Development and Evaluation of Parsimonious Solvation Models for the Estimation of Partitioning Properties of Passive Samplers

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A thesis submitted in partial fulfillment of requirements for the degree of
Master of Science
In
Environmental Science

Institute of Environmental Sciences and Engineering (IESE)

School of Civil and Environmental Engineering (SCEE)

National University of Sciences and technology (NUST)

Islamabad, Pakistan

(2019)

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DEDICATION

This thesis is dedicated to my affectionate parents.

Acknowledgements

This research work would not have been possible without the guidance of Allah Almighty, the most beneficent and merciful.

I would like to express my utmost gratitude to my Supervisor, Dr. Deedar Nabi for his understanding, wisdom and patience and for pushing me farther than I thought I could go. I would also like to express my gratitude to my GEC members, Dr. Yousuf Jamal and Dr. Zeshan. Their guidance and expertise generously helped me during my research.

My siblings, friends and research group fellows for helping me in stressful times and not letting me give up.

Lastly, I would like to thank my parents for their unconditional love, support and encouragement.

(Qasim Saeed)

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Abbreviation	Meaning
ASM	Abraham Solvation Model
TWA	Time weighted average
K_{POM-w}	Polyoxymethylene-Water Partition Coefficient
K_{PE-w}	Polyethylene-Water Partition Coefficient
K_{PA-w}	Polyacrylic-Water Partition Coefficient
K_{PDMS-a}	Polydimethylsiloxane-Air Partition Coefficient
K_{PUF-a}	Polyurethane Foam-Air Partition Coefficient
log Kow	Octanol-Water Partition Coefficient
log Kaw	Air-Water Partition Coefficient
log Koc	Organic carbon-Water Partition Coefficient
LFERs	Linear Free Energy Relationships
op-LFER	One Parameter Linear Free Energy Relationship
pp-LFER	Poly Parameter Linear Free Energy Relationship
2p-LFER	Two Parameter Linear Free Energy Relationship
QSARs	Quantitative Structure Activity Relationships
QSPRs	Quantitative Structure Property Relationships
ANOVA	Analysis of variance
VIF	Variance Inflation Factor
RMSE	Root Mean Square Error
LOOCV	Leave One Out Cross Validation

ABSTRACT

In this thesis, a (2p-LFERs) two parameter Linear Free Energy Relationship have been designed and applied for varied sets of aquatic and air passive samplers. LFER models for polyethylene passive sampler to water, polyoxymethylene passive sampler to water, polyacrylic passive sampler to water, polydimethylsiloxane passive sampler to air and polyurethane foam passive sampler to air were designed.

For water system the new 2p-LFER models excellently explained partitioning variability in the datasets with R^2 and root mean square error (RMSE) ranging from 0.81 to 0.94 and from 0.45 to 0.53 log units respectively. For air system my 2p-LFER models exhibited R^2 and root mean square error in the range of 0.94 to 0.93 and from 0.38 to 0.54 log units. All models designed in this study were found statistically robust after testing by using four independent cross validations tests.

The models developed provide us how the traits of hydrophobicity, volatility – octanol-water partition coefficient (Kow), air-water partition coefficient (Kaw) and organic carbon partition coefficient (Koc), manage the transfer of contaminants from one phase to another and indicates the dominance of octanol-water partition coefficient (Kow), hydrophobicity, in both aquatic and air phases.

The significance of my research models is that they have a benefit over the predefined estimation approaches. The previous models either require super-fast computers, or parameter demanding, or the required parameters are not experimentally accessible or they are remarkably expensive. Whereas, the suggested LFER methods in this study are not only simple and accessible but also productive than different multi-parameter estimation methods.

My 2p-LFER model is not only statistically potent but also theoretically-accurate and compliments the principle of parsimony.

Chapter 1

INTRODUCTION

1.1 Passive Sampling

Organic and inorganic environmental pollutants monitoring is a great challenge today. It requires quite large number of samples from a location of interest over time duration when using active sampling methods, when finding out quality of different environmental compartments like atmosphere, indoor air, water basins, soil or biota. Such type of approach requires large number of resources as well as it is requires a great amount of time (Namies´nik *et al*., 2005).

The discharge of contaminants into the environment is inevitable cost of human development. Innumerable amounts of various commercial chemicals are produced each year (Mackay *et al*., 1997). The micro organic chemicals are a serious potential hazard to human health and to other exposed organisms. Thus, development of an effective monitoring tool to protect the environment is very important (Vrana *et al*., 2005).

Passive sampling is an alternate solution for such situations; it is the measure of analyte concentration represented as weighted average over the sampling time. Passive sampling methods are immune to unintentional, extreme differences or variations of pollutant concentrations as the analyte concentration is integrated over the exposure time. The data that is attained in such manner is appropriate for obtaining a long-term overview of pollutant levels in a given environmental compartment.

In order to use passive samplers' certain calibration parameters are required such as partition coefficients, sampling rates and loss rate constants, which are usually determined in the laboratory or at the sampling site (Phi and Hiramatsu, 2012). Thus, to get useful information out of passive samplers we need partition and diffusion coefficients for field application.

1.2 Partition Coefficient

Equilibrium Partition coefficient (P) is the ratio at equilibrium of compound concentration in a mixture of two immiscible phases. It is therefore a measure of differences in solubility of compound present in two phases. (Kwon, 2001).

The transport and distribution of chemicals in environment are greatly influenced by equilibrium partitioning properties (Schwarzenbach *et al.*, 2002). Therefore, fate models for environmental behaviors and ecological impact assessment of chemicals typically engage partitioning properties, defined as follows;

$$Pxy,i = \left\{\frac{Cx,i}{Cy,i}\right\}_{\text{equilibrium}}$$

Where $P_{xy,i}$ is partition coefficient between two phases x and y, and $C_{x,i}$ and $C_{y,i}$ are the concentrations of contaminant i at partitioning equilibrium present in these phases. Thus, to assess the chemical exposure and transport in the environment, Equilibrium partition coefficients are required (Schwarzenbach *et al.*, 1993).

Partitioning of nonionic organic compounds between water and natural organic phases, which are the two phases is credited as hydrophobicity of compound i which is targeted compound. It is expressed as K_{ow} i.e. octanol/water partition constant or coefficient. Likewise, K_{oa} or octanol/air partition constant is a function of compound volatility which is partitioning of compound i between air and liquid or solid. In order to find out unknown equilibrium partition coefficient between two phases such partitioning constant parameters are used in one-parameter Linear Free Energy Relationships (LFERs). As one-parameter LFERs use only one such parameter so it has limited predictive power because as we know that a single parameter does not or has no ability to completely all the molecular interactions which govern the equilibrium partitioning of a compound between any two phases. So, for different regression coefficients for different compound classes is required in LFERs (Goss and Schwarzenbach, 2001).

Therefore for handling of variability of both compound and sorbent, there is a need of a much refined approach than those of op-LFERs for quantification and improved prediction of equilibrium partitioning. A very useful tool exist for describing partitioning data of large and diverse data sets of compounds using an equation known as poly-parameter linear free energy relationships pp-LFERs (Abraham *et al*., 1999).

The Abraham solvation model (ASM) has been widely explored in environmental chemistry to estimate several partitioning and transport properties. The model parameterizes the solution's cavity model, and is based on the neutral molecules transfer from the gas phase to a condensed phase. There are many methods available for estimation of partition coefficients but there are limitations for them like discussed before for one-parameter LFER. Abraham solvation model has its own limitations. It has a limited database; only 8000 abraham solute descriptors are available for chemicals and are unavailable for many existing and emerging nonpolar environmental pollutants such as polychlorinated n-alkanes (PCAs), polyhalogenated dibenzo-pdioxins (PHDDs), dibenzofurans (PHDFs) (Greim *et al*., 1997; van den Berg *et al*., 2013).

The aim of the study is to find a simple, inexpensive method of estimation by taking few important and easily accessible descriptors.

1.3 Problem statement

When it comes to freely dissolved chemicals and their presence in trace and ultra-trace level in our environment the existing sampling and estimation methods have certain limitations and there is a need for an easily-accessible, computationally inexpensive estimation approach.

1.4 Objectives of the study

Objectives of this study are

- To develop theoretically-rigorous, robust and parsimonious models to estimate partition coefficient for widely-used passive samplers.
- To understand which set of environmental properties control the partitioning behavior of chemicals to the passive samplers.

1.5 Scope of Study

The study is divided into two phases for aqueous and air system

- In first phase two-parameter linear free energy estimation models were developed for diverse set of passive samplers for aqueous system.
- In second phase two-parameter linear free energy estimation models were developed for diverse set of passive samplers for air system.

REVIEW OF LITERATURE

2.1 Experimental Methods

Traditional methods for environmental monitoring such as active sampling and spot or grab sampling (air, water, sediments) offer some difficulties. The information obtained from grab samples is less representative because it provides a snapshot at a particular instant and no temporal and spatial variations in contaminant concentrations is provided. Since contaminants are present in trace amounts, large volumes of samples are required in spot or grab sampling. This limitation can be overcome either by increasing sampling frequency or by installing automatic sampling systems. But this approach could be costly as well as impractical as it requires a safe location site and certain pre-treatment for water analysis. Depending upon the applied pre-treatment (e.g. filtration), spot/grab sampling yields different concentrations of contaminates but gives no information regarding truly dissolved or bioavailable fraction (BAF) of contaminants (Vrana *et al*., 2005).

