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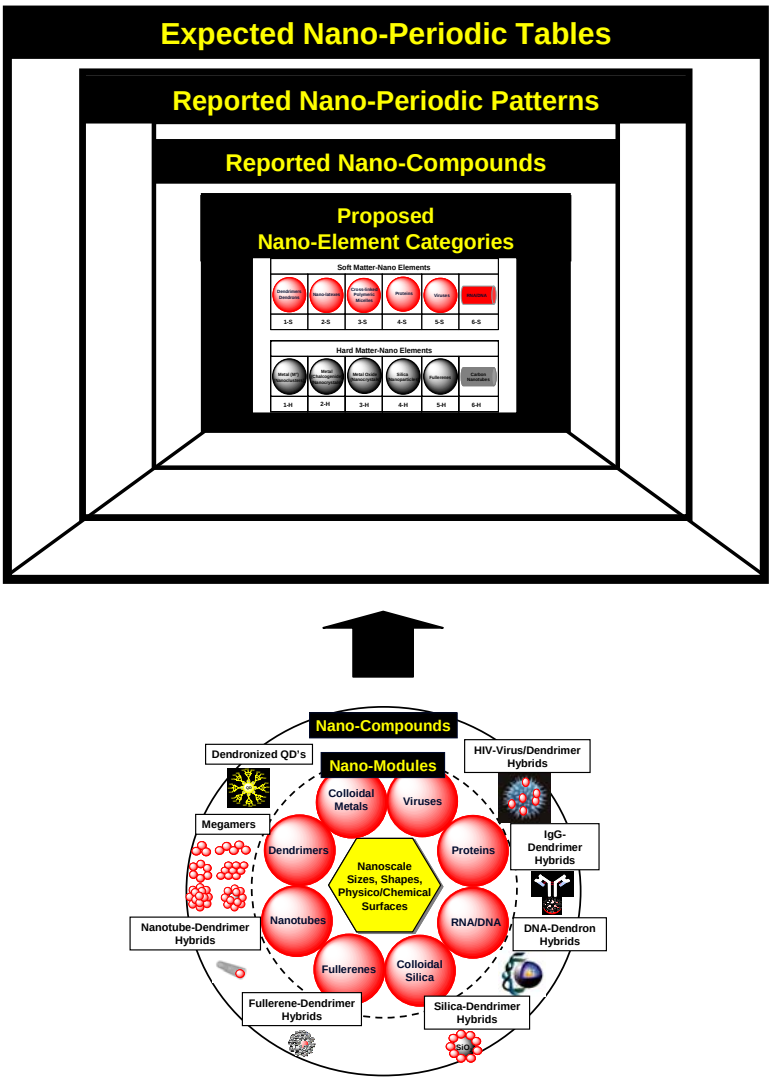
Periodic Patterns, Relationships and Categories of Well-Defined Nanoscale Building Blocks

Report on a National Science Foundation Workshop
September 24-25, 2007



Periodic Patterns, Relationships and Categories of Well-Defined Nanoscale Building Blocks

Report on a National Science Foundation Workshop

September 24-25, 2007

Central Michigan University, Mt. Pleasant, MI 48858

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Sponsored by

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Preface

The NSF Workshop entitled: ***Periodic Patterns, Relationships and Categories of Well-Defined Nanoscale Building Blocks*** was initiated by a serendipitous meeting with Dr. M. C. Roco, (Senior Advisor, Nanotechnology (NSF)) in September 2006. This meeting occurred at the 2nd Annual American Academy of Nanomedicine Conference (AANM) held at the National Academy of Sciences in Washington, DC. It was at that time, we had an opportunity to dialogue on the remarkable progress that NNI, NSF, other federal agencies and academia had made in many areas of basic nanoscience/technology research. However, we both agreed that there still remained several major voids and unanswered questions concerning "big picture issues for nanoscience/technology." *Foremost was –What wisdom could be gained by examining the historical stages and the growth steps that led to the initiation of a "central dogma" for traditional chemistry and its evolution to the Mendeleev Periodic Table? What steps could be taken to advance nanoscience/technology based on such historically proven principles and rationale? Could we conceptualize a similar "central dogma" for nanoscience (chemistry)? If so, could it be used as a scientifically grounded strategy to develop a so-called Nano Periodic Table(s)?*

It was readily apparent that nanotechnology/nanoscience was growing rapidly, but missing such an important perspective. As this issue was discussed, there arose a number of very provocative questions that included the following:

1. Could a *nano-chemistry dogma* be evolved based on historical precedence/example, much as John Dalton initiated for traditional atom based chemistry with his seminal *New System of Chemical Philosophy* (1808)?

2. Could *nano-matter classifications* be defined much as traditional inorganic/organic classifications? If so, would their properties allow them to be considered *hard or soft-type nano-matter*?

3. Could *well defined nano-module categories* be identified that exhibited sufficient *atom mimicry* that they could be treated as so-called *nano-elements*?

4. Could these nano-elements be used as reactive building blocks to synthesize/assemble more complex *nano-compounds?*

5. Would these nano-elements and their nano-compounds exhibit *nano-periodic patterns*? If so, could these patterns be used for predicting critical *nano-physical, chemical, medical, toxicological, electronic or magnetic properties? Could such periodic patterns be used for predicting the existence or design of new nanoscale materials and complexity? Finally, could such periodic patterns collectively lead to a grand vision of nanoscience (chemistry) with predictive value similar to our traditional Mendeleev Periodic Table?*

It was this initial meeting with Dr. M. Roco and similar discussions with key individuals in other Federal agencies that led to the encouragement and active support to organize this NSF Workshop. In that regard, we invited key nanoscience experts who had either published recent work or were active in critical areas related to these provocative questions cited above.

I wish to thank all the plenary speakers for their outstanding presentations and meeting the impossible task of providing short informative talks on focused topics yet allowing ample time for discussion. I am especially grateful to Dr. Mike Roco (NSF) for welcoming the workshop participants and catalyzing the entire event, as well as Dr. Piotr Grodzinski (NCI) and Dr. Scott McNeil (NCL) for their outstanding plenary lectures and participation. I also wish to thank those individuals who participated in the workshop, as well as those who unselfishly engaged in many stimulating discussions, offered informed opinions and provided important scientific consensus in the post workshop evolution of this final report.

Finally, I want to express my gratitude to Richard Canady (FDA), Scott McNeil (NIH-NCL), Anil Patri (NIH-NCL), Martin Fritts (NIH-NCL), Raul Cachau (NIH-NCL), Sally Tinkle, (NIEH), Wendy Sanhai (FDA), Nakissa Sadrieh (FDA), Nicholas Turro (Columbia University), Jorn Christensen (University of Copenhagen, Denmark), Linda Nixon and others for their interest, valuable discussions and encouragement in this effort.

