Macromolecular, Supramolecular, and Nanoscale (MSN) Systems in the Curriculum

Context

Much of the traditional undergraduate curriculum in chemistry focuses on the synthesis and characterization of small discrete molecules. But many types of materials are not well-described from this perspective. These include macromolecules (whether synthetic or biological), supramolecular systems and nano/mesoscale systems. In some of these materials, the boundaries between discrete molecular and bulk behavior are blurred, which impacts the ways that we can describe and characterize their structure and physical properties. In others, though the molecular boundaries may be clear, understanding key behaviors relies on understanding the role of non-covalent and intramolecular interactions. Recognizing the differences between small molecule vs. larger systems is key to understanding many important materials that are pervasive in our society and in modern chemistry. Because of the importance of these large scale chemical systems, the ACS guidelines require that exposure to aspects of MSN chemistry be included in the undergraduate curriculum.

The 2015 ACS guidelines state that students be exposed to MSN content covering three broad areas: 1) structure, synthesis and/or preparation, 2) characterization, and 3) physical properties. Coverage of at least two types of MSN systems, such as synthetic polymers, biological macromolecules, supramolecular aggregates, and/or meso- or nanoscale materials is required. To be counted towards the requirement, MSN material must focus on aspects in which large scale chemical systems are significantly different than small molecules. Contrasting examples include:

- Simply referencing the types of condensation or addition reactions that can be used to synthesize polymers does not address their unique properties.; but the requirement could be met by discussing the impacts of these synthetic routes on the properties of the final polymer, the high extents of reaction (>99%) necessary to achieve high molecular weight polymers by condensation polymerization or the impact of various types of addition polymerization reactions on molecular weight distribution, stereochemistry, etc.
- Studying the kinetics of an enzyme catalyzed reaction where only the catalytic impact of the enzyme is covered would not contribute to student’s understanding of MSN systems; inclusion of the impact of the tertiary structure on its catalytic role would.
- Superconductors composed of solid state oxides are not supramolecular systems; metal-organic frameworks (MOFs) are valid examples of MSN systems.
- Laboratories that utilize polymeric systems, such as polysiloxanes, epoxies, or other polymers without covering the relationship of the properties of these systems do not fulfill

the MSN requirement; labs which focus specifically on the synthesis, characterization, or evaluation of properties that are uniquely related to MSN materials would. It is expected that laboratories used for the MSN requirement include related background, either in lecture courses or significant pre-lab assignments to ensure that the students have a solid understanding of the MSN aspects of the laboratory content.

Some chemistry programs provide coverage of this material in polymer chemistry, materials chemistry, and/or supramolecular chemistry courses which may be used to satisfy the MSN requirement. However, *IT IS NOT NECESSARY FOR DEPARTMENTS TO DEVELOP A SEPARATE COURSE*, as it is equally acceptable to introduce these concepts into existing foundation and in-depth courses across the curriculum. While MSN content may be incorporated into any of the standard subdisciplines, it is not required that the exposure spans *every* subdiscipline.

If not covered through a stand-alone course(s), the combined coverage of these topics should be the equivalent of approximately one-fourth of a standard semester course distributed through the required curriculum, where the coverage of any single type of MSN system will be counted for no more than half of the MSN coverage. This supplement suggests ways to introduce these concepts in either a distributed or stand-alone format throughout the chemistry curriculum.

Conceptual Topics

Three general subject areas in MSN chemistry are recommended for meeting the MSN requirement. While some content from all three general subject areas is expected, CPT recognizes that most approved curricula will not cover all of the topics suggested below.

Structure, synthesis, reactions, and preparation of MSN materials

- Basic synthetic approaches for the preparation of MSN materials such as synthetic polymers, biological macromolecules, inorganic polymers, framework materials, and nanoparticles.
    - Step growth (condensation) polymerizations - molecular weight dependence on extent of conversion (Carothers Equation), reaction kinetics, broad MW distributions, branching
    - Chain growth (radical, ionic, or coordination) polymerizations – reaction kinetics, catalysts, living polymerization, MW control, stereochemistry
    - Nanostructures - top-down milling (e.g., milling, e-beam patterning, chemical etching), bottom-up synthesis (solution synthesis of nanoscale particles, sol-gel growth, pyrolysis, vapor phase growth, e-beam deposition))
    - Quantum dots – solution phase synthesis
    - Supramolecular inclusion complexes (e.g., cyclodextrins, curcuribitils, etc.)
    - Endohedral complexes
    - Metal organic frameworks

- Polymer composition (homo vs copolymer) structure (linear, branched, star, crosslinked/network) and morphology (amorphous, semi-crystalline), and the role of covalent and non-covalent interactions in determining molecular interactions
- Isolation, purification and size separation techniques for synthetic and biopolymers (solubility, size exclusion, etc.).
- Nanoparticle structure - single component, core-shell

