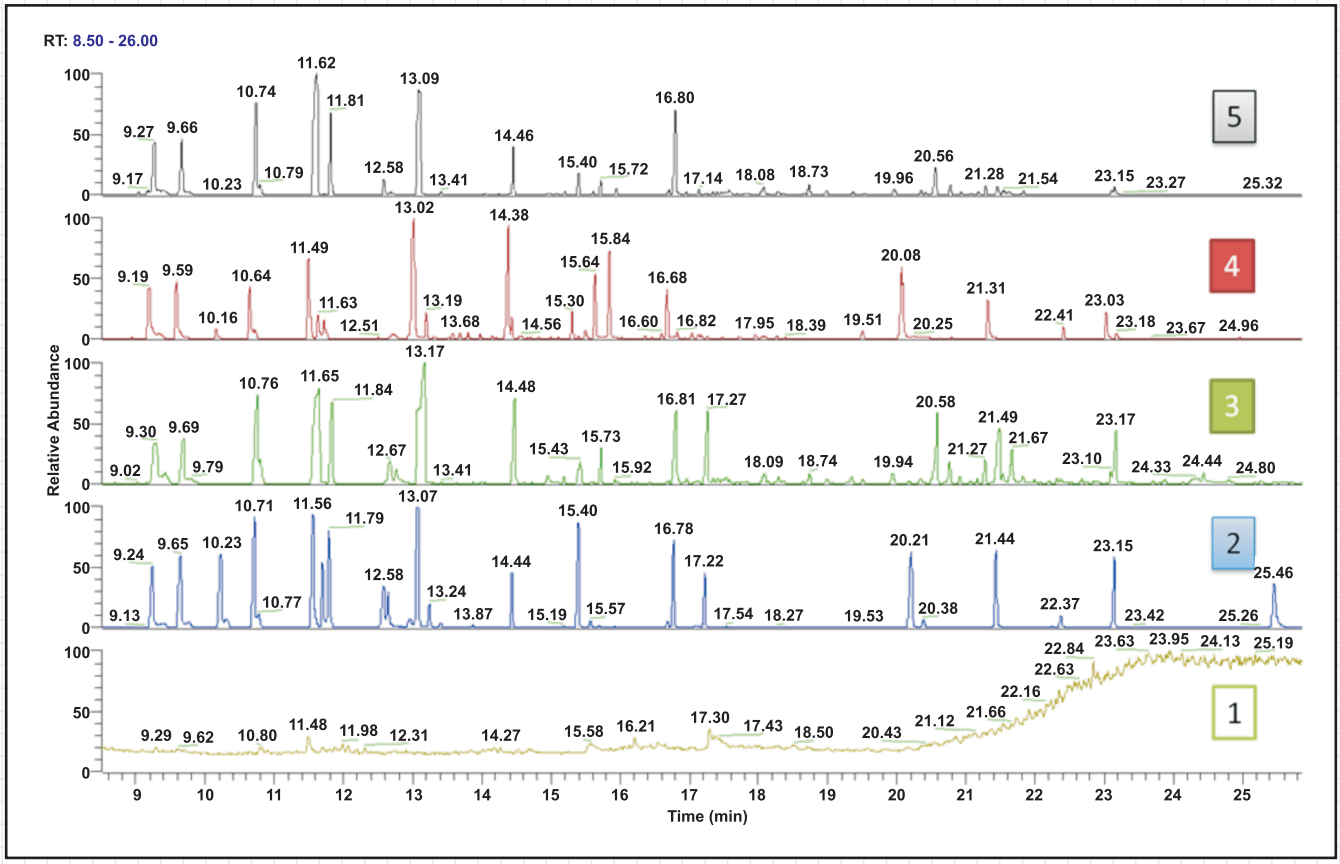
Solid-phase microextraction-gas chromatography-mass spectrometry (SPME-GC-MS) methods using derivatization