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August 15, 2008

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Executive Summary

This report overviews the results of the CMU-NSF (National Science Foundation) Workshop held on the campus of Central Michigan University, September 24-25, (2007) entitled: *Periodic Patterns, Relationships and Categories of Well-Defined Nanoscale Building Blocks.*

These workshop results are presented in nine sections as follows: **Section 1** introduces a workshop roadmap and mission objectives with a brief statement on workshop deliverables. **Section 2** overviews nomenclature used throughout the report, specifically focusing on nanomaterial dimensionalities, proposed nano-matter roadmap classifications and nano-periodic pattern objectives. It is concluded with a glossary of proposed nanoscience terminology. **Section 3** reviews historical background concerning the "central dogma" for traditional chemistry. Structural control of Critical Atom Design Parameters (CADP) and Critical Molecular Design Parameters (CMDP) are presented followed by a demonstrated new strategy for structural control of Critical Nanoscale Design Parameters (CNDP) based on dendritic polymer systems. **Section 4** presents a comprehensive Nanomaterials Roadmap for classifying nano-matter into hard and soft categories based on composition and consideration of band gap properties. An overview of atom mimicry and proven structure control of Critical Nanoscale Design Parameters (CNDP) documented for dendritic systems are presented as part of the selection process for proposing nano-element categories. **Section 5** proposes a Nanomaterials Classification Roadmap, as well as a selection pathway for proposed nano-element categories. It is concluded by a list of proposed criteria for defining nano-elements. **Section 6** is an overview of the synthesis and key features associated with proposed nano-element categories with a focus on hard and soft nano-matter elements. **Section** 7 presents criteria for defining nano-compounds. It is followed by a presentation of three combinatorial grids for reported examples and yet to be discovered examples of: (1) hard matter nano-compounds, (2) soft matter nano-compounds and (3) soft matter-hard matter nano-compounds. **Section 8** briefly reviews selected examples of reported nano-periodic property patterns. These examples include six categories of nano-periodic property patterns. They include (1) physical properties, (2) chemical reactivity, (3) photonic properties, (4) electronic properties, (5) magnetic properties and (6) toxicological properties. **Section 9** concludes by reflecting on the historical chronology that was involved in the initiation of the "central dogma for traditional chemistry" and the time required for evolution to the Mendeleev Periodic Table.

In conclusion, we believe the results presented in this report offer a viable concept for evolving a *central dogma* for nano-chemistry. Literature documented nano-periodic patterns confirm that the first steps may have already been taken toward the evolution of a proposed **Nano-Periodic Table(s).** With this workshop concept, we have proposed well defined **Nano-Elements** and identified literature reported **Nano-Compounds**, as well as many unique and critical **Nano-Periodic Patterns**. The traditional **Mendeleev Periodic Table** has been used extensively for the past ≈150 years as an important tool for predicting reactivity, toxicology and associated risks and benefits for the atom based elements. This present work should provide optimism for taking similar first steps toward defining and predicting important **Nano-Element** reactivity, toxicology parameters for a range of **Hard and Soft Nanomaterials**. The ability to predict "risk-benefit" boundaries[76] for nanomaterials, both known and yet to be discovered, should be of very high priority and interest to the National Nanotechnology Initiative (NNI) and many federal agencies including the FDA, EPA, NIH and NSF, to mention a few.[77]

Workshop Program

Periodic Patterns, Relationships and Categories of Well-Defined Nanoscale Building Blocks
September 24-25, 2007

Central Michigan University, Center for Applied Research and Technology
2625 Denison Drive, Mt. Pleasant, Michigan 48858 USA

DAY 1: Monday, September 24, 2007

11:00-12:20 - Meet and Greet at the CMU-RC Bldg. Auditorium (Luncheon)

12:20-12:45 – Dr. Mihail C. Roco (NSF) - *NNI Context and Workshop Goals*

12:45-1:10 – Dr. Donald A. Tomalia (Dendritic Nanotechnologies, Inc./CMU) - *The Big Picture: From Synthetic Small Molecule Chemistry (1808) to Synthetic Nano Chemistry (2008)*

1:10-1:35 – Dr. William A. Goddard (Cal. Tech.) - *Theory and Simulation Applied to Nanoscale Building Blocks*

1:35-2:00 – Dr. Virgil Percec (Univ. of Pennsylvania) - *From Complex Self-Assembling Dendrons and Dendrimers to Supramolecular Nanostructures, Functions and Systems*

2:00-2:15 - Coffee/Beverage Break

2:15-2:40 – Dr. Stephen O'Brien (Columbia Univ.) - *Nanocrystal Superlattices*

2:40-3:05 – Dr. Dmitrii F. Perepichka, (McGill Univ.) - *Surface Nanopatterns with Tunable Periodicity via Molecular Engineering Approach*

3:05-3:30 – Dr. Emmanuel P. Giannelis (Cornell Univ.) - *Nanoparticle-Based Ionic Materials (NIMS)*

3:30-3:55 – Dr. Dwight S. Seferos (Northwestern University) - *Nanoparticle Gene Regulation Agents*

3:55-4:20 – Dr. Donald T. Haynie (Artificial Cell Technologies/Central Michigan University) - *Organic Superatoms in the Green Manufacture of Nanostructured Materials*

4:20-5:05 - Dr. Piotr Grodzinski (NCI) - *Interfacing Bio-inspired and Composite Materials - Emergence of Nanotechnology-Based Diagnostic and Therapeutic Solutions for Cancer*

6:30pm – Dinner

DAY 2: Tuesday, September 25, 2007

7:30-8:15 - Continental Breakfast

8:15-8:30 – Dr. Donald A. Tomalia – Overview/Housekeeping/Workgroup Sessions

8:30-8:55 - Dr. Theodore Goodson III (University of Michigan) - *Scalable Optical Properties with Novel Organic*

8:55-9:20 – Dr. Bradley D. Fahlman (Central Michigan Univ.) - *Low-Temperature Routes to Carbon Nanofibrous Growth and Metal Oxide Nanoclusters*

9:20-9:45 - Dr. Ulrich Wiesner (Cornell Univ.) - *Nano Silica*- Nano Relationships, Chemistry, Nano-hybrids

9:45-10:10 - Dr. Scott McNeil (NCL) - *NCL Data: Trends in Bio Compatibility and Toxicity*

10:10-10:30 - Coffee/Beverage Break

10:30-Noon - Workgroup Sessions

12:00-1:30 - Lunch

1:30 -3:30 - Workgroups Reconvene - *Nano-module Category Reports*

4:00 – Wrap-up/Adjourn

1.0 Introduction

Exactly 200 years ago (1808), traditional chemistry was in nearly the exact stage of development that we find nanoscience (technology) today. Traditional chemistry/physics was in the first stage of transition from alchemy (i.e., ill-defined materials, recipes, ideas, transpositions) to a rational science of well defined elemental building blocks, stoichiometries, combining ratios, etc. that now constitute the main dogma of these traditional sciences. These elemental picoscale building blocks were exploited extensively as fundamental building blocks for the synthesis of endless varieties of higher molecular structure and complexity. Much of this higher molecular complexity is taken for granted today as familiar functional materials, structures and compounds such as: pharmaceuticals, natural products, dyes, monomers, macromolecules, supramolecular chemistry, etc.). As a consequence of the quantized order, systematic architecture/structure exhibited by these picoscale building blocks they were later shown to exhibit unique periodic chemical/physical patterns (i.e., Mendeleev's Periodic Table (1869)). These periodic relationships/patterns have provided invaluable predictive tools for anticipating reactivity, toxicology, physical properties, etc.

Today this traditional electron driven chemistry remains the same; however, the functional dimensions associated with these new emerging nanoscale entities have increased by a factor 10^3. Although these new nanomaterial dimensions possess traditional compositions and bear traditional chemical functionality, an over-riding consequence of this dimensional enhancement must be completely new scaling relationships with literally all other hierarchically defined materials (i.e., from pico to macroscale). As such, one must ask- *What new understanding, rules, concepts, dynamics, scaling features, etc. must one consider in order to practice chemistry, physics, biology, medicine, engineering, etc. at this new higher dimensional level of hierarchical complexity? How does one predict reactivity, hazards, stoichiometries, physical properties, toxicology and physiology at these new dimensions?* These are among the many questions that we attempted to address as the objectives and mission for this NSF Workshop entitled: ***Periodic Patterns, Relationships and Categories of Well-Defined Nanoscale Building Blocks.***

1.1 Workshop Roadmap and Objectives

1.1.1 Workshop Objectives

The spirit and mission of the NSF Workshop entitled: ***Periodic Patterns, Relationships and Categories of Well-Defined Nanoscale Building Blocks*** (September 24-25, 2007) was intended to be a two step event.