Characterization of macromolecules and mesoscale structures

- Structure and characterization of polymers/macromolecules:
    - Techniques for determining molecular weight and molecular weight distributions (steric exclusion chromatography, light scattering, MALDI-MS)
    - Identification of phases (amorphous, microcrystalline) and phase changes including glass transition, crystalline melting, and degree of crystallinity
    - Network formation and degree of crosslinking
    - Thermo-mechanical properties such as toughness, yield strength, stress-strain behavior, and degradation temperature
    - Electrical properties of conjugated systems
- Structure and characterization of biopolymers:
    - Gel electrophoresis
    - Nucleotide melting
    - Circular dichroism/thermal melts
- Structure and characterization of nanoparticles
    - Particle size and electronic properties of nanoparticles by UV/Vis spectroscopy
    - Particle size and morphology by SEM, TEM, and AFM
    - Particle size distribution by aerosol MS
    - XRD for crystallinity, chemical composition, and particle size
    - Mobility measurements by zeta potential
    - Particle size and morphology by light microscopy and optical spectroscopy
    - Elemental profiling by XPS, EDX, or nano-SIMS

Physical properties of MSN systems

- Impacts of size on the evolution of properties as MSN materials grow larger on:
    - Mechanical properties: impacts of entanglements, new phase changes (glass, microcrystalline and liquid crystalline transitions), strength-to-weight ratio, thermoformability, durability, etc.
    - Optical properties: impact of polymer morphology
    - Thermal properties: glass transition temperature, segmental motion, relationship of backbone structure and aromaticity on thermal stability
    - Electrical properties
    - Surface plasmon resonance in metal nanoparticles
- Impact of non-covalent interactions in determining key properties and behaviors
    - Intra-molecular interactions and relationship of structure and function (especially for biopolymers)

    - Impact of stereoregularity on crystallization and material properties for synthetic and biopolymers
    - Impact of chain ordering on optical and electrical properties
- Properties of solutions and mixtures
    - Thermodynamics of mixtures/phase separation of macromolecules
    - Thermodynamics of solution formation and rheology, non-Newtonian behaviors
    - Behaviors of composite material and alloys, and the impact of length scale
- Biocompatible and biodegradable polymers and their applications

Practical Topics

MSN can be used to illustrate a myriad of principles throughout the classroom and laboratory components of the chemistry curriculum. The brief listing below provides examples appropriate for each subdiscipline.

Analytical Chemistry

- Size exclusion chromatography – determination of synthetic polymer molecular weight and molecular weight distribution
- Study of structural stability, phase changes, morphology by DSC
- Stability, gas absorption capacity using thermogravimetry (TGA)
- Molecular weight by functional-group titration
- Size determination by light scattering methods
- Determination of copolymer composition by pyrolysis gas chromatography
- Determination of additive levels using ultraviolet or infrared spectroscopy
- Determination of structure, long-range order in framework materials by X-ray methods
- Determination of nano/mesoscale structure and composition by microscopies and scanning probe methods

Biochemistry

- Structure, stabilizing factors, folding and biosynthesis of key biopolymers including proteins, carbohydrates, cellulose, RNA, and DNA
- Influence of molecular bonding on structure and properties (carbohydrates vs cellulose, crosslinking of lignin, DNA, etc.)
- Impact of intramolecular interactions on protein structure, folding, influence on biological function
- Intermolecular interactions of biopolymers and influence of polymer primary, secondary, and tertiary structure (DNA, RNA, proteins, etc.)
- Determination of molecular weight and structure for natural polyamides
- Self-assembly of large-scale biological systems (lipids, cell walls, etc.)
- Natural, modified natural and synthetic macromolecules used for bioactive applications
- Purification of proteins: size exclusion, solubility (precipitation via salt or molecular crowding); laser light scattering (aggregation state, pre-crystallization conditions)
- Thermodynamics of protein folding and superstructure organization

- Allosteric regulation of proteins; e.g., hemoglobin
- Intrinsically disordered protein domains
- Protein aggregation polymerization, e.g., prions, actin, sickle cell, protein aggregation and disease
- Heteropolysaccharides (cartilage) and homopolymer saccharides (gelation etc.)
- Secondary/quaternary structure without ternary structure
- Supramolecular structure of collagen
- Lipid bilayer viscoelastic properties

Inorganic Chemistry

- Coordination – catalyst formation, metalloenzyme structure, structure of metal-organic frameworks (MOFs), control of porosity and framework size, control of gas adsorption properties
- Ziegler-Natta, metallocene catalysts for olefin polymerization – impact on industrial/materials development
- Structure/bonding/property relationships in silicon or phosphorous based polymers and semiconductors, including backbone flexibility, conductivity, and molecular orbital and band theory compared to C based analogs
- Utilization of X-ray and calorimetry to determine percent crystallinity
- Polymer/inorganic natural systems such as chitin/calcium carbonate composites
- Absorption properties of metal nanoparticles (e.g., colloidal gold used to color stained glass windows)
- Quantum dots – effect of size on optical properties, electrical properties, effect of core-shell structures