The collected samples volumes is limited in traditional methods which is ≤5 L, because of handling, processing, preserving, transport and extraction issues, the exposure assessment of organisms involve laborious multiple sample collections. As a consequence, for trace (≤ 1 μg L−1 or mg m−3) or ultra-trace (≤1 ng L−1 or μg m−3) hydrophobic organic chemical levels the method quantification limits (MQL) might not be sufficient. Low quantification limits are of particular importance when it comes to assessment of chemicals which can bio-concentrate (the uptake by skin absorption or respiration) or bio-accumulate (the uptake via skin diet, respiration and absorption) and other organic materials that are highly toxic (Huckins et al., 2006).

For the trace and ultra-trace Suspended-Volatile-Organic-Compounds (SVOCs) analysis the applicability of grab sampling in air is limited. In addition, the sampling methods that might be chosen for assessment of global-atmospheric transport of pollutants are restricted by the sampling gadget's size, weight and portability and the need of electrical power for their use (Górecki and Namieśnik, 2002).

It can be summarized, that active and spot or grab sampling methods provide useful and reliable information about the total airborne or waterborne concentration of contaminants in a brief interval of time but no information regarding time-weighted average (TWA) concentrations of contaminants is provided. This shortcoming strictly limits their use for exposure analysis of organisms (Huckins *et al*., 2006).

Bio-Monitoring organisms (BMOs or test organisms) for chemical risk and exposure analysis are another approach to investigate the bioavailable fraction of contaminants. They can be extended for longer periods of time and provide bioaccumulation and equilibrium level of waterborne chemicals but this approach also has limitations. The degree and inconsistency of chemical concentration hoarded in tissues can be influenced by the site-exposure conditions. The results can also be affected by BMO species specific physiological, anatomical and behavioral characteristics i.e. metabolism, excretion, stress, etc. Furthermore, prior to instrumental analysis the extraction of analytes from organisms is complex (Vrana *el al*., 2005).

In regulatory toxicology, certain tests are carried out on animals for hazard assessment and are used to classify the toxicity properties of chemicals that are exposed to humans or our environment through a specific product or purpose. Presently for safety, certain regulatory testing of drugs and chemicals is compulsory to performed and for this standardized animal tests are there firstly for the protection of workers during the production phase and secondly for the protection of consumer and environment from that chemical product. The animals used in these laboratory tests are exposed to hazardous chemicals which cause considerable pain and distress and might lead to death. (Liebsch and Spielmann, 2002)

2.2 Passive Sampling

Passive sampling is a sampling technique in which a sampling device is used to capture freely flowing analyte molecules from the sampling medium which is due to the analyte chemical potential difference present in two media. The process of analyte molecules movement between two mediums is a result of equilibrium that is established or till the time when sampling stops (Mackay *et al*., 1997).

Passive sampling combines the three steps into one which are sampling, analyte isolation and pre concentration, simplifying the need of pre-treatment of sample before it is deployed. It also requires no or very little solvent. Passive sample determines time-weighted average (TWA) concentrations so the response speed is the result of duration for which time weighted average is determined over time (Gorecki and Namiesnik, 2002).

The quantity of analyte being collected by sampler depends upon two things; firstly its concentration of analyte in the sampled medium and the other is the exposure time. Time weighted average TWA can easily be calculated if we have the information about the relationship between the rate of sampling and the concentration of analyte. But for such certain conditions must meet which are

- There should not be any release of trapped molecules that has been captured even if the concentration of analyte reaches zero and this is called “zero sink”.
- The rate of sampling must be constant throughout the time. This is achieved quite easily when the analyte is absorbed or chemisorbed but problems are there when there is a process of physical adsorption involved in collection of analytes.

2.2.1 Types of Passive Samplers

There is a wide range of passive sampling devices present that can be for sampling of different contaminants that are present in different environment. It is also of great importance to select an appropriate passive sampling device for a particular sampling environment. Different materials are used as sorbents in passive sampling devices as it provides the device with a specific property which is good for example polyethylene passive samplers which are ethylene sheet based passive samplers are great when it comes to capturing of hydrophobic compounds. Sampling devices such as semipermeable membrane devices (SPMD) (Turgut *et al*., 2017), low density polyethylene (LDPE) film (Carls *et al*., 2004; Cornelissen *et al*., 2008; Zhu *et al*., 2015), polyacrylic (PA) plastic sorbent (DiGiana *et al*., 1988; Namies´nik *et al*., 2005), polyoxymethylene (POM) devices (Beckingham and Ghosh, 2013), polydimethylsiloxane (PDMS) fibers (Zhang *et al*., 2014) and polyurethane foam (PUF) device (Bartkow *et al*., 2004; Nabi and Arey, 2017) can be used in different as well as more than one environment depending upon what type of compounds we are looking for.

2.2.2 Passive sampling as an alternative monitoring tool

Passive sampling is an alternative monitoring tool, which is affordable, reliable and produce quality representative data comparable between time and locations. Passive samplers can be places at site for extended time from few days to months and yields time weighted average concentrations of pollutants. From analytical point of view passive sampling offer many advantages over traditional methods, as it significantly simplifies sampling procedures by eliminating sample preservation and preparation, provides cleaner extracts with less use of solvents, speed up the processing time, eliminates power /electricity supplies, and evidently reduces the costs of analysis. It a greener technology with less matrix effect as it provides better detection and quantification limits as compare to other methods. This technique is in particular appropriate for the determination of time-weighted average concentrations of contaminants (Górecki and Namieśnik, 2002) and has a great potential because of the simplicity of the principles underlying its function and structure and the low cost involved (Greenwood *et al*., 2007).

In order to use passive samplers' certain calibration parameters are required such as partition coefficients, sampling rates and loss rate constants, which are usually determined in the laboratory or at the sampling site (Phi and Hiramatsu, 2012). Thus, to get useful information out of passive samplers we need partition and diffusion coefficients for field application.

2.3 Equilibrium partition coefficient

Mathematically partition coefficient is defines as the ratio of substance concentration in one phase versus the concentration in another phase at equilibrium written as

$$Partition\ Coefficient\ (P) = \left(\frac{C1}{C2}\right) equilibrium$$

The concentration units may be unalike. In inhalation toxico-kinetics different partition coefficients are used like for gases blood-air partition coefficient and for all other substances tissue-blood partition coefficient. For gas and a liquid which are at low concentration at equilibrium the partitioning between these is “Henry’s Law Constant” and it is a denotation particularly for vapor-liquid. In toxicology henry’s law at higher concentrations there may be deviations despite it is can be applied over the concentration range of interest. (Schlosser and Medinsky, 2010).

When there is an interaction of organic compound with two immiscible solvents i.e. it dissolves in both of these solvent phases and it is measured by distribution coefficient or by the partition coefficient which is defined as the ratio at equilibrium of the substance present in mixture of two phases that are immiscible. This ratio tells us about the solubility of the substance that how differently it interacts with the two phases of which one is water and the other is hydrophobic.

Therefore, the partition coefficient gives us information about the hydrophobic and hydrophilic property of that chemical substance present in the two phases.

Compounds hydrophobicity gives us information that the hydrophobic compound can get into the groundwater and pollute it. In hydrogeology, K_{ow} can be used for modeling and prediction of migration of organic compounds with hydrophobic properties in groundwater and soil as it gives us information about specie mobility. (Speight, 2017)

Different environmental phases interact with each other in a complex manner. However, at chemical equilibrium, the distribution of mixtures among different phases is due to their thermodynamic properties. This is defined by equilibrium partitioning theory. There are many conditions in the environment where it is appropriate to consider equilibrium, for example, the distribution of contaminants among the three phases of the sediment-water system: the pore water dissolved organic matter and amorphous organic carbon portions of the sediment. Even in situations when equilibrium is not attained, knowing the equilibrium partition coefficient is very useful in order to know a chemical’s tendency for accumulation in a specific phase. Equilibrium partition coefficients also tell us the exact direction in which the chemical moves in a complex environment. They also calculate the rate of mass transfer across different interfaces.

2.3.1 Octanol-water partition coefficient (K_{ow})

For aqueous system octanol–water partition coefficient (K_{ow}) is mostly applied partition coefficient and it also has its major role in air and other media like soil and others. In air system we have many organic compounds i.e. carbon-carbon or carbon-hydrogen bond molecules and as we know like solvents dissolve like solutes so, the solubility can be differentiated as these under normal conditions of pressure and temperature can easily get dissolved into organic solvents. In such case we term it as hydrophilic or lipophilic as organic compounds can easily dissolve into water or lipids and if they do not readily dissolve into organic solvent under normal conditions it is termed as hydrophobic or lipophobic.