Step one, was to invite experts in the field of nanotechnology to examine/analyze critical paths taken by 19th-20th century scientists in the initiation, research, development and characterization of elemental (atomic), picoscale, building blocks as non-Newtonian, quantized precursors to our present traditional chemistry/physics (sub-nanoscale) molecular complexity. Particular emphasis was placed on those unique periodic features that led to the evolution/development of the traditional (Mendeleev type) picoscale elemental periodic table.

The second step was to identify analogous "well defined", Newtonian quantized, nanostructures (nano-elements) and determine whether certain unifying features based on "atom mimicry", core-shell structures/architecture, composition (i.e., hard/soft matter), periodic properties/patterns (i.e., reactivity, valency, stoichiometry, sterics, nano-containment, aggregation, self-assembly, surface area or other physical behavior) could be identified. Finally, it was proposed that identification of certain ubiquitous/universal nano-periodic patterns would provide the basis for evolving rational strategies for *a*

priori prediction of important nanoscale risk/benefit properties of importance to nanotoxicology, environmental impact, commercial manufacturing and nanomedicine, etc.

1.1.2 Workshop Breakout Sessions

Nanoscience experts in the field were invited to present recent results/observations, share scientific understanding and examine contemporary perspectives in the following four broad focus areas:

SESSION I: Periodic Internal Structure and Surface Patterns in Well-Defined Nanostructures (Nano-elements)
SESSION II: Periodic Internal forces, Dynamic Behavior Patterns in Well-Defined Nanostructures (Nano-elements)
SESSION III: Reactivity, Self-Assembly, Stoichiometric Relationships of Well Defined Nanostructures (Nano-elements) to Form Nano Compounds (Hybrids)
SESSION IV: Well Defined, Nanostructures (Nano-elements): Classifications and Terminology

The following discussion points were recorded from the breakout sessions listed above:

Breakout Session- I: Periodic Internal Structure and Surface Patterns in Well-Defined Nanostructures (i.e., nano-element categories).

Discussion Leader: Stephen O'Brien (Columbia University)

Session Members:
Dmitrii Perepichka (McGill University)
Robert Rodriquez (Cornell University)
Donald A. Tomalia (Central Michigan University)
Ulrich Wiesner (Cornell University)

- Core-shell architecture appears to be pervasive through most well defined nanostructures. (i.e., nano-element categories) What features contribute to their structural control? Architecture /function within the core-shell motif must be considered.
- What determines a well defined nanostructure (i.e., nano-element category)? Can a nomenclature system be developed to describe these categories?
- Define fundamental core-shell building principles in the nano-regime.(i.e., nano-element categories).
- Dimensionality (i.e., 0-D and 1-D) should be considered.
- What defines hard and soft nano-matter? Flexibility, polarizability, ability to interdigitate?
- Nano-shapes must be considered –regular vs. irregular, ruggedness, nano-cusps vs. nano-clefts, conformational shape changes, cyclic shape changes, clusters from different shaped cores/objects, patterns vs. non-patterned particles, helical shapes.
- What affect does internal composition vs. outer shell composition impose?

- Consider inorganic-organic hybrids. Are these nano-compounds? What determines a nano-compound? (i.e., a criteria). Stoichiometry and combining masses must be considered. Reducing the surface symmetry of a nanoparticle will be important for defining nanoparticle valency.

- What role do nano-connectors (i.e., ss-DNA, etc.) play vs. traditional functional groups in the assembly of nano-compounds?

- How does one desymmetrize a homogenous nano-element surface to design specific valency? Janus nanoparticles, spherical, isotropic, anisotropic surface patterns?

Break-out Session -II: **Periodic Internal Forces, Dynamic Behavior Patterns in Well Defined Nanostructures (i.e., nano-element categories).**

Discussion Leaders: William Goddard (California Institute of Technology), Ted Goodson (University of Michigan)

Session Members: Donald A. Tomalia (CMU), Mihail C. Roco (NSF)

- How does interior nanoparticle composition affect size, shape, surface reactivity (i.e., self-assembly) under perturbing conditions? pH, magnetic fields, pressure, temperature?

- What defines hard and soft nano-matter? Inorganic vs. organic?

- What effect does interior flexibility/polarizability impose on well defined nanostructure size, reactivity, aggregation dynamics, aggregation hierarchy, solution behavior?

- How does interior composition/architecture/geometry influence certain photonic/electronic and magnetic events?

- Are there combinatorial "quantum confinement effects" involving size, shape and composition? Need to understand quantum confinement effects in a larger diversity of nanostructures. (i.e., hard vs. soft nano-matter).

- Need to better understand geometry/symmetry connection to new materials and properties.

- The variety of bottom-up, building block strategies (i.e., key intermediates, complexes, transition states, phases, etc.) may have to be examined and understood in order to evolve common or unifying dynamics patterns.

- Try to classify forces that act both internally and externally on nano-matter to produce known properties. Can periodic patterns be identified to allow predictions?

- Electronic Structure - As gold/other metals are reduced in size the "material" behaves differently. There is still no articulate "quantum description" along that continuum. Molecular properties are observed but not well defined. Need a better understanding of fundamental electronic properties (i.e., emission, NLO, HOMO, LUMO, etc,).

- Geometry- Geometry-symmetry connections to real properties are important for applications. Geometry and hierarchical nature of an aggregate, dendrimer, nanoparticle, nanocomposite makes a significant difference in its properties. Define a few common geometries that describe the limits, both theoretically and experimentally in these systems. For example, two-photon imaging with aggregates in NIR has been accomplished. What could be done to enhance performance?

- Forces- The nature of a particular force is very important in determining (predicting) size and shape dependent properties. Forces such as: coulombic, excitonic, "long range" charge delocalization, etc. are critical forces that can be "induced" by designed synthesis (i.e. for aggregates, etc.). These forces may be weak, uniform or heterogenous and used as tools for driving dynamics in a system.

Breakout Session- III: Reactivity, Self-Assembly, Stoichiometric Relationships of Well Defined Nanostructures (nano-elements) to Form Nano-Compounds (Hybrids).

Discussion Leaders: Virgil Percec (University of Pennsylvania) and Bradley Fahlman (Central Michigan University)

Session Members:
Donald Haynie (Artificial Cell Technologies)
Dwight Seferos (Northwestern University)
David Giljohann (Northwestern University)
Erik Wiener (University of Pittsburgh)
R. Kannan (Wayne State University)
Anil Patri (Nanotechnology Characterization Laboratory, NIH\NCI)
Choon Lee (Central Michigan University)
Alan Jackson (Central Michigan University)

The following parameters were discussed as they relate to defining internal structure and self assembly:

- Internal Structure Patterns– characterization of the core of the nanostructure (chemical composition associated with properties), mass, charge and ligand densities of the structure, packing/organization (free volume, shape) softness (conformationally flexible)/hardness, surface reactivity and properties.
- Self assembly – stereochemistry of subunits, interparticulate distance, size/shape (conformational effects, S effects), size dependent miscibility, aspect ratio, experimental conditions (e.g., growth temp./pressure, solvent evaporation conditions, etc., properties of nanocomposite vs. discrete nanostructural building blocks (C_{60} vs. dendrimer), solvent, colloidal growth considerations.