Organic Chemistry

- Step growth polymerizations including common types of polymers (nylon, PET, polycarbonate, polyurethane, etc.)
- Types of chain growth polymerization (radical, cationic, anionic, and coordination) and common types of polymers (polyethylene, polypropylene, PVC, polystyrene, etc.)
- Ring-opening polymerizations
- Living polymerizations and control of molecular weight/distribution
- Biocompatible materials (e.g., glycolic acid/lactic acid polyesters as absorbable sutures, bone scaffolding, etc.)
- Green chemistry, sustainability, materials from renewable biosources
- Role of hydrophobic/hydrophilic interactions in governing self-assembly processes (latex polymerizations, surfactant behavior)
- Role of π-stacking in self-assembly
- Properties of extended conjugated systems (polyacetylene, graphite, graphene)

Physical Chemistry

- Polymerization kinetics by various synthetic methods and impact on polymer structure and polydispersity

- Thermodynamics of polymer/solvent and polymer/polymer solutions with respect to phase separation and solution properties – comparison to small molecule/ideal analogs
- Dilute solution viscometry – determination of polymer molecular weight, hydrodynamic radius, chain branching, solvent interactions/ideal solutions
- Non-Newtonian properties of polymer melts and solutions
- Thermomechanical properties including differential scanning calorimetry (DSC) – observation of phase changes, determination of percent crystallinity, dynamic mechanical analysis (DMA) – determination of viscoelastic properties of elastomers, and thermogravimetric analysis (TGA) – determination of thermal stability/degradation
- Influence of linearity, stereochemistry, tacticity on polymer crystallinity and density
- Kinetic vs thermodynamic aspects of nanocrystal growth and morphology, and impact on physical properties
- Optoelectronic properties of nanostructures such as surface plasmon resonance and surface enhanced Raman scattering (SERS)

References

Below is a list of references that may be useful in incorporating macromolecular content:

- M.M. Coleman and P.C. Painter, “Fundamentals of Polymer Science: An Introductory Text”, 2nd Ed., Technomic Publishing/CRC Press LLC, Boca Raton, FL, 1997.
  [An excellent elementary text that can function as a source of material to augment/ enhance/ increase interest in any foundational chemistry course.]
- C.S. Brazel and S.L. Rosen, “Fundamental Principles of Polymeric Materials”, 3rd Ed., John Wiley and Sons, Inc., Hoboken, N.J., 2012.
  [A classic beginning textbook.]
- H.R. Allcock, F.W. Lampe and J.E. Mark, “Contemporary Polymer Chemistry”, 3rd Ed. Prentice Hall, 2003.
  [A classic textbook that may be at a slightly higher level than desired for foundation courses, but is good for in-depth courses and a good reference for instructors]
- H.A. Wittcoff, B.E. Reuben and J.S. Plotkin, “Industrial Organic Chemicals”, 3rd Ed., John Wiley and Sons, Inc., Hoboken, N.J., 2013.
  [An outstanding textbook which not only treats polymeric materials but places them in context as to origin, prominent place in the chemical industry, and importance to societal well-being.]
- J.A. Tyrell, “Fundamentals of Industrial Chemistry”, John Wiley and Sons, Inc., Hoboken, N.J., 2014, Ch. 7-9.
  [Provides a brief overview of polymeric materials in chapters 7-9, which can be drawn on to provide supplemental material for any foundational course.]
- B.A. Howell, Ed., “Introduction of Macromolecular Science/Polymeric Materials into the Foundational Course in Organic Chemistry”, American Chemical Society (Symposium Series 1151), Washington, D.C., 2013.

[This volume contains several chapters illustrating how polymeric materials are currently being incorporated into the beginning organic course. It is a wonderful source of material/approaches for any organic instructor.]

- Sandler, S.R; Karo, W.; Bonesteel, J.; Pearce, E.M. *Polymer Synthesis and Characterization: A Laboratory Manual*; Academic Press: San Diego, CA, 1998.
  [Laboratory manual for polymer synthesis and characterization]
- Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry;* 2nd Ed., Wiley and Sons: New York, 2009.
  [This text focuses on the main categories of supramolecular systems.]
- Steed, J.W.; Gale, P.A. *Supramolecular Chemistry: From Molecules to Nanomaterials*; Wiley and Sons: New York, 2012
  [An eight-volume reference work covering supramolecular and nanoscale materials, including tutorial articles]
- Diederich, F.; Stang, P.J.; Tykwinski, R.R., Eds. *Modern Supramolecular Chemistry: Strategies for Macrocycle Synthesis*; Wiley and Sons: New York, 2008
  [Covers experimental procedures for most major classes of supramolecular compounds]

Literature articles on supramolecular systems:

- Nguyen, S. T.; Gin, D. L.; Hupp, J. T.; Zhang, X. “Supramolecular chemistry: Functional structures on the mesoscale,” *PNAS* **2001**, *98*, 11849.
- Smith, D. K. “A Supramolecular Approach to Medicinal Chemistry: Medicine Beyond the Molecule,” *J. Chem. Educ.* **2005**, *82*, 393.
- Breslow, R. “Bioorganic Chemistry: A Natural and Unnatural Science,” *J. Chem. Educ.* **1998**, *75*, 705
- Diederich, F. “Molecular Recognition in Aqueous Solution,” *J. Chem. Educ.* **1990**, *67*, 813.
- Hamliton, A. D. “Molecular Recognition,” *J. Chem. Educ.* **1990**, *67*, 821.

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