K_{ow} is defined as ratio of concentration of a substance in octanol to the concentration of substance in aqueous phase at equilibrium. In general octanol is a surrogate for solvents that are lipophilic and this is because it has affinity for water as well as organic compounds which is termed as amphibilic. It is also an indicator which is of importance in environmental partitioning (Vallero, 2014).

2.3.2 Organic Carbon Water Partition Coefficient (K_{oc})

Organic carbon water partition coefficient (K_{oc}) is unit less which is the ratio of concentration of chemical that is absorbed per unit mass of soil to its concentration in second phase which is aqueous phase. K_{oc} is the representation of distribution coefficient (K_d) which is normalized to total organic carbon content. The K_{oc} value for most "Persistent Organic Pollutants" is high as it explains partitioning of POPs that are present in soils with high organic matter contents. The binding of chemical with organic matter is controlled by the chlorination (or bromination), higher the chlorination (or bromination) more will it bind and it's a general rule (O'Sullivan and Megson, 2014).

2.3.3 Air Water Partition Coefficient (K_{aw})

In environment the transport of organic compounds is affected by the transfer between the atmosphere and aqueous systems (Schwarzenbach *et al.,* 2004). Henry's law constant KH or K_{aw} is the air-water partition ratio for neutral compounds that are present in pure water at dilute solution concentrations. But as we know we don't have pure water but aqueous solutions which contain many chemicals, for this "air-water distribution ratio" is used, which is determined by approximating Henry's Law constant. K_{aw} is a unit less defined as the ratio of substance abundance in air phase to that of aqueous or water phase at equilibrium. The compound's transfer depends upon the value of K_{aw}; it will get into air phase from water or aqueous phase if K_{aw} value is large (Ji *et al*., 2008).

2.4 Two-Dimensional Gas Chromatography (GCxGC)

For several thousand compounds that are present in complex mixtures, two-dimensional gas chromatography (GC×GC) is an analytical technique of choice. Two-dimensional gas chromatography has two columns; one is primary which through a modulator is combined with the second column. The function of the modulator is to act as an inlet for the second dimension, cutting the primary broader peak into sub peaks and it does it continuously. The sub peaks are further separated in the secondary column.

The length of both primary and secondary columns is different. The secondary column is kept shorter so that the separation that is achieved in the first dimension is preserved. Analytical detection limits in two-dimensional gas chromatography (GCxGC) are improved because as a result of different chemical selectivity of stationary phase in secondary column than that of primary column produces very sharp peaks but requires fast sampling detectors making it expensive (Nabi, 2014).

2.5 Abraham Solvation Model

The Abraham solvation model (ASM) is equation involving different parameters that can be used for the estimation of numerous transport properties and for estimation of partition coefficient in environmental chemistry. It is based on the parameters of cavity model and other intermolecular interactions. It is written as

$$\log SP = c + e\mathbf{E} + s\mathbf{S} + a\mathbf{A} + b\mathbf{B} + l\mathbf{L} \text{ (eq. 1)}$$

Depending upon the different type of intermolecular interactions the parameters can be chosen for example in case of transfer between two condensed phases it is written as

$$\log P = c + e\mathbf{E} + s\mathbf{S} + a\mathbf{A} + b\mathbf{B} + v\mathbf{V} \text{ (eq. 2)}$$

The letters that are lower case are system constants whereas the capital letters are solute descriptors. Partition constant and other free energy terms describe the solute property which is log P. The complimentary interactions between the solute and solvent are described by lowercase letters. The solute descriptors are **E** describing the solute polarizability, **S** describing the solute polarity, solute’s hydrogen bond interactions are represented by **A** and **B** where **A** represents hydrogen accepting capacity and **B** is hydrogen bond donating capacity. **V** tell us about the cavity formation by solute in solvent and **L** is the solute’s hexadecane-air partitioning constant at 25^{o}C (Bradley *et al*., 2015).

Using the Abraham solute descriptors Goss gave a single model telling about the transfer between condensed phases and transfer from gas to condensed phase. In Goss equation (eq. 3) **V** and **L** descriptors are used eliminating **V**. Both are these descriptors tell about dispersion interactions and contributions from the process of cavity formation in the process.

$$\log SP = c + s\mathbf{S} + a\mathbf{A} + b\mathbf{B} + v\mathbf{V} + l\mathbf{L} \text{ (3)}$$

Goss model provide a good fit when it comes to experimental data but it has its limitations when it comes to describing the physical significance of factors that contribute to the process. Goss model is an additional estimation equation for calculating partition coefficients and helps in understanding the processes which involve closed thermodynamic cycles not replacing the Abraham model (Poole *et al*., 2013)

2.6 One Parameter-Linear Free Energy Relationship

Currently using the double logarithmic correlations present between the constants that is not known and the partition constant of compound that is known, equilibrium partitioning can be evaluated. To understand this example can be taken that for organic matter and water or, air and water partitioning, it can be correlated with octanol-water and air-water partition coefficient.

The limitations of such relationships which is one parameter linear free energy relationship or op-LFER is that it only predicts the variability of compound in only one substance class as a single coefficient is used. This limitation of op-LFER is because of two reasons; the first reason is that as partitioning is a result of many independent and different kinds of interactions so a single parameter cannot describe compound variability completely. The second reason is that the phase that is being studied is not represented in variable parameter but it is represented in intercept and slope of double logarithmic correlation. Due to these reasons op-LFER gives us no understanding regarding the variability in between two substance classes as well as no information about the variability between two or different natural organic phases making this approach good for estimating certain properties for certain families alone. (Goss *et al*., 2001)

2.7 Estimation Methods

Ab-initio, LFER like op-LFER and pp-LFER, fragmental and group methods are some of the estimation methods that are widely used for screening of chemicals.

At optimized level the mechanical structures of molecules can be found out using a quantum mechanical modeling method known as “Ab-initio” method. This method can be used to assess the chemical’s structural measurement and the difference of one chemical from another. Different other modeling methods like envelop function and bead function are used for the scattering of data as it is based on simulation of system that explores other various available methods. (Nedyalkova, 2019; Singh, 1986)

Solvent activity in polymer is used by group estimation method. The group method estimation is carried out in different stages, in the first stage the first order group assessment is carried out and later second order group gets assessed in advantage stage giving the value. To determine the properties isomer estimation and identification with precise application is used. (Constantinou, 1994).

Poly-parameter LFERs (pp-LFERs) uses different parameters and considers all the interactions that are involved in partitioning, and complete compound variability can be predicted by a single equation also giving information about sorption characteristics in different natural phases (Goss *et al.*, 2001). In many technical systems pp-LFERs model for estimation of partition coefficient has greater efficiency as it has ability to define and tell about the linear relationship between many properties of environment. The model equation of also has ability to tell and describe descriptors strong relationship present between them. (Endo, 2014; Endo, 2009).

For development of Quantitative Structure Activity Relationships or QSAR model, fragmental method has quite wide and extensive operation. This is use to estimate and to get information about chemicals physical and biological properties as well as its site specific physiochemical profiling. Chemicals functional group and active skeleton can also be estimated using this method. (Japertas, 2003). Quantum-Chemical Descriptors based on Quantitative Structure Activity Relationships or Quantitative Structure Property Relationships (QSAR/QSPR) require superfast computers which are not readily available and are highly expensive. These descriptors could have serious drawbacks depending on the nature of the chemical structures or processes involved (Poole *et al.*, 2013).

Chapter 3

METHODOLOGY

3.1 Acquisition of Data

The experimental values of for both water and air system were collected from the literature (Abraham and Ibrahim, 2006; Nabi *et al.*, 2017) Once the data set collected for each passive sampler was collected it was carefully curated to remove any duplication and organized according to its type and properties.

For each chemical in 5 data set, its smiles code and cas number were collected. Smile codes are single line representation for chemical specie and cas number is a numeric identifier assigned to a chemical specie.

After compiling our data sets the values for intermolecular descriptors such as octanol-water partition coefficient K_{ow} (Hydrophobicity), air-water partition coefficient K_{aw} and organic carbon partition coefficient K_{oc} were taken from different modules of EPI Suite™ which are KOWWIN v1.68 for K_{ow}, HenryWin v3.20 for K_{aw} and KOCWIN v2.00 for K_{oc}.

Using smile code of chemicals Abraham solute descriptor values were collected from UFZ-LSER Database.

The data sets for both water and air system used in the study is diverse. The diversity is an important attribute which describes the data representativeness. The diversity for the data sets of water system is diverse and ranges over several orders of magnitude like in Polyethylene-Water Partition Coefficient ($K_{PE\text{-}w}$) it is 6 orders of magnitude, for Polyoxymethylene-Water Partition Coefficient ($K_{POM\text{-}w}$) it is 5 orders of magnitude and for Polyacrylic-Water Partition Coefficient ($K_{PA\text{-}w}$) it is 6 orders of magnitude. Similarly for air system the data set for

Polydimethylsiloxane-Air Partition Coefficient (K_{PDMS-a}) is 11 orders of magnitude and for Polyurethane Foam-Air Partition Coefficient (K_{PUF-a}) it is 6 orders of magnitude.