Breakout Session IV: **Well Defined Nanostructures (i.e., nano-element categories); Classification and Terminology.**

Discussion Leader: Martin Fritts (Nanotechnology Characterization Laboratory, NIH-NCI)

Session Members:
Scott McNeil (Nanotechnology Characterization Laboratory, NIH-NCI)
Mike Roco (NSF)

Anton Jensen (Central Michigan University)
Chiming Wei (Johns Hopkins University)
Lajos Balogh (Roswell Cancer Center)

- Need a nanostructure/nano-informatics data base
- What information is needed to define a well defined, nano-building block structure (i.e., nano-element)? Elemental composition, architecture, molecular structure, shapes, size and compositional homogeneity, size polydispersity, physical state, surface chemistry, etc.

What information is needed to define a nano-compound--terminology, descriptors, etc., building blocks involved? How complex is the structure? What is the assembly motif? What kind of chemical bonding?

1.1.3 Post Workshop Concept and Report Development

The above breakout session notes merely provided the initial basis and premises for developing this report. Considerable post workshop interaction (i.e., e-mail, phone conversations and person to person dialogue) was required to assemble and organize this report into its final form. A Workshop Mission Roadmap (Figure 1.0) was developed to outline the process and pathway taken from the initial workshop discussions.

The objective of this report is to review contemporary progress with referenced examples and offer a consensus for future directions and recommended research where appropriate.

First Picoscale (Atoms) Defined vs. Material Mixtures
"Traite Elementaire de Chemie" – A Lavoisier (1789)

First Chemical Strategy Proposed for Forming Elemental (Atom) Compounds
"New System of Chemical Philosophy" – J. Dalton (1808)

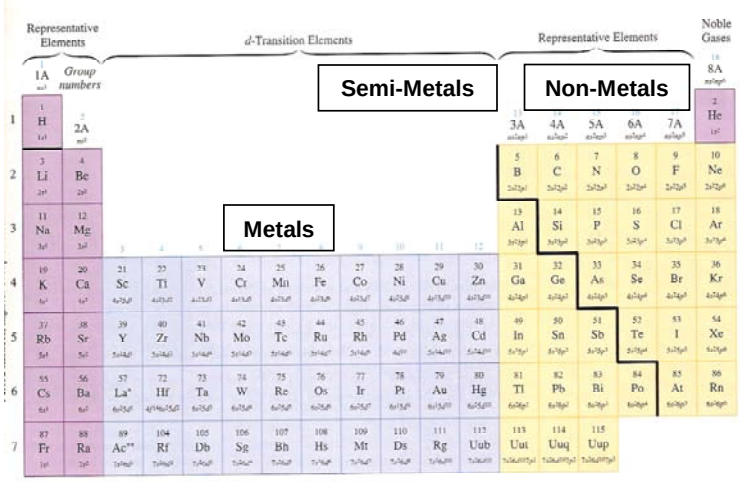
Traditional Chemistry (1808-)

Picoscale Elements (Atoms)

- **Homogeneous, Monodispersed Structures**
- **Non-Newtonian Quantized, Core-Shell Structures** → **Non-Newtonian Quantum Mechanical Physics (1922-)**
- **Quantized- Critical Atom Design Parameters (CADPs)**
  (a) size, (b) shape, (c) surface chemistry, (d) polarizability

Observed Picoscale Periodic Patterns
(a) reactivity, (b) toxicology, (c) physical properties → **Nuclear Chemistry (1898-)**

- **Picoscale Periodic Table**
  Predictable: (a) reactivity, (b) toxicology, (c) physical properties
  Mendeleev (1869)



Traditional Colloid Chemistry (1914-)

Traditional Polymer Chemistry (1920-)

Feynman (1959)

Nano-Materials

- **Heterogeneous, Polydispersed Structures**
  Nanomaterial Mixtures

- **Homogeneous, Monodispersed Structures**
  Nanomaterial Elements → **Quantum Confinement Nano-Physics**
  Nanomaterial Element Categories
  - **Newtonian Quantized, Core-Shell Structures**
  - **Quantized- Critical Nano-Design Parameters (CNDPs)**
    (a) size, (b) shape, (c) surface chemistry, (d) flexibility → **Newtonian Mechanical Nano-Physics**

Observed Nanoscale Periodic Patterns
(a) reactivity, (b) toxicology, (c) physical properties → **Synthetic Nano-Chemistry**

Nano-Periodic Tables
Predictable: **(a) reactivity, (b) toxicology, (c) physical properties** → **Nano-Toxology**

Workshop Breakout Sessions:
IV.
I.
II.
III.

Figure 1.0. *Workshop Roadmap Overview*

2.0 Terminology and Nomenclature

Analogous to the period in this sentence, *zero-dimensional* (0-D) structures are the simplest building blocks that may be used for nanomaterial design. These materials with dimensions from 1-100 nm have been denoted by a wide variety of descriptors such as: nanostructures, nanoparticles, nanoclusters, nanocrystals, etc. and are used synonymously in the literature. In order to share a common language in this report, we will attempt to provide a platform of explicit definitions and examples to avoid the current nomenclature ambiguities (*vide infra*) (Sections 2.4-2.5).

Figure 2.0 illustrates the intriguing similarities between discrete atoms and nanoscale building blocks. In order to synthesize a "well defined 0-D nanostructure", one must control the assembly of individual molecular/atomic sub-units as a function of: (a) size, (b) shape and (c) surface chemistry while avoiding bulk solid formation *via* a variety of well known processes (i.e., Ostwald ripening, cross-linking, aggregation, etc.). Many recent strategies have been developed to accomplish these controlled assemblies involving both covalent and non-bonding self assembly methodologies. For example, controlled stepwise polymerizations (i.e., poly(peptide), poly(nucleotides) and dendrimer polymer synthesis) to produce "well defined" soft nanomaterials or the use of entraining/stabilizing agents (i.e., metallic/compound nanoparticles and nanoclusters) to produce "well defined" hard nanomaterials.

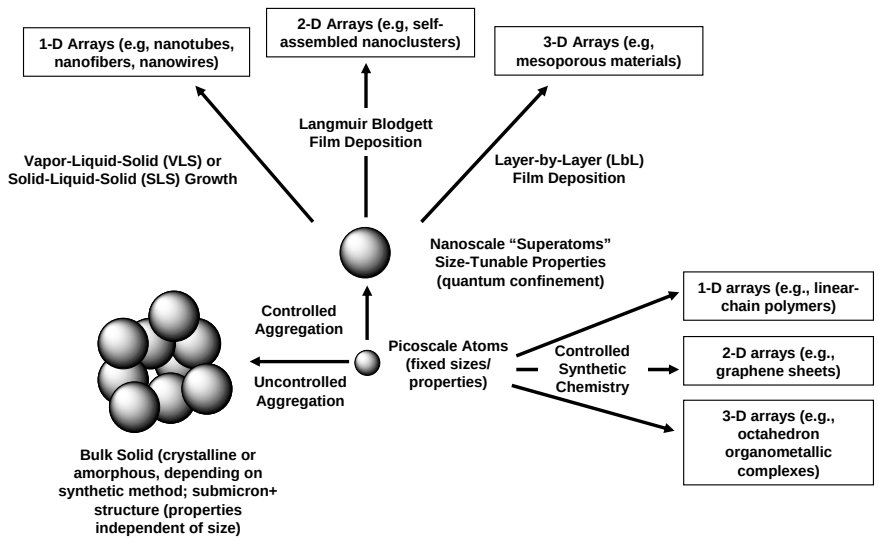


Figure 2.0. *Overview of picoscale atom based elements into various 0-D, 1-D, 2-D and 3-D nano-assemblies.*

An attractive feature of 0-D nanostructures (i.e., quantum dots) is their ability at small nano-dimensions to tightly confine electrons much like the behavior of picoscale 0-D atoms (i.e., quantum confinement). As illustrated in Figure 2.1, confining dimensions leads to dramatic discretionization of energy states compared to 1-D, 2-D and 3-D. It is very well recognized that by simply controlling the nano-dimensions of such a quantum dot, one can control the frequency or color of the light emitted upon excitation.