A rapid and sensitive analytical method was developed for trichloroethylene metabolites viz. dichloroacetic acid, trichloroethanol and trichloroacetic acid in human plasma. The metabolites were converted to their methyl ester derivatives using methyl chloroformate and subsequently extracted by SPME followed by GC-ECD and GC-MS analysis.
Mudiam et al.; Journal of Chromatography B; 2013; 925; 63-69

Similarly, 20 amino acids in hair, urine and soybean samples were derivatized using ethyl chloroformate and extracted by SPME followed by GC-MS analysis. The method was fast, simple and solvent free.
Mudiam et al.; Journal of Chromatography B; 2012; 907; 56-64

Dispersive liquid-liquid microextraction-gas chromatography-mass spectrometry (DLLME-GC-MS) method using derivatization

DLLME is a recent microextraction technique which is fast, economic and eco-friendly liquid-liquid extraction technique. A simultaneous derivatization cum extraction method based on ultrasound assisted-DLLME was developed using ethyl chloroformate as derivatizing reagent for the determination of 20 amino



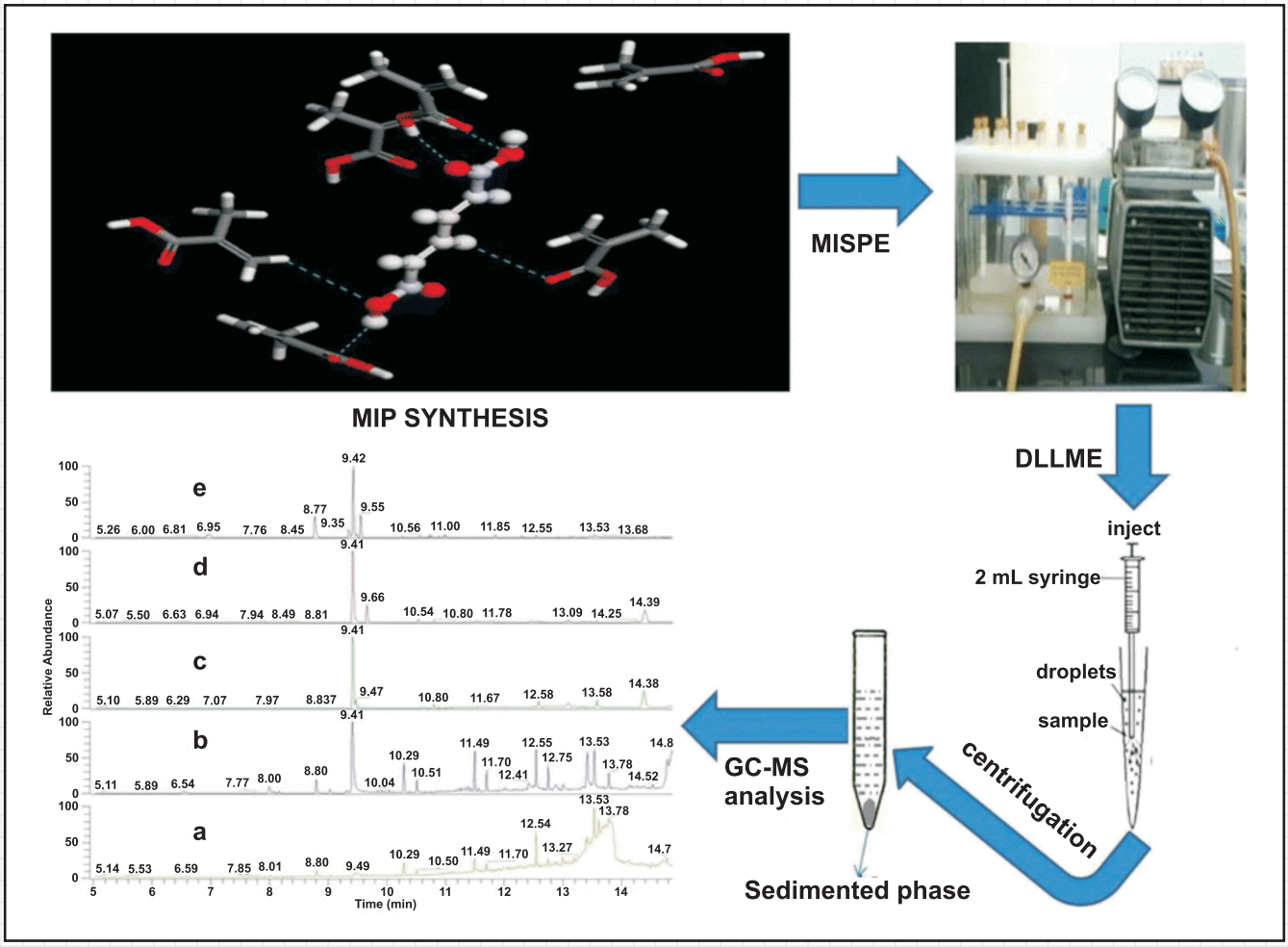
Separation profile of amino acids using UA-DLLME/GCMS in 1) blank sample 2) standard 3) Hair sample 4) soybean sample 5) urine sample