3.2 Statistical Analysis

Before starting analytical analysis certain statistical criteria's were set to which the model has to comply with. The model should bring in minimum "Akaike Information Criterion (AIC)". F test and t-value of the variable coefficient is less than or equal to the critical t-values reported at the significance level i.e. p-value <0.05 and the confidence interval to be 95%. Variance inflation factor (VIF) for independent data should be <5.

Keeping in view the statistical criteria, statistical analysis like step-wise regression, multi linear regression, cross validation tests and dimensionality analysis or principal component analysis were performed using R program. First of all step-wise regression was carried out followed by multiple linear regression. The significance of the selected variables and the criteria set was checked and variables were selected. After the selection of variables, regression diagnostics like studentidized residuals, hat values and cook's distance were from regression analysis marked influential values or outliers that have influence on our model. The models after removing the outliers were rechecked and certain outliers which were representing major information were left.

3.3 Cross Validation

After selection of best model, Four different independent cross validation tests were carried out which are leave one out test, K- fold test, repeated K-Fold test and bootstrapping algorithm after selection of best model. For each of these tests the data set is split randomly into two sets i.e. training set and test set and regression is performed by the software.

Leave one out cross validation (LOOCV) is n-1 i.e. out of total number of observations one observation is removed and on the remaining regression is performed and in similar manner the exercise continues for numerous times. The final result is the average of each regression run and nearness of the final result with the real model is checked. R^2 and root mean square error value is indicator for it.

In K-Fold test and repeated K-Fold test the data set is randomly divided into folds or k groups of almost equal size. For the testing the first fold or group is kept and the model is trained on k-1 folds or group. This process is repeated K times and in each, for validation, there is a different fold or group of data is used. In this study for K-Fold test the K=3 whereas for repeated K-Fold test K=10.

In bootstrapping algorithm the software resamples the data set and each time it the sub sample is different existing sub sample with sample size n. Analysis is performed on these sub samples and average is given as a final result. In this study Bootstrapping was carried out as n=100, n=500 and n=1000 on R program.

3.4 Dimensionality Analysis

Principal component analysis is a compressing tool that covers maximum information without compromising any loss in it while highlighting to us which set of variables are important.

Dimensionality analysis using Abraham solute descriptors was carried out before finalizing 2p-LFER model equations. Using R program principal component analysis was run on the collected Abraham solute descriptors. It was used to indicate whether our 2p-LFER model is as efficient or not and how much information is being covered in it.

RESULTS AND DISCUSSION

4.1 Phase 1- Aqueous System

4.1.1 Polyoxymethylene passive sampler to water

Polyoxymethylene passive samplers are used for polar chemicals and for chemicals which have H bond donating capacity.

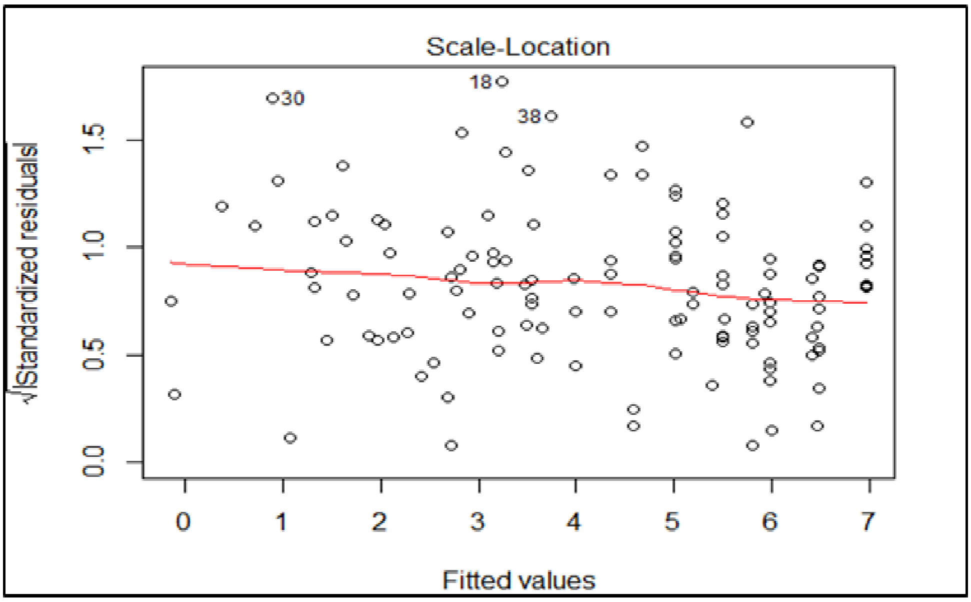

Figure 4.1: Scale Location Plot for polyoxymethylene passive sampler to water

For polyoxymethylene passive sampler to water stepwise and multi linear regression was carried out on the data set of 124 observations. Partition coefficient value was held as dependent variable and log K_{ow} and log K_{oc} was taken as independent variable for our final 2p-LFER model. Statistical analysis was also carried out while taking log K_{ow} and log K_{aw} but it did not comply with the statistical criteria that we set for our model.

The anova result for my model showed that p value for both the independent variables are significant. The p value for my model is $< 2.2e-16$ which is well less than 0.05.

Different regression diagnostics were run on the data set. Figure 4.1 is a scale location plot which tells about “Homodescasity”. It is an important assumption for a linear model, which is the equal distribution of variance across the data space. We can see in our scale location plot that there is an equal distribution of residuals along the red line across all the fitted values. The outliers can also be seen in the plot. In similar way other linear diagnostics plots like residuals v/s fitted values, normality plot, cook’s distance, residuals v/s leverage, cook’s distance v/s and leverage and influence plot were also generated to ensure that our data set is good and arranged linearly. These plots also give us information about the studentized residuals which gauges the influence arising from dependent variables, HAT values which are matrix of leverages that indicate the influence stamping from independent variables and cook’s distance, which is the measure of influential data points.

The value for R^2, Adjusted R^2 and Q^2 is 0.94 log units. The root mean square error for my data set is 0.45 and Press root mean square error is 0.44 log units. The Q^2 and press root mean square are R^2 and root mean square value of leave one out test that was used for cross validation. Four independent cross validations were carried out that support our values.

The final model equation (eq. 4.1) after carrying out all the analysis for polyoxymethylene passive sampler to water is

$$\mathbf{\log K_{POM\text{-}w}} = -0.70(\pm 0.12) + 0.59(\pm 0.04)\log K_{ow} + 0.50(\pm 0.06)\log K_{oc} \quad \text{(eq. 4.1)}$$

The bar plot (figure 4.2) is giving us information about the hydrophobicity. We can see that log K_{ow} is exerting dominant effect and as we know higher the K_{ow}, more hydrophobic are the compounds. log K_{oc} which is a proxy for residual intermolecular interactions also exerts the same response as of log K_{ow}.

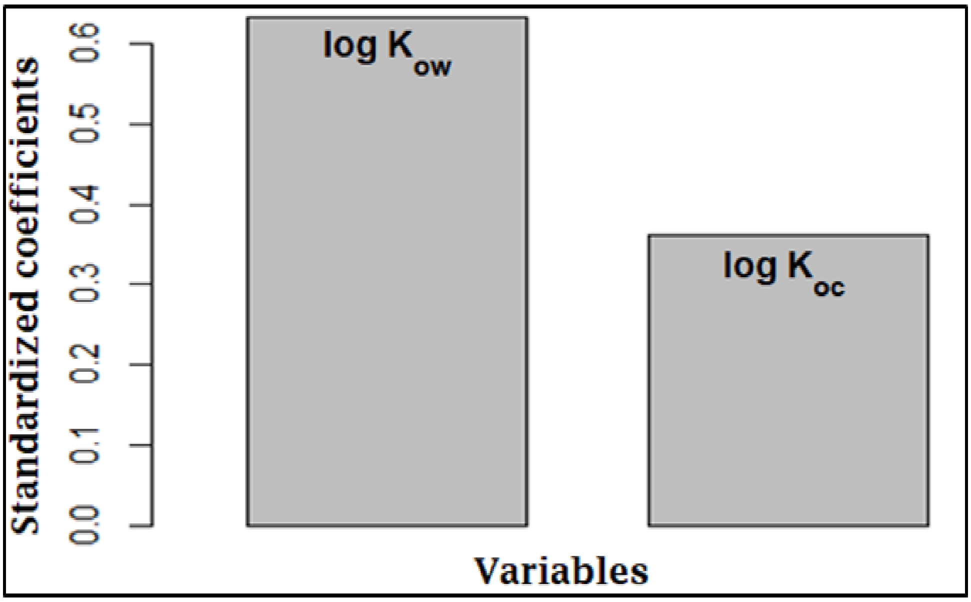

Figure 4.2: Bar Plot for polyoxymethylene passive sampler to water.

Dimensionality Analysis - Justification for 2p-LFERs

Dimensionality analysis was carried out after successful development of 2-p LFER model on Abraham solute descriptors that were collected from UFZ-LSER Database. This was carried out to ensure that 2p-LFER model is covering maximum information without losing any information.