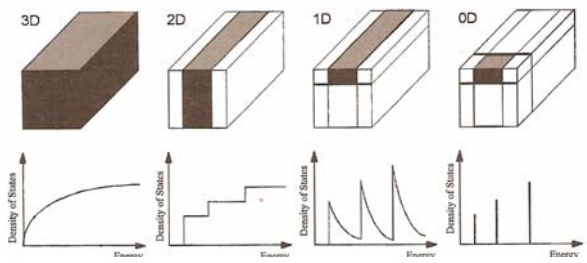


Figure 2.1. *Formation of zero-dimensional (0-D) quantum dot by the formal reduction of dimensions correlating with the continuing discretization of the energy states.*[1]

Many of these 0-D nanostructures have been referred to as *artificial atoms or superatoms*.[71, 78, 79] These terms and comparisons were initially made because of the similar influence that these entities impose upon electrons. Concurrently, it was also noted that these 0-D nanostructures resembled atoms in that they could be assembled into more complex 1-D, 2-D and 3-D arrays.[21, 59, 70] Whereas, individual atoms assemble into well defined molecular arrays based on their intrinsic combining properties, 0-D nanostructures may be constructed and designed to form preferred "nano-molecular like" organizations of varying dimensions based on the conditions used for assembly. Furthermore, as described later, many well-defined 0-D nanostructures possess core-shell type architectures which are reminiscent of atoms. Most noteworthy, is that nanoscale superatoms are also most reactive at the periphery (i.e., outer shell), analogous to the valence-shell electrons of discrete atoms. For instance, it is the presence of outer shell, surface amino groups on a dendrimer that facilitates chemisorption and surface assembly onto a mica substrate to yield a patterned 2-D array of the dendrimer.[80, 81]

An important feature that differentiates nanoscale-superatoms from traditional atomic units is the size-tunable properties of the former. Whereas, picoscale atoms have a distinct size and intrinsic chemical/physical properties, nanoscale-superatoms may be designed and fine-tuned to possess desired chemical and physical properties (i.e., conductivity, melting point, surface area, magnetism, chemical combining ratios, self-assembly features, etc.) by simply varying the size, shape and surface chemistry and not necessarily the composition. Perhaps the best illustration of discrete nanoscale size benefits is the design of semiconductor quantum dots. In order to alter the bandgap of a bulk semiconductor such as silicon, one has to appropriately dope the material with an *n*- or *p*-type dopant requiring specialized, high-temperature ion bombardment/post-annealing procedures. However, one can easily synthesize/engineer the diameter of a semiconducting nanocrystal (a quantum dot) and alter the bandgap as a function of diameter by adjusting the concentration of reactants, stabilizing agents, etc. in the solution phase, thus resulting in a lower cost and more facile modification.[16, 37]

2.1 Specific Examples of Zero Dimensioal (0-D), One Dimensional (1-D), Two Dimensional (2-D) and Three Dimensional (3-D) Nanoscale Dendrimeric Materials

Dendrimers have been viewed as "well defined, nano-mimics" of atoms.[21, 59] This comparison is based on their core shell structures, monomer shells (i.e., generations) that are systematically and mathematically quantized as a function of molecular weight, degree of polymerization (i.e., dendrimeric number) and systematic, well-defined sizes. As such, they may be considered 0-D nanostructures much as a buckminsterfullerene. Therefore, organizations of these 0-D structures into linear configurations, sheets or lattices may be viewed as examples of 0-D, 1-D, 2-D and 3-D nano-objects as illustrated in Figure 2.2.

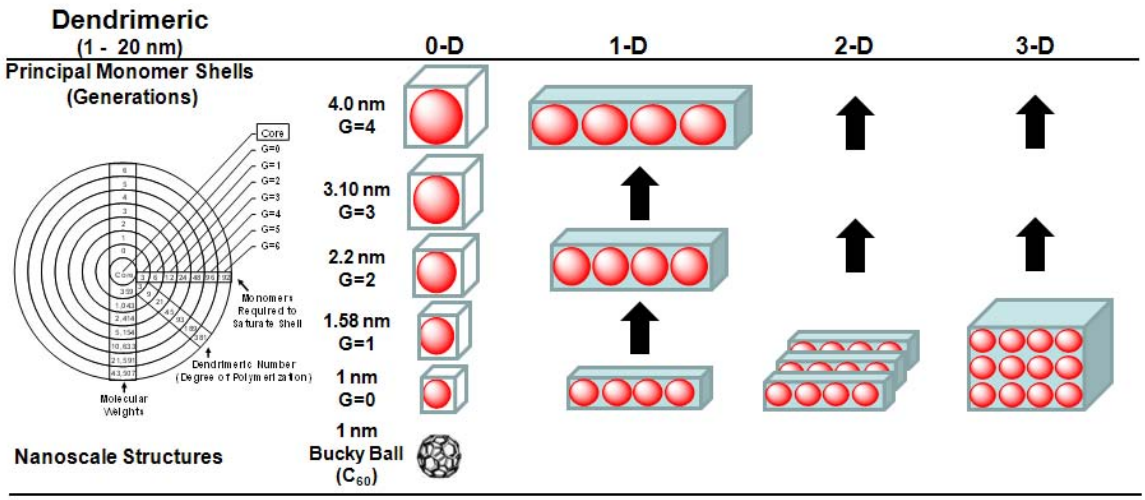


Figure 2.2. *Comparison of poly(amidoamine) (PAMAM) dendrimer core-shell structures with monomer shells, generational diameters and buckminsterfullerene. Comparison of possible spacial dimensionality arrangements (i.e., 0-D, 1-D, 2-D and 3-D).*

Historically, it is universally recognized that traditional small molecule chemistry was initiated 200 years ago with J. Dalton's proposed use of atom modules as 0-D building blocks for the synthesis of molecular level complexity. In 1808, Dalton described his *New System of Chemical Philosophy*[5] a provocative hypothesis for its time, that has since led to the synthesis of literally millions of small inorganic/organic molecular structures of incalculable value. Based on his envisioned atom modules (i.e., 0-D wooden spheres) and their propensity to form chemical bonds (i.e., electronic connections), an unlimited number of mathematically defined small-molecule compositions, shapes, architectures, and chemical functionalities have been combinatorially assembled at the picoscale and sub-nanoscale level. These molecular structures generally manifested chemical/physical properties very different from their building blocks,[82] as well as adhering to new and different combining rules (Figure 2.3).

Approximately eight decades ago (1926), Herman Staudinger broke a second important complexity barrier encountered by all synthetic organic chemists at the time, when he introduced his *macromolecular hypothesis*. This profound complexity breakthrough demonstrated that quantized, 1-D sub-nanoscale molecules (i.e., *linear*-monomer) building blocks could be catenated (polymerized) into mega-sized covalent structures (i.e., *linear*-random coil polymers) of nanoscale proportions, albeit with broad, statistical molecular weight distributions (Figure 2.3). Four major macromolecular architecture categories have evolved from Staudinger's hypothesis, namely; (I) linear, (II) bridged (crosslinked), (III) branched and more recently (IV) dendritic architectures.[21, 39, 83] It is interesting to note that each of these seminal breakthroughs encountered resistance at their inception and in some instances the pioneering scientists faced severe peer criticism.[84, 85]

Nearly three decades ago, dendrimers/dendrons, the first members of the dendritic polymer class were discovered and found to be perhaps the first examples of precise (soft matter) nanoscale structures that can be controlled as a function of: (a) size, (b) shape, (c) surface chemistry and (d) flexibility (polarizability).[21, 39, 56] Subsequently, one of us[21, 58, 59] has hypothesized the principles for a dendrimer-

