George Mason University **Prof. Abul Hussam**
CHEM 424/624: Principles of Chemical Separation **Planetary Hall 337/402**
Spring 2020, T,R 5:55- 7:10 PM, PH 310 **ahussam@gmu.edu**

This course is designed to introduce the theory and practice of chromatographic science with emphasis in analytical separation. Analytical separation techniques are now used in every laboratory doing chemical analysis. It involves separation, quantitation, and identification of chemical species in gas, liquid, aqueous, polymer, biological systems, and any complex matrix. The techniques used are Gas-Liquid Chromatography, Ion Chromatography, Size Exclusion Chromatography, Capillary Electrophoresis, and their variations. This graduate level course assumes a background in Instrumental Analysis, Physical Chemistry, and Calculus I. The topics covered are from the assigned text book, journal articles, and posted materials. Class lectures are augmented by in-class problem solving. The final grade is determined by your performance in class exams, homework, and presentation.

Syllabus and schedule

Lecture	Topics	Resources
Jan 21-Jan 30	**Lecture 1,2** H-22 and PMBB: Distribution between two immiscible phases (solvent extraction), Definitions of partition and distribution coefficient, fractions left in phases after n^{th} extraction. Effect of pH on the distribution of weak acids and bases. The role of fractional distribution on partition coefficient, K. and capacity factors, k. Distribution of metal complexes for separation of metals. Know all terms and symbols in equation for D. Types of chromatography. Categories and variations (G10.1). Know mobile phase, supporting material (alumina and silica), stationary phase, and dimensions of open tubular column. Know retention time, void time, capacity factor, resolution, separation factor, phase ratio, retention volume, linear velocity, properties of a Gaussian peak, resolution and theoretical plates. Resolution between two adjacent peaks, its relation to column length, and cycling technique. **Lecture 3,4** **H23: Gas chromatography**, basic instrumentation, column types- capillary columns and dimensions, stationary phase materials, polarity of stat phase and functional group, examples of separation of compounds, isothermal and temperature programmed techniques, injection techniques, split, splitless injection and column overloading, detectors, flow rate sensitivity of TCD, MS as detector and its primary advantages. HPLC: Basic instrument, column material, silica as supporting materials and its nature, role of silanol group, deactivation and bonded C-18 phase as stationary phase. Mobile phase in HPLC and control of retention by mobile phase composition. Supercritical CO_2 as mobile phase **G-10: Chromatographic migration**. Fractional concentration in mobile and stat phase (R), zone velocity, average velocity, retention time of solute, unretained solute, retention volume. Relations between partition coefficient, capacity or retention factor, retention volume, and phase ratio. Relation between capacity factor and change in standard chemical potential. Origin of non-linearity in chromatography and peak tailing. Effect of gas compressibility and pressure –gradient correction factor on retention volume. Effect of gradient on R_f in TLC and PC. Non equilibrium zone spreading, effective diffusion coefficient and its effect on plate height. Understand all basic equations to solve problems.	G-9.13, G-10, H-22, H23, PMBB
Feb 4,6	**Sept 16: Lecture 3** Temperature dependence of retention factor (k'). Enthalpy and entropy driven	G-1, G-2, H21-1,

	separations. Linear free energy relation to number of methylene group increment in homologous series. **G-1:** Separation criteria and thermodynamic limitations. Entropy control and the origin of size exclusion chromatography (more in next class **G2:** Equilibrium thermodynamics in closed and open systems, concept of partial molar free energy and chemical potential, different concentration unit based partition coefficients (K_c, K_x, K_a etc), and standard states.	Handout
Feb 11,13	**Lecture 4** Partition coefficient and its relation to vapor pressure and activity coefficient for gas-liquid, liquid-liquid, and liquid-solid systems based on chemical potential. Understanding of standard states and the use of appropriate units. Retention factor and separation factor- relation to the above parameters. The role of interfacial surface tension and infinite dilution activity coefficient of solute in sorption chromatography (NPLC and RPLC). Excess free energy as a measure of solute-solvent interactions. Origin of intermolecular forces. Concept of functional group contributions and linear free energy relations. Solubility parameter as a measure solvent strength and solute-solvent interactions, its relation to chemical potential and retention factor. Supercritical CO_2 as mobile phase in chromatography.	G-3
Feb 18,20	**Lecture 5** **Chapter 2: Equilibrium drive force for separation** Measurement of activity coefficient by GC and Headspace GC. Relation between solubility parameter (δ) and activity coefficient (or infinite dilution activity coefficient). How to use the δ for solvent selection in separation? Entropy effect in separation (G-2). Principle of size exclusion chromatography and separation of large molecules. **G-3**: Molecular transport, basic driving forces, Langevin equation, Stokes equation, Fick's first law and transport with flux, origin of diffusion equation.	G-3, H-25.6
Feb 25,27	**Lecture 6** **Chapter 3: Separative transport** Fick's second equation. Basic transport equation and concept of zone velocity. Moving coordinate in transport eq. Know the difference among displacement under external and internal potential gradient, bulk displacement with transport medium, and diffusional displacement.	G-3
March 3-12	**Lecture 7,8** **Chapter 4: Flow transport and viscous phenomena** Origin of flow and viscosity. Flow through capillary and packed column. Flux density and Darcy's law, Hagen Poiseuille law. Capillaric flow model in TLC and paper chromatography. Compressible flow in GC- know average velocity eq. Electroosmotic flow. Laminar and turbulent flow- Reynold's number. Viscosity of liquids and gases- Stokes equation. Ways to reduce viscosity in liquid- implication on LC and SFC.	G4
March 17	**Midterm: 90 minute exam includes material covered until March 12 (**G-9.13, G-10, H-22, H23, PMBB, G-4, H-25.6, G-1, G-2, H21-1, Handout, G3, G4)	
March 19-31	**Lecture 9,10** **Chapter 5: Zone formation and resolution** Solve Fick's second equation and generate C(x,t) as a Gaussian function. Properties of	G-5