The factor plot (figure 4.3) is showing that the nonspecific Abraham descriptors E, S and V are imparting major information to the first dimension. Whereas the hydrogen bonding interaction parameters A and B are bringing in major information to the second dimension. Very weak contributions from the Abraham Solute descriptors from 3rd to 5th dimension can be observed.

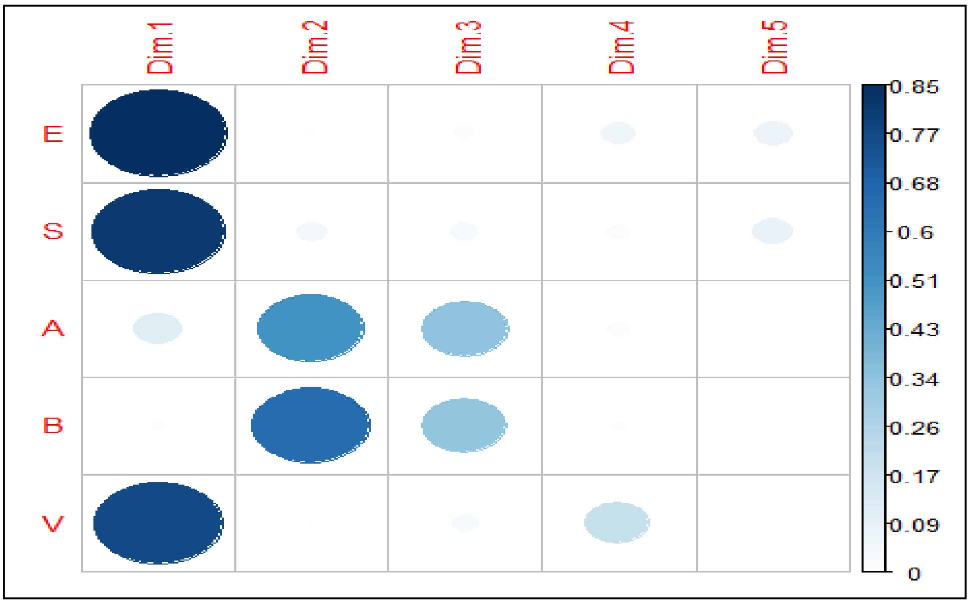

Figure 4.3: Factor Plot for polyoxymethylene passive sampler to water.

The dimensionality analysis justify the two parameter model as it tells that only two dimensions are enough to explain 75.4% of the information encoded in the Abraham solute descriptors for organic chemicals.

4.1.2 Polyethylene passive sampler to water

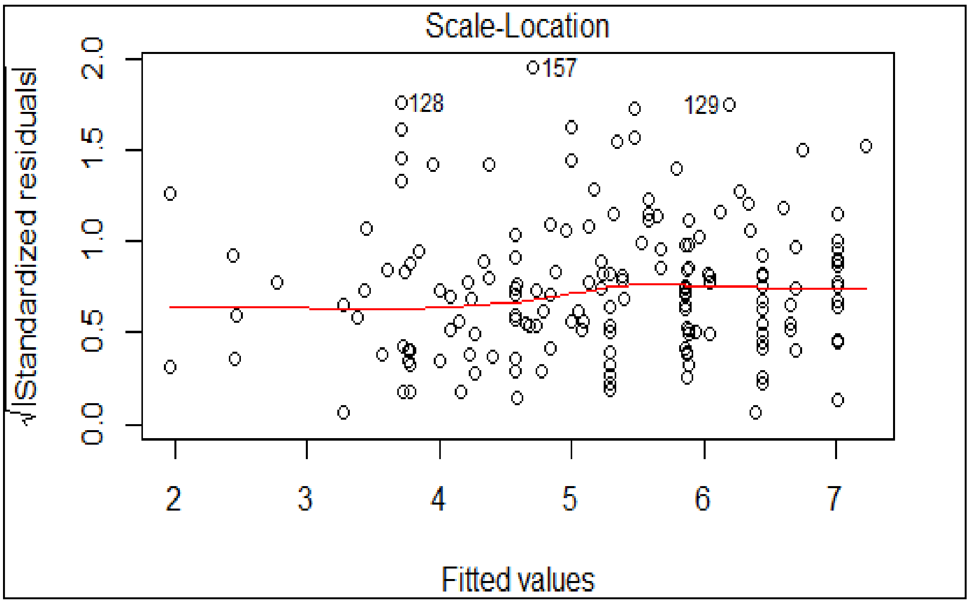

Figure 4.4: Scale Location Plot for polyethylene passive sampler to water

Polyethylene passive samplers are ethylene sheets which are cheap and good for hydrophobic chemicals . For polyethylene passive sampler to water the total number of data set was of 192 observations which was reduced to 170 after removing a outliers and problematic data like PCB 180, PCB 204, PCB 208, PCB 187, PCB 170, BDE 196, BDE 204, BDE 207, BDE 208, BDE 209, BDE 126, BDE 138, BDE 153, BDE 154, BDE 166, BDE 181, BDE 183, BDE 190, dieldrin, α-endosulfan, endrinaldehyde and n-decylcyclohexane. Partition coefficient value was held as dependent variable and log K_{ow} and log K_{aw} was taken as independent variable for our final 2p-LFER model.

Stepwise and multi linear regression was carried out on the data set and the results were found positive as all the regression diagnostics plots and other values showed that the data set is linear and diverse. The value for R^2, Adjusted R^2 and Q^2 is 0.83 log units. The root mean square error for my data set is 0.52 and Press root mean square error is 0.52 log units. Cross validation tests support our results. The p value for my model is < 2.2e-16 which is well less than 0.05 and telling us that it is very significant.

The final model equation (eq. 4.2) for polyethylene passive sampler to water is

$$\mathbf{log\ K_{PE\text{-}w}} = -0.90(\pm0.24) + 0.76(\pm0.05)\log K_{ow} + 0.39(\pm0.08)\log K_{aw} \quad \text{(eq. 4.2)}$$

In the bar plot (figure 4.5) we can see that log K_{ow} and log K_{aw} both are indicating that compounds will prefer to get to the other phase from aqueous phase that is our sampler. This indicates that the compounds are hydrophobic. Here one thing is to be noted that polyethylene passive samplers is used for super hydrophobic compounds.

Dimensionality Analysis - Justification for 2p-LFERs

The dimensionality analysis for polyethylene passive sampler to water indicates only two dimensions cover 68.3% of total information. Factor plot (figure 4.6) is showing contribution of Abraham solute descriptors in two dimensions justifying the 2p-LFER.

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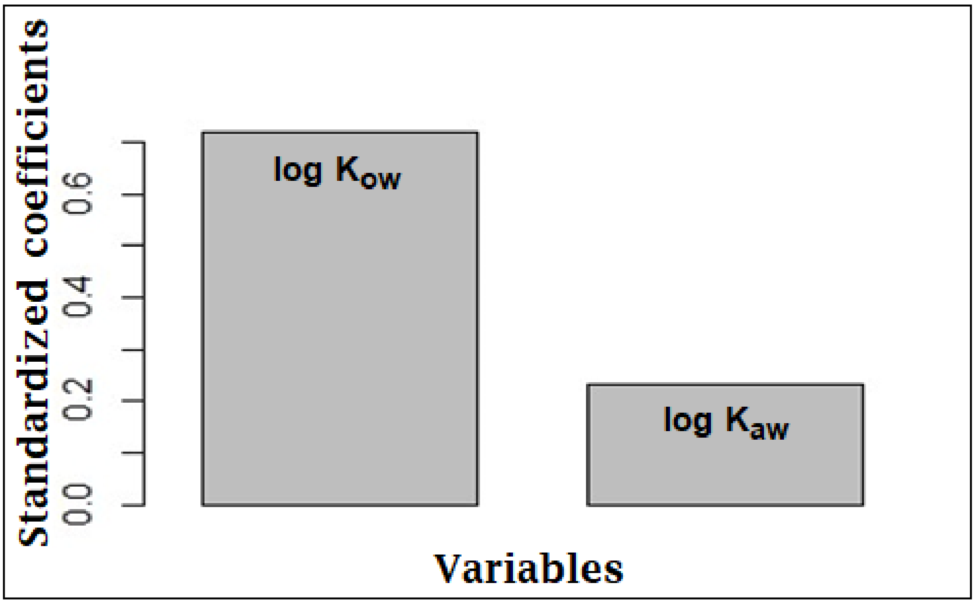

Figure 4.5: Bar Plot for polyethylene passive sampler to water.