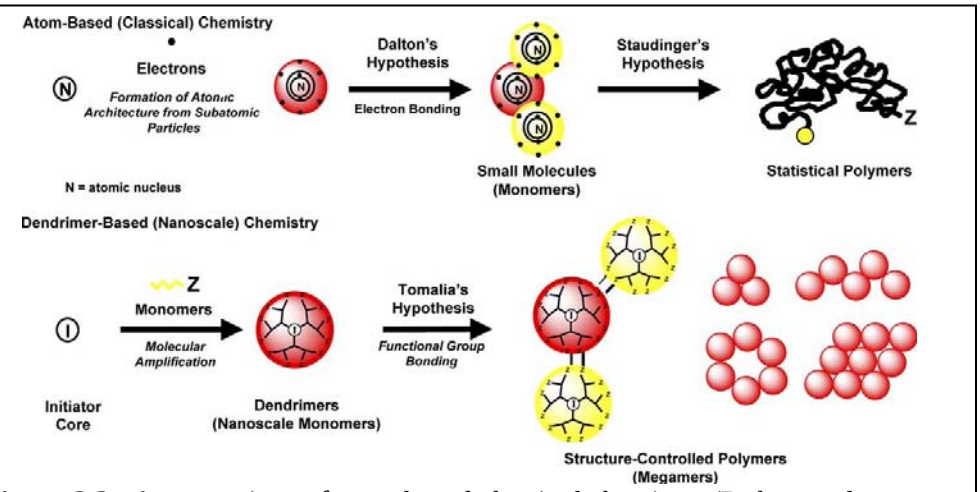


Figure 2.3. *A comparison of atom-based classical chemistry (Dalton and Staudinger hypotheses) with dendrimer-based nanoscale chemistry (Tomalia hypothesis) for synthesizing higher-complexity structures.*[21]

based nanoscale chemistry platform; wherein, dendrimers are viewed as *nanoscale atom mimics* which may be used to construct a wide diversity of so called *nanoscale compounds* (i.e., megamers) by both chemical bond formation and self assembly (Figure 1.4). Furthermore, it is believed that these principles may be applied to other "well defined" nanomaterial categories of both *soft and hard nano-matter*.

2.2 Nano-Matter Roadmap Classification and Nano-Periodic Pattern Characterization Objectives

In this report, we will consider only *well defined* nanomaterials. These nanomaterials will be examined topologically as either 0-D nano-spheroids or 1-D nano-tube/rod/wire analogues of traditional 0-D, elemental atoms or traditional 1-D polymers, respectively, in an effort to evolve a first step toward shape classification of nanoscale building blocks. These building blocks were then further sub-divided according to compositions that defined their intrinsic chemical and physical properties. We accomplished this by basing these classifications on traditional *band gap continuum* criteria that has evolved for classifying molecular/bulk matter, namely; (a) metals (conductors), (b) semi-metals (semi-conductors) and (c) non-metals (insulators). Efforts to develop these nanoscale electronic/physical property classifications based on molecular orbital behavior should allow the separation of fundamental nanoscale building blocks properties into a so-called a *nanoscale band gap continuum*. We propose that this continuum will reside between the two extreme property boundaries that we refer to as *hard and soft nano-matter*.

Next, all well defined 0-D nanoscale modules were examined relative to early historical criteria advanced by J. Dalton, et al.,[5, 8] for defining picoscale elements and their ability to combine stoichiometrically to form traditional molecular structures and compounds. This examination produced a short list of proposed *0-D nano-elements* and *1-D nano-polymer structures* that may be classified into the three major *band gap continuum* categories described above. Examination of the literature has revealed that a very extensive list of nano-compound examples derived from chemically bonded combinations/permutations of these nano-elements and polymers has already been reported (see Section 7.0). Based on *nano-element* criteria, formation of these nano-compounds appear to be following rational nano stoichiometry/mass (molar) combining rules which are reminiscent and analogous to the traditional picoscale systems.

Finally, selected examples of nano-periodic patterns are presented for several well defined (nano-elements) to demonstrate real observed progress toward the evolution of a *nano-periodic table* based on the mission and within the context of this NSF Workshop.

2.3 Nomenclature

The term *nanoparticle* is generally used to encompass all 0-D nanosized building blocks (regardless of size and morphology), or those that are amorphous and possess a relatively irregular shape.[62] Herein, we will define nanoparticles as amorphous or semicrystalline 0-D nanostructures with dimensions larger than 10 nm, and relatively large (≥ 15%) size dispersion. For amorphous/semicrystalline nanostructures smaller in size (*i.e.*, 1-10 nm) with a narrow size distribution, the term *nanocluster*[86] is more appropriate. This distinction is a simple extension of the term *cluster*, which is typically used in inorganic/organometallic chemistry to indicate small molecular cages of fixed sizes. In this respect, one can consider a nanoscale object as being "mesomolecular" or "mesoatomic" – an aggregate of smaller molecular/atomic subunits. Analogous to bulk materials, the agglomeration of noncrystalline nanostructural subunits should best be termed a *nanopowder*.

It is also important here to note the difference between nanoparticles/nanoclusters and traditional *colloids*, which dates back to the early 1850s[87] (Table 2). We are all familiar with the term colloid, which is used to describe solid/liquid and solid/gas suspensions such as milk, paints, butter, smoke and smog. Although both types of materials have sizes within the nano-regime, the leading difference is the control one has over composition and morphology. It is widely recognized that stabilization of metal based nanostructures requires a protective stabilizing agent to prevent agglomeration. This is also the case for colloids; wherein, polydispersed organic polymers or other ionic species may be adsorbed onto the colloid surface.[88, 89] Such a variation in the nature of the encapsulating environment, often leads to a large polydispersity in overall morphology and properties of colloids. By contrast, in order for nanomaterials to be suitable for "bottom-up" design, their synthesis must lead to monodispersed entities with structure controlled features that will exhibit properties that are reproducible. This is often accomplished through the use of stabilizing agents with well-defined structures, that do not react with or surface deactivate the entrained nanostructures (e.g., dendrimers, polyoxoanions, etc.).

Table 2.0. *Comparison of 0-D Nano-Architectures with Traditional Colloids*[88]

Nanoparticles/Nanoclusters	Colloids
Size: 1 – 100 nm (nanoclusters: 1 – 10 nm)	Typically > 10 nm
Homogeneous molecular composition	Poorly defined compositions
≤ 10% size dispersion (more mono-dispersity for nanoclusters relative to nanoparticles)	> 10% size dispersion
Reproducible synthesis (control over size, shape, and composition)	Non-reproducible, uncontrollable morphology/composition
Reducible physical properties and catalytic activity	Non-reproducible properties (especially non-reproducible catalytic activities)
Soluble in polar/non-polar organic solvents (depending on stabilizing agent)	Typically only soluble in polar solvents
Contain clean surfaces	Contain surface-adsorbed species such as –OH, -X, H_2O , etc.

Thus far, we have defined nomenclature for amorphous 0-D nanostructures. Analogous to bulk materials, any nanomaterial that is crystalline should be referred to as a *nanocrystal*. This term should be reserved for those materials that are single-crystalline; if a particle exhibits only regions of crystallinity, it is better termed a nanoparticle or nanocluster depending on its dimensions. Transmission electron microscopy, especially in tandem with electron diffraction is most useful for determining the crystallinity of any nanostructure. Figure 2.4 illustrates a variety of 0-D structures as a function of sizes ranging from picoscale to macroscale (i.e., bulk materials).