	Gaussian function in relation to chromatographic separation. Statistical moments and their significance. One dimensional random walk, and band broadening, and the origin of diffusion coefficient. Mechanisms of band broadening- a first look. Plate height, H, number of theoretical plates, and index of separation. H in elution system, Peak resolution, peak capacity and their relation to H and N. Non-Gaussian effect.	
April 2-9	**Lecture 11** **Chapter 8: Separation by external fields** Separation by external field: Transport and theoretical plate. Electrophoresis- types and examples. Separation power- N, H and n_c. Debye-Huckel equation and the origin of effective charge and its consequence in electrophoretic mobility. Origin of surface charge and modification of equilibrium expression for surface complexation reaction. Surface pH and surface potential. Electroosmotic and electrophoretic mobility. Capillary electrophoresis: Principle, technique, application (Harris 25.6) and power point slides as PMBB. Check example problems in Harris. Laboratory visit to see different GG, HPLC, GC-MS and other separation techniques.	G-8.1-8.5, H-25.6, PMBB
April 14-16	**Lecture 12** **Chapter 11: Chromatography from a molecular viewpoint** Random walk model and molecular basis of band broadening. Band broadening due to longitudinal diffusion, sorption-desorption, and flow and diffusion in the mobile phase. The role of these processes in packed and capillary column.	G11
April 23-28	**Lecture 13** **Chapter 12: Optimization in chromatography** Plate height equations: packed and capillary columns. Corrections in GC. Derivation of reduced plate height. Optimization of resolution: parameters to optimize. Relation between resolution and thermodynamics. Complex multicomponent separation, minimizing plate heights, and faster separation.	G 12
April 30 May 4	**Presentation of papers by students**	
May 7	**Final exam 4:30 – 7:15 PM** Covers materials discussed after the midterm	

Notes: **G -10**: Giddings- Chapter 10; **H-22**: Harris- Chapter 22; **PMBB**: Posted materials on Blackboard;

Required Text

Unified Separation Science, J. Calvin Giddings
Publisher: Wiley-Interscience; 1st Edition
ISBN-10: 0471520896, ISBN-13: 978-0471520894

Chapters 22-25

Quantitative Chemical Analysis, 8th or 9th Edition, Daniel Harris
ISBN-10: 142925436X, ISBN-13: 9781429254366

Homework Problems

Students are responsible to work out the following problems. These problems are also solved in class after the chapter is covered. Exams are primarily based on the problems solved in class and materials discussed.
Chapter 1: Introduction: 1, 2, 3, 4, 5, 6
Chapter 2 Equilibrium: 1, 2, 3, 4, 5, 6
Chapter 3: Separative Transport: 1, 4, 7, 8, 9, 11, 12, 13

Chapter 4: Flow and Transport: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13
Chapter 5: Zone Formation and Resolution: 5, 7, 8, 10, 11, 13, 14, 15, 19, 20, 22, 24
Chapter 8: Separation by External Fields: 1, 3, 6, 7
Chapter 10: 3, 4, 5, 6, 7, 8, 9, 10, 11
Chapter 11: 1, 2, 3, 4, 5, 7, 8, 9
Chapter 12: 1, 3, 4, 5, 6, 7, 8,

Assigned homework and projects to be submitted

1. Limonene (L, a lime flavor) has a partition coefficient of 50.0 between water (phase 1) and chloroform (phase 2). The initial concentration of L is 0.050 M in 100.0 mL water. It is then extracted 5 times with 10.0 mL portions of chloroform. Find the fraction of solute remaining in aqueous phase and the fraction extracted.
2. Show that the distribution constant (D) of a weak acid between two phases is given by $D = K [H^+] /([H^+] + K_a)$. What is D when pH= pK_a? Plot a graph of log D vs. pH (2-12, intervals 0.5), when K = 4.0 and pK_a = 5.0 (Use Excel).
3. Giddings: Problem 1.5

G1: 2, 3, 4, 5, 6.
G2: 3
G5: 1, 6, 8, 9 (data plot and explanation), 16, 23
G8: 6 – parts
G-10: 3, 4, 5, 6, 9, 10, 11

Paper presentation

Select a full-length paper on separation science published in last five years from a list of journals given below. Write a 2 page review of the paper and present the paper in class. The ten minute 'power point' presentation should emphasize the purpose of the work, the separation technique used, the problem solved, and the results of interest. You should submit the journal reference of your selection to me by March 17, 2020 for approval and the review by April 23, 2020. I will post the title on the 'blackboard'. The final presentation will be held on April 30 and May 4.

The following journals are recommended:
Analytical Chemistry (ACS Publications) **and other ACS Publications**
www.pubs.acs.org/journal/ancham
Journal of Chromatography A - Elsevier
www.journals.elsevier.com/journal-of-chromatography-a/
Journal of Chromatography B - Elsevier
www.journals.elsevier.com/journal-of-chromatography-b/
Journal of Chromatographic Science: Oxford Journals ...
www.chromsci.oxfordjournals.org/
Analytica Chimica Acta - Journal - Elsevier
www.journals.elsevier.com/analytica-chimica-acta

Grading

Midterm 20%, Final 40%, HW and Project 20%, Paper presentation 20%