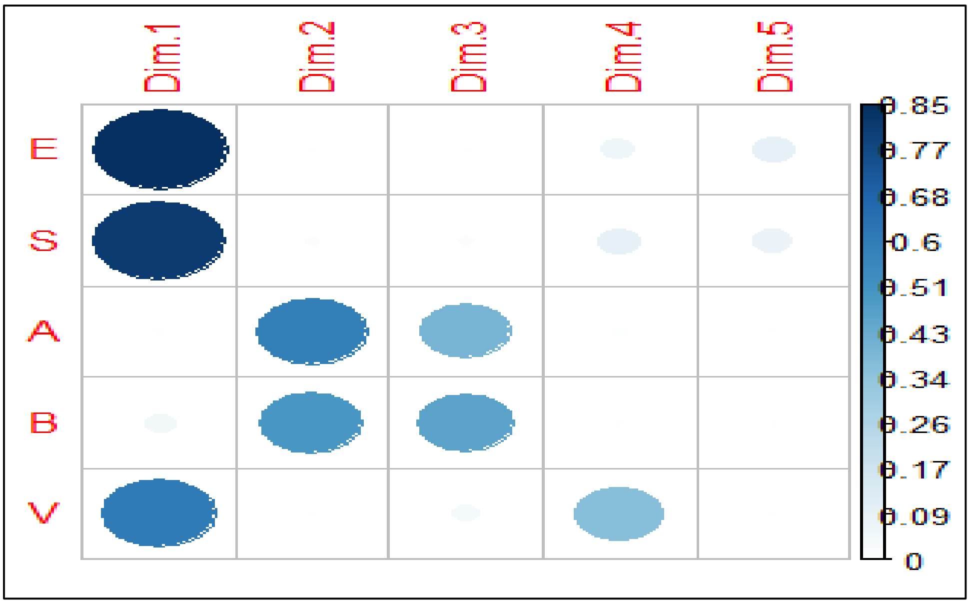

Figure 4.6: Factor Plot for polyethylene passive sampler to water.

4.1.3 Polyacrylic Passive Sampler to Water

Polyacrylic passive samplers are acrylic based samplers used for polar chemicals and chemicals with H bond accepting capacity.

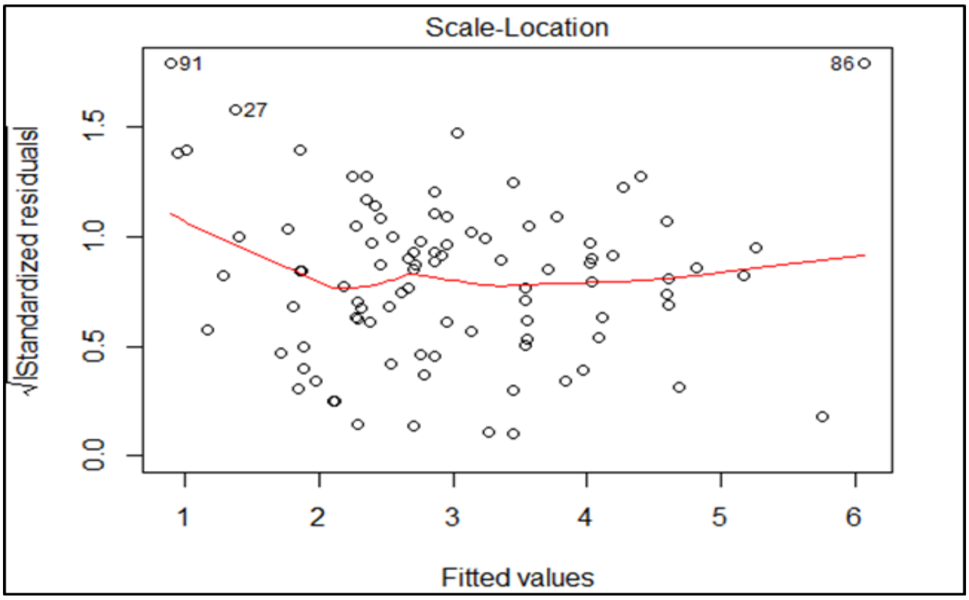

Figure 4.7: Scale Location Plot for polyacrylic passive sampler to water.

For polyacrylic passive sampler to water the total number of data set was of 96 observations. log K_{ow} and log K_{aw} was taken as independent variable for our final 2p-LFER model. Stepwise regression and multi linear regression was carried and the criteria set for model was checked. All the regression diagnostic plots confirmed that the data is linearly arranged and diverse. VIF for the data set was less than 5 while the p value was also less than 0.05 i.e. is $< 2.2e-16$.

All four cross validations tests support the values that were attained from running regression. The value for R^2 and Adjusted R^2 is 0.81 log units whereas Q^2 is 0.80 log units. The root mean square error for my data set is 0.53 and Press root mean square error is 0.52 log units.

The final model equation (eq. 4.3) for polyacrylic passive sampler to water is

$$\mathbf{log\ K_{PA\text{-}w}} = 0.001(\pm 0.19) + 0.87(\pm 0.04)\log K_{ow} - 0.08(\pm 0.02)\log K_{aw} \quad \text{(eq.4.3)}$$

In the bar plot (figure 4.8) we can see that log K_{ow} is exerting dominant effect which is telling about hydrophobicity of the compounds while log K_{aw} indicates that compounds would not get to the sampler phase.

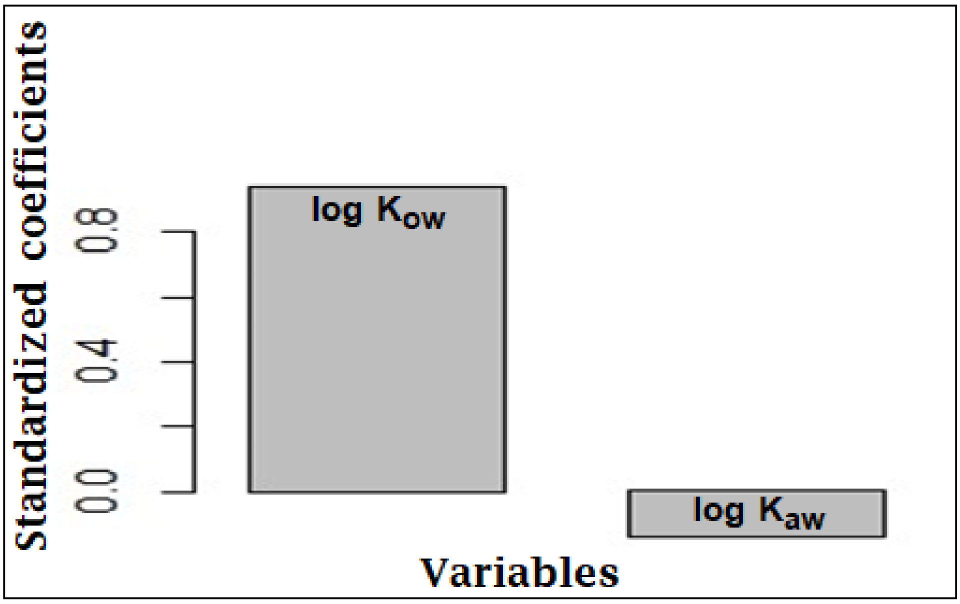

Figure 4.8: Bar Plot for polyacrylic passive sampler to water.

Dimensionality Analysis - Justification for 2p-LFERs

The dimensionality analysis carried out using Abraham solute descriptors covers 70.4% for polyacrylic passive sampler to water showing that not much information is lost. Factor plot (figure 4.9) shows that the 2p-LFERs are justified as two dimensions are covering most of the information.

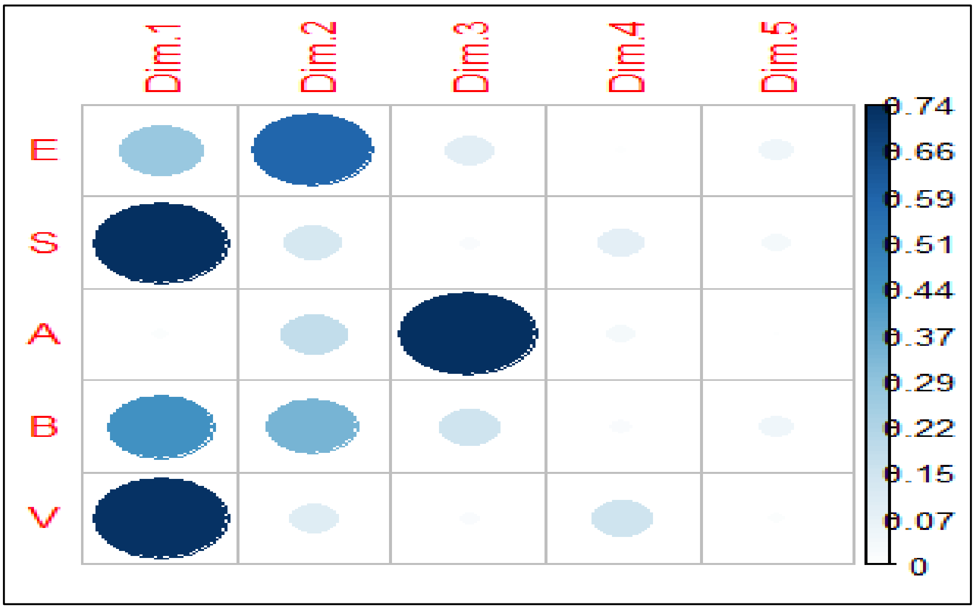

Figure 4.9: Factor Plot for polyacrylic passive sampler to water.