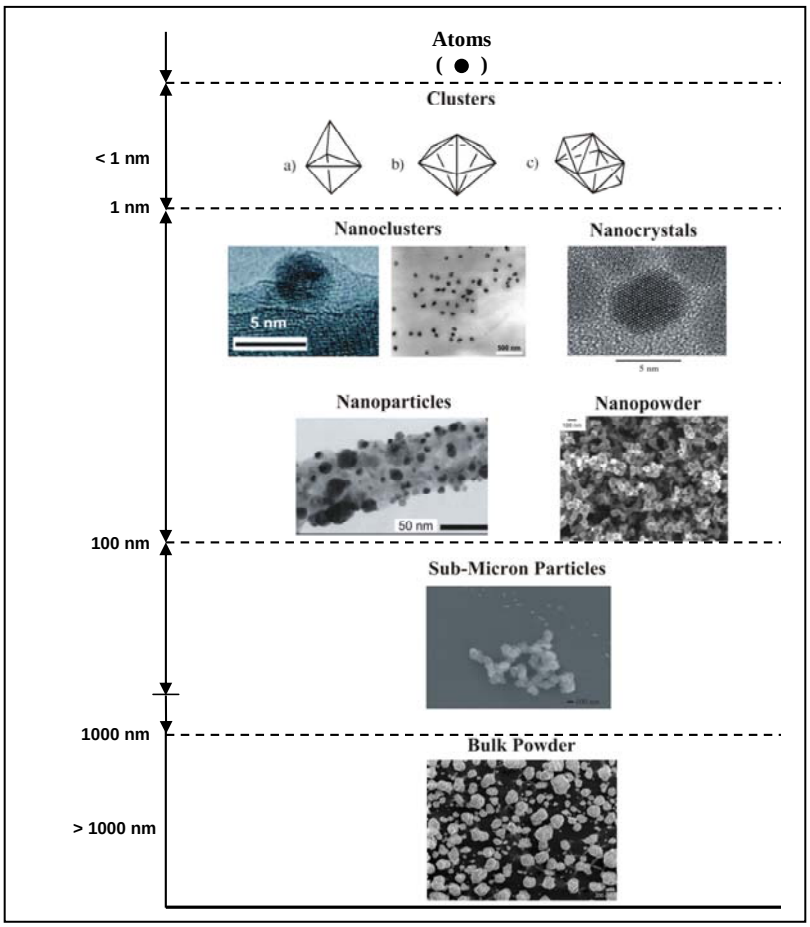


Figure 2.4. *0-D nanostructure nomenclature. Shown are the well-defined cage sizes of molecular clusters ($Os_5(CO)_{16}$), ($Os_6(CO)_{18}$), [$Os_8(CO)_{22}$][90] Comparatively, nanoclusters should be used to describe 0-D nanostructures of a homogeneous size distribution.[91] By contrast, nanoparticles exhibit a greater range of sizes/shapes.[92] Nanocrystals are characterized by the presence of an ordered lattice array of the constituent subunits, as illustrated by a single nanocrystal of CdSe.[93] In stark contrast to a nanocrystal, an example of a nanopowder is shown that consists of microscopic grains each comprised of nanoscale amorphous units.[93] The size regime that is intermediate between the nano- and micro-regimes is best referred to as sub-micron.[94] The bulk powder scale bar is 200 μm.[62]*

2.4 One-Dimensional (1-D) Nanoscale Dimensionality

It is easy to be confused by the common synonymous use of the terms nanotube, nanofiber, nanowire, nanoribbon and nanorod. In essence, these descriptors are defining crude nano-topologies. If you think of the analogous bulk materials without the prefix *nano*, there should be no ambiguity regarding the topology and proper use of these descriptors (Figure 2.5). In essence, these nanostructures may be

viewed as 1-D nano-polymers. They are usually derived from the propagation or polymerization of picoscale elements (i.e., metals, carbon, metal compounds) or short 1-D organic monomers (i.e., amino acids, nucleic acids, etc.). The common feature among all of these structures is that their diameters must be within the 1 – 100 nm range; typically, their lengths are such that they present an aspect ratio of 10 or more. In some instances, the aspect ratio may be very large with lengths of a micron or larger. Topologically, a *nanotube* is a 1-D structure that contains a hollow core; whereas, the other three nanoarchitectures are solid throughout. The term *nanofiber* should be reserved for 1-D nanostructures that are amorphous (and usually nonconductive) such as polymers and other non-graphitized carbonaceous structures. By contrast, a *nanowire* designates a structure that is crystalline, with either metallic or semiconductive electrical properties.

A *nanorod* is typically a crystalline 1-D nanostructure possessing low aspect ratios, (i.e., the overall length is not much larger than its width (< 10) with both dimensions < 100 nm). As their name implies, another feature of nanorods is their rigid sidewall structures. However, since crystalline nanorods exhibit the same overall shape as needle-like bulk crystals, the term *nanocrystal* may be more appropriate for these structures (or, more explicitly: rod-like nanocrystals). Whereas, nanowires, nanofibers, and nanotubes may exhibit flexible/deformable lengths such as in an interwoven array, nanorods are completely linear and assumed to exhibit a less flexible morphology. As such, nanorods are capable of stacking onto each other to yield interesting 2-D and 3-D arrays – not usually as accessible with the more "spaghetti-like" morphologies of the other 1-D nanostructures.

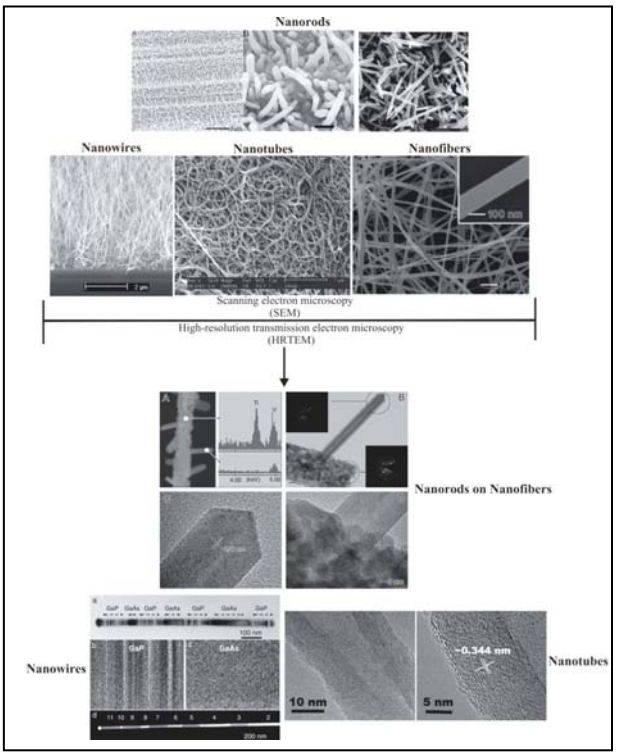


Figure 2.5. *Classifications of 1-D nanostructures. The top portion shows SEM images of various nanostructures. Whereas, the morphology of nanowires, nanotubes and nanofibers look identical by SEM, nanorods are notably different, with much shorter lengths and straight sidewalls. The bottom portion shows high-resolution TEM images, which provide morphological details of the nanostructures. The top TEM image shows crystalline nanorods grown on the surface of amorphous nanofibers. The bottom two TEM images illustrate the difference between nanowires/ nanotubes – the latter contains a hollow core. It should be noted that crystalline nanorods may also be termed "nanocrystals", as their morphology resembles that of needle-like bulk crystallites.*[62]