acids in complex matrices such as hair, urine and soybean followed by GC-MS analysis.
Mudiam et al.; Journal of Chromatography A; 2013; 1291; 10-18

A single step derivatization and extraction method for the analysis of parabens was developed using isobutyl chloroformate as derivatizing reagent and DLLME as extraction technique followed by GC-MS analysis.
Jain et al.; Food Chemistry; 2013; 141; 436-443

Optimization of UA-DLLME by experimental design methodologies for the simultaneous determination of endosulfan and its metabolites in soil and urine samples by GC-MS

A simple, economical, rapid and sensitive analytical method has been developed for the simultaneous determination of endosulfan (α- and β-) and its metabolites (endosulfan ether, endosulfan hydroxy ether, endosulfan lactone, endosulfan alcohol and endosulfan sulphate) in complex samples, such as soil and urine, based on ultrasound assisted dispersive liquid–liquid microextraction (UA-DLLME) followed by gas chromatography–mass spectrometric (GC–MS) analysis. The method parameters have been optimized using response surface design experiments. Trichloroethylene (TCE) and acetone were chosen as extraction and disperser solvents respectively. After UA-DLLME, the sediment phase obtained was directly analyzed by GC–MS without any further cleanup and preconcentration procedure. Several factors which can affect the UA-DLLME extraction were screened and optimized by 27–4 Plackett–Burman design (PBD) and central composite design (CCD) experiments respectively. Based on these experiments the optimized parameters for UA-DLLME extraction were as follows: extraction solvent, (TCE, 58 µL), disperser solvent (acetone, 1.27 mL) and ionic strength (Na_2SO_4, 7%, w/v). Intra- and inter-day precision were expressed as percent relative standard deviation (% RSD) and were found to be less than 6.33%. The limit of detection (LOD) of all the analytes in soil and urine were found to be in the range of 0.316–2.494 ng g^{-1} and 0.049–0.514 ng mL^{-1} respectively. The proposed method was successfully



applied in the analysis of soil samples contaminated with endosulfan. The method may find wide application for the routine determination of endosulfan and its metabolites in environmental and biological samples.
Mudiam et al.; Analytical Methods; 2012; 4; 3855-3863

Molecularly imprinted polymer-dispersive liquid-liquid microextraction (MIP-DLLME) methods for polar analytes

A simultaneous derivatization and preconcentration method for the selective determination of *t, t*-muconic acid (a biomarker of benzene exposure) after selective extraction from urine samples using MIP was developed using GC-MS for detection and identification.
Mudiam et al.; Analytical and Bioanalytical Chemistry; 2013; 405; 341-349

MIP-DLLME-HPLC method was developed for telmisartan in rat plasma samples. A selective MIP was synthesized for telmisartan which was used as sorbent for solid-phase extraction of telmisartan; the extract was subjected to DLLME for preconcentration followed by HPLC analysis.
Mudiam et al.; Bioanalysis; 2013; 5; 847-858