4.2 Phase 2- Air System

4.2.1 Polydimethylsiloxane passive sampler to air

In air system the first passive sampler is a silicone polydimethylsiloxane passive sampler compatible with wide spectrum of polar and non-polar chemicals. The data set consisted of to 140 observations. Stepwise regression and multi linear regression carried out on the data set indicated that the data set is linear. Considering the criteria log K_{ow} and log K_{oc} are taken for the final equation 2p-LFER after all the regression diagnostic plots and cross validations. R^2 and Adjusted R^2 is 0.94 log units whereas Q^2 is 0.93 log units. Root mean square error for data set is 0.54 and Press root mean square error is 0.53 log units. The anova result for 2p-LFER model is significant which is < 2.2e-16.

The 2p-LFER model equation (eq. 4.4) for polydimethylsiloxane passive sampler to air is

$$\textbf{log K}_{\textbf{PDMS-a}}=-0.07(\pm0.08) + 0.98(\pm0.02)\log Kow - 0.7(\pm0.02)\log Kaw \quad \text{(eg. 4.4)}$$

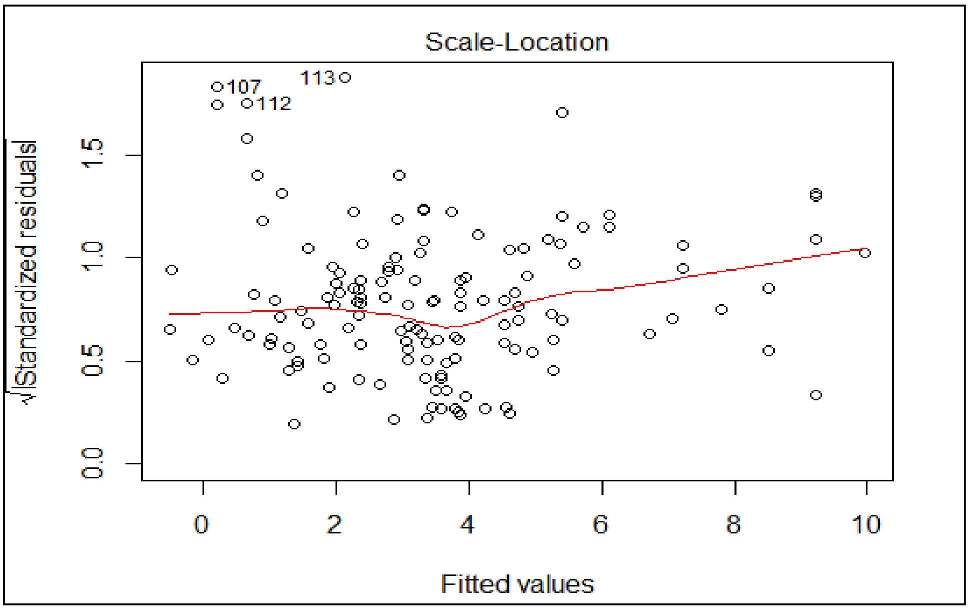

Figure 4.10: Scale Location Plot for polydimethylsiloxane passive sampler to water.

The bar plot (figure 4.10) is showing that log K_{ow} has dominant effect and as we know higher the K_{ow}, more hydrophobic the compounds. In air system log K_{aw} is showing hydrophilic nature of the compounds.

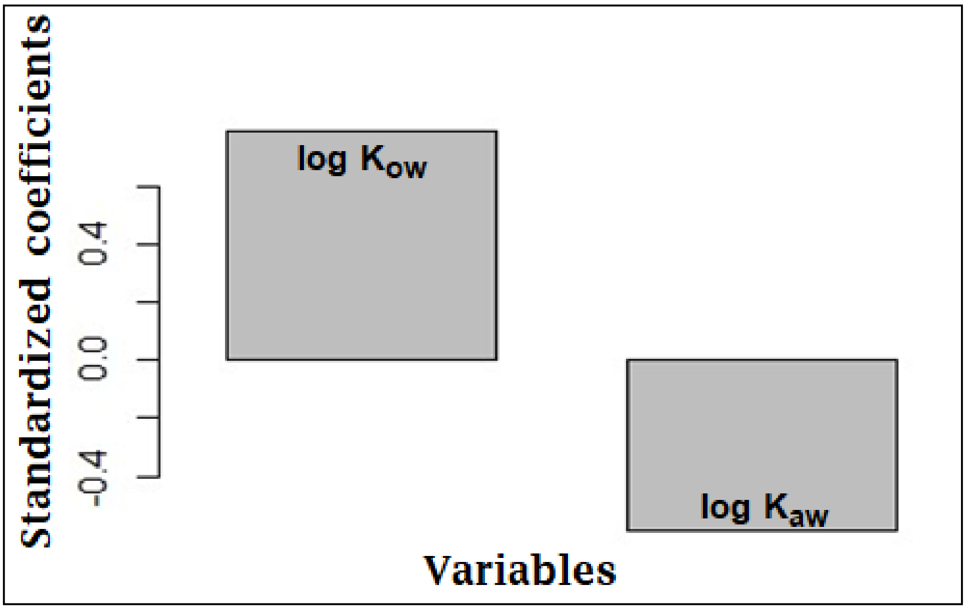

Figure 4.11: Bar Plot for polydimethylsiloxane passive sampler to water.

Dimensionality Analysis - Justification for 2p-LFERs

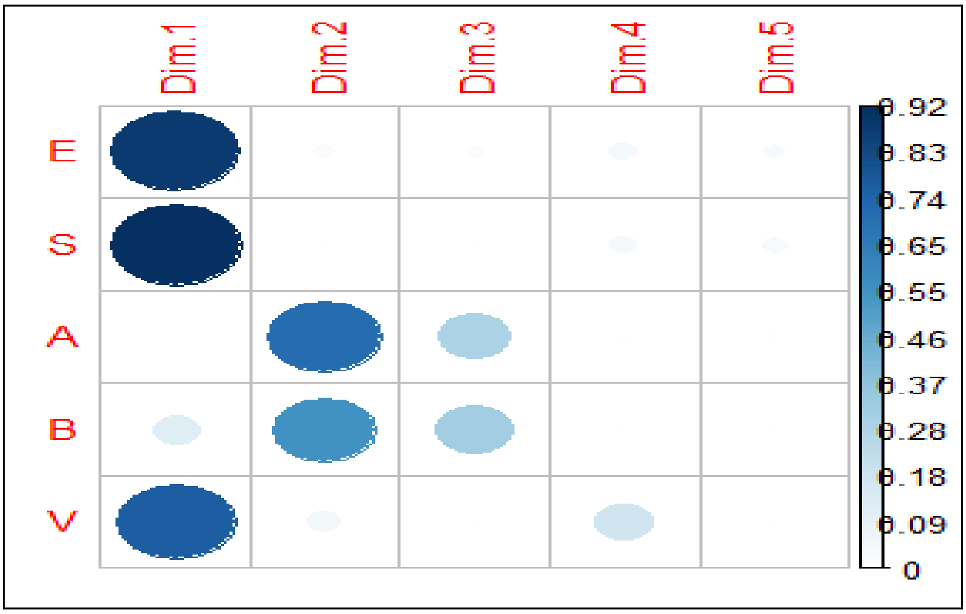

Figure 4.12: Factor Plot for polydimethylsiloxane passive sampler to air.

The factor plot (figure 4.12) justifies 2p-LFER model as only two dimensions are bringing in strong information. The dimensionality analysis of polydimethylsiloxane passive sampler to air shows that 81% of information is covered in only two dimensions.

4.2.2 Polyurethane Foam Passive Sampler to Air

For polyurethane foam passive sampler stepwise regression and multi linear regression carried out on 104 observations while taking log K_{ow} and log K_{aw} as independent variables for 2p-LFER model equation (eq. 4.5).

$$\textbf{log K}_{\textbf{PUF-a}} = 0.21(\pm 0.12) + 1.05(\pm 0.03)\log Kow - 0.90(\pm 0.02)\log Kaw \quad \text{(eq 4.5)}$$

Polyurethane foam passive samplers are widely used and are easier to manage. The p value is < 2.2e-16, less than 0.05 telling the significance. The variance inflation factor for log K_{ow} and log Ka_{w} is 2.106 which is less than 5. The value for R^2, adjusted R^2 is 0.93 log units and the root mean square error for data set is 0.38 log unit attained from running regression analysis. The diagnostic plots interpretation indicates clearly about the linear arrangement of data. The cross validations tests support the value attained from regression analysis as Q^2 is 0.93 log units and press root mean square error is 0.36 log units.