2.5 Other Terminology

Aerosols: *A substance consisting of very fine particles or liquids (i.e., usually polydisperse particles) suspended in a gas.*
Anion: *A negatively charged elementa/lmolecular species that contains more electrons than protons.*
Atom: *Smallest particle of an element that retains the chemical properties of that element.*
Atom (Artificial): *Nanoscale particles or structures that exhibit certain features or characteristics of a traditional atom.*
Atom (Super): *See super atoms or artificial atoms.*
At**om Mimicry:** *The mimicry of certain structural, chemical or physical features of traditional picoscale atoms at any other dimensional level (i.e., nano-, micro- or macroscale).*
Atom Mimicry (heuristic): *Noted mimicry of certain structural, chemical or physical features of atoms (elements) by higher dimensional entities (i.e., dendrimers, metal nanoclusters) that serve as a guide to discover or reveal new relationships. Valuable for stimulating or conducting empirical research, but unproved or incapable of proof.*
Atom Mimicry (proven): *Noted mimicry of certain structural, chemical or physical features of traditional picoscale atoms (elements) at higher than picoscale dimensions that have been experimentally proven.*
Atom Mimics (Reactive) – *Nanoscale, 0-D entities that mimic reactivity associated with unsaturated electron shells in atoms (i.e., dendrimers, core-shell tecto(dendrimers), etc.).*
Atom Mimics (Noble Gas): Nanoscale, *0-D entities that mimic lack of reactivity associated with saturated electron shells in atoms.*
Bonding (metallic): *Chemical bonding that holds the atoms of a metal together. Metallic bonds are formed from the attraction between mobile electrons and fixed, positively charged metallic atoms. Whereas, most chemical bonds are localized only between specific neighboring atoms, metallic bonds extend over the entire molecular system.*
Bonding (covalent): *A chemical bond which is formed when electrons are shared between two atoms.*
Cation: *A positively charged elemental/molecular species that contains fewer electrons than protons.*
Chalcogenide: *A chemical compound consisting of at least one chalcogen ion and at least one more electropositive element. Although all group 16 elements of the periodic table are defined as chalcogens, the term is more commonly reserved for sulfides, selenides, and tellurides, not oxides.*
Colloids: *Aggregates of atoms or molecules ranging from 1-1000 nm that may be dispersed in a continuous phase (i.e., usually polydisperse particle sizes). They will exhibit a statistical size distribution if not properly stabilized, usually by a protective surfactant. Discovered by M. Faraday in 1857.*
Core-Shell Structures (Architecture): *Architectures consisting of a central domain (core) surrounded by concentric shells (i.e., much like an onion). Some examples include picoscale (atoms) and nanoscale dendrimers.*
Critical Atomic Design Parameters (CADP): *The parameters involved in the structure control of atoms, namely; (a) size, (b) shape, (c) surface chemistry and (d) flexibility (polarizability).*
Critical Molecular Design Parameters (CMDP): *The parameters involved in the structure control of molecules, namely: (a) size, (b) shape, (c) surface chemistry and (d) flexibility(polarizability).*
Critical Nanoscale Design Parameters (CNDP): *The parameters involved in the structure control of nanoscale structures, namely: (a) size, (b) shape, (c) surface chemistry and (d) flexibility (polarizability).*
Dendrimer: *A highly branched, dendritic core-shell type molecular structure originating from a polyvalent core. These structures possess two or more dendrons and amplify their structures in concentric shells (i.e., generations) around the core by the iterative bonding of monomers (i.e., branch cell monomers). They present terminal groups according to the mathematical expression:* $Z=N_cN_b^G$; *where: N_c=core multiplicity, N_b=branch cell multiplicity and G=generation.*
Dendritic Effects: *A chemical or physical property of dendrimers/dendrons that varies in a systematic/periodic manner as a function of generation (G) (i.e., size or polyvalent surface chemistry).*

Dendron: *A dendritic molecular structure reminiscent of a "molecular tree". These dendritic structures originate from a monovalent core (i.e., the trunk of the tree) and amplify their structure by iterative bonding of monomers (i.e., branch cell monomers) to produce concentric layers (i.e., generations) of branched monomer shells (i.e., the branches of the tree) that are terminated by functional groups that are reminiscent of the leaves on a tree. The terminal groups (Z) amplify according to the mathematical expression:* $Z=N_cN_b^G$; where: N_c=core multiplicity = 1, N_b=branch cell multiplicity and G=generation.
Elements-(Dictionary Definition): *The simplest components of a subject of study.*
Elements-(Picoscale Chemical Definition): *Substances that cannot be decomposed into simpler substances by chemical or physical means.*
Elements-(Pseudo Elements): *Polyatomic entities that mimic or imitate certain features or behaviors of an element (i.e., pseudo halogens such as –CN, -N_3, -SCN,-OCN, etc.).*
Elements- (Para Elements): *See pseudo elements.*
Functional Groups: *A group of atoms substituted for hydrogen in the formula of a hydrocarbon that gives the compound its characteristic chemical/physical properties; a reactive part of a molecule that undergoes characteristic reactions (i.e., -CO_2H, -NH_2 , -OH, etc.).*
Hard Matter/Nanomaterials: *Nano-matter comprised of elements that manifest electron conducting or semi-conducting properties. Usually metals, semi-metals, inorganic compounds such as metal chalcogenides or carbon allotropes containing extended pi systems (i.e., fullerenes, carbon nanotubes, etc.).*
Hybridized Nano-Compounds (Structures): *See nano-compounds.*
Macromolecular Self assembly: *Self assembly of macromolecules (polymers) to produce larger or more complex organizations (i.e., supra-macromolecular structures).*
Macroscale, Atom Mimics: *Macroscale spheroidal/shaped objects used to imitate atoms (e.g., Corey-Pauling-Koltun (CPK) models).*
Major Polymer Architectures: *Four major* polymer *architectures exhibiting distinct topological features (i.e., linear, cross-linked, branched, dendritic). They manifest differentiated properties that are determined by these topologica/architectural features.*
Megamer: *Multiples of two or more dendrimers associated by chemical or non-bonded connectivity.*
Mesoscale: *Dimensions involved at the boundary between nanoscale and microscale.*
Metalloids: *Also referred to as semi-metals. They are elements that exhibit properties intermediate between metals and nonmetals (i.e., Si, As, or Sb). They are semi-conductors in that they conduct electrons, but not as well as metals.*
Microscale: *Dimensional range of* 10^{-6} *meters.*
Molecular Self assembly: *Non-bonding assembly/organization of molecular structure driven by a variety of factors including; hydrogen bonding, dipole-dipole interactions, hydrophobic/hydrophilic interactions, Van derWaal forces, etc.*
Monodisperse Nanoparticles: *Arbitrarily defined as a predominately homogeneous population of nanoparticles with >90% uniformity in size distribution (see Mirkin, et al.).*[65]
Monomer: (Traditional Definition) - *A small 1-D molecule of any class of compounds, usually organic, that can react with other similar or dissimilar compounds to form very large linear, 1-D macromolecules or polymers.* **(Nanoscience Definition)** – *One-D atoms of any elemental class, usually metal or carbon that can react with similar or dissimilar atoms to form very large 1-D rods, wires or tubes (i.e., carbon nanotubes*).
Monomer (Branch Cell): *Molecular level structures possessing a branch point and three or more reactive sites that may be used in polymerization processes. A critical intermediate used in the synthesis of dendrimers.*
Nano Aggregation: *Non-bonding association of nanoscale particles to form either well defined or non-descript domains of higher dimensionality.*
Nano Clusters: *Finite collections or arrays of bonded atoms that tend to be spheroidal and defined by so-called "magic number" values that reflect stabilized, low energy states (i.e., shells surrounding a core) yet exhibit dimensions from 1-100 nm.*

Nano-Compounds: *Nanostructures/particles resulting from the chemical bonding of two or more nano-elements to produce larger more complex nanostructures/particles that exhibit well defined, reproducible mass combining ratios and stoichiometries.*