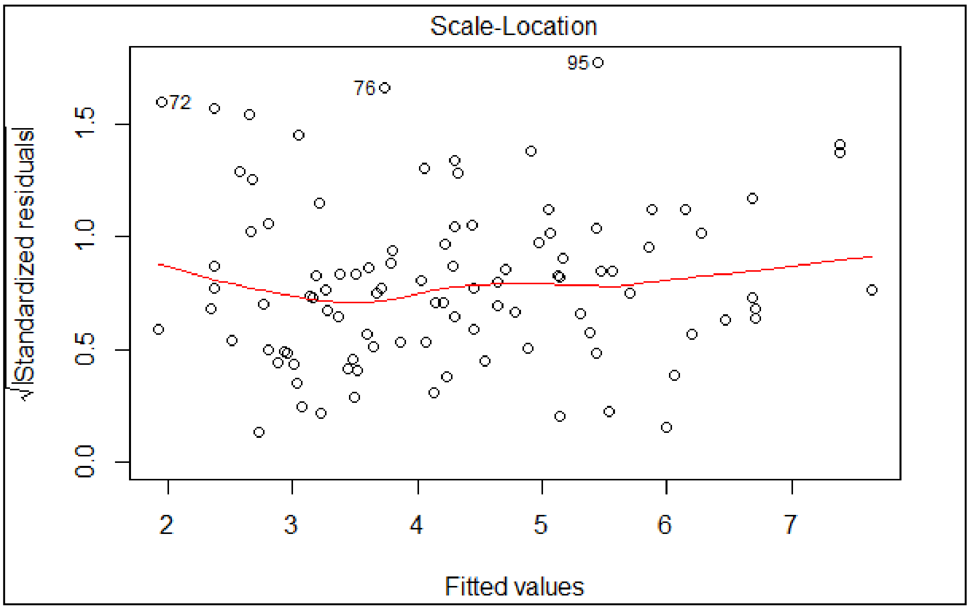

Figure 4.13: Scale Location Values Plot for polyurethane foam passive sampler to water.

The bar plot (figure 4.14) for polyurethane foam passive sampler like polydimethylsiloxane passive sampler to air indicates that log K_{ow} is rationalizing the hydrophobicity while log K_{aw} is indicates that the compounds will prefer to stay in air phase than to get the sampler.

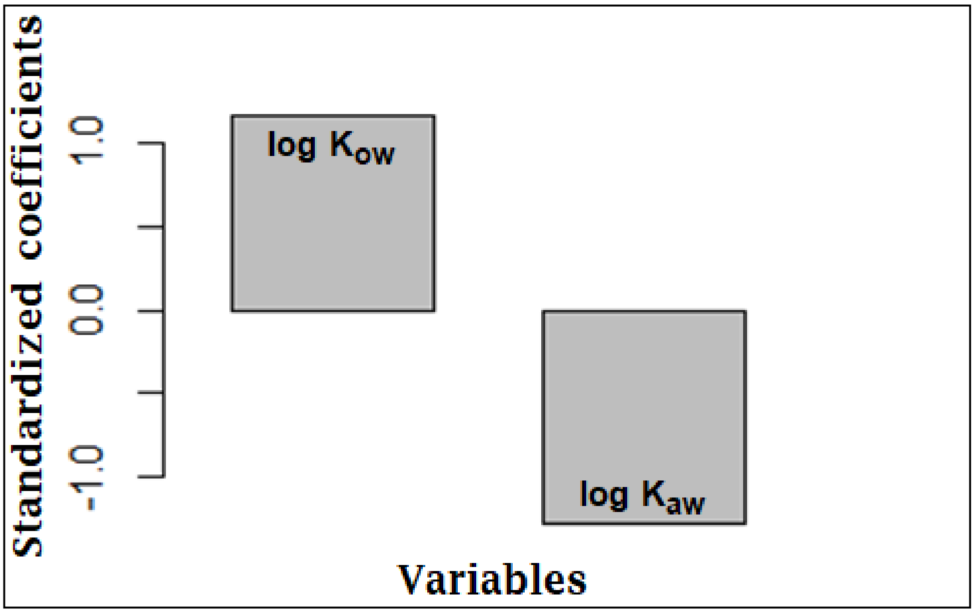

Figure 4.14: Bar Plot for polyurethane foam passive sampler to water.

Dimensionality Analysis - Justification for 2p-LFERs

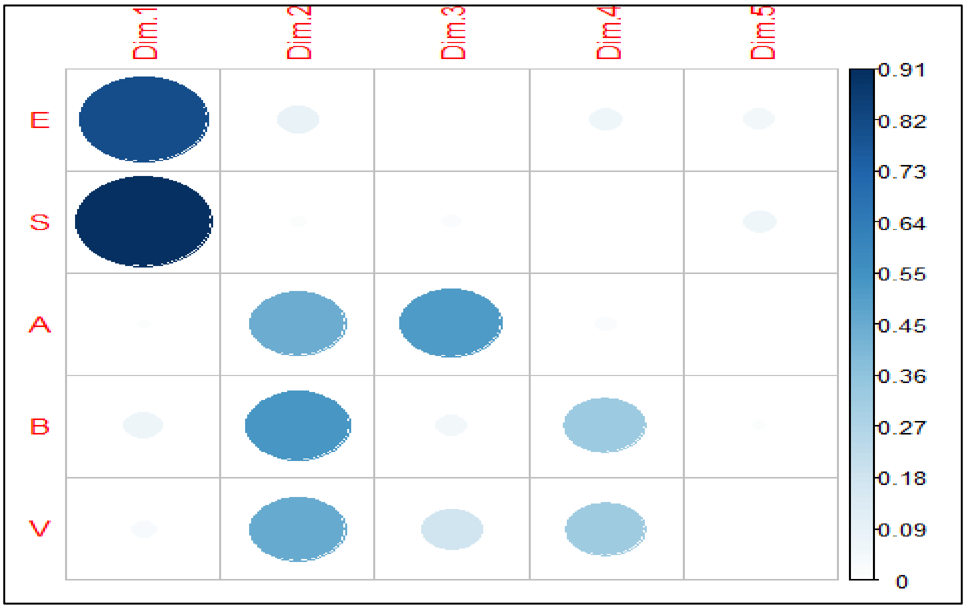

Figure 4.15: Factor Plot for polyurethane foam passive sampler to water.

The factor plot (figure 4.15) is showing that Abraham solute descriptors are mostly covered in first two dimensions. In polyurethane foam passive sampler it can be observed that descriptor V is being covered in second dimension as before it was covered in first dimension. The sorbent difference tells us that the descriptors may behave differently depending upon the type of sorbent material used. The first and second dimension brings 67.5% of information which justifies the 2p-LFER.

4.3 Results Summary

Table 4. 1: Results summary

Passive Samplers					
	POM-water	**PE-water**	**PA-water**	**PDMS-air**	**PUF-air**
Regression Analysis (Stepwise/Multi Linear Regression)					
No. of Observations	123	170	96	140	106
R^2	0.94	0.83	0.81	0.94	0.93
Adj. R^2	0.94	0.83	0.81	0.94	0.93
RMSE	0.45	0.52	0.53	0.54	0.38
VIF	log K_{ow} = 2.601 log K_{oc} = 2.601	log K_{ow} = 2.665 log K_{aw} = 2.665	log K_{ow} = 1.114 log K_{aw} = 1.114	log K_{ow} = 1.006 log K_{aw} = 1.006	log K_{ow} = 2.106 log K_{aw} = 2.106
Cross Validation Tests					
LOOCV					
R^2	0.94	0.83	0.80	0.94	0.93
RMSE	0.44	0.52	0.52	0.53	0.36
K-Fold CV					
R^2	0.94	0.85	0.82	0.93	0.94
RMSE	0.43	0.52	0.50	0.52	0.35
Repeated K-Fold CV (k=10)					
R^2	0.95	0.84	0.84	0.94	0.94
RMSE	0.43	0.50	0.50	0.52	0.35
Bootstrapping (n=500)					
R^2	0.94	0.83	0.81	0.94	0.93
RMSE	0.45	0.52	0.53	0.53	0.37

CONCLUSION AND RECOMMENDATION

5.1 Conclusion

Models developed in this study are theoretically-rigorous and statistically robust respecting the principle of parsimony. The dimensionality analysis provides the statistical support for the justification in reducing 5p-ASM to 2p-LFER as it can be observed that it covers most of the information and supports the fact that only few information is lost. 2p-LFER models for aquatic passive samplers and air passive samplers with RMSE range 0.45 to 0.55 log units and 0.38 to 0.54 log unit were successfully developed in this study.

The LFERs developed in this study unanimously shows that the log Kow has a positive effect on the uptake for both water and air samples. The proposed LFER methods are accessible, simple and efficient than different multi-parameter estimation methods with very low cost as compare to other estimation techniques like Abraham Solvation Method that requires experimental values and Quantitative Structure Activity Relationships or Quantitative Structure Property Relationships model which require superfast computer and are highly expensive.

5.2 Recommendations

Though my 2p-LFER model has its limitation for ionize chemicals, metallic and organometallics chemicals but this model can be used for passive samplers such as EVA - Ethylene vinyl acetate passive sampler. This sampler can be modeled using the same principles.

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Supporting information of my thesis can be accessed using the link. It comprises of all tables, plots, figures and other relevant details.

https://drive.google.com/file/d/1-11GoiarzSKw98uKGj7pLwym7CUhtcKf/view?usp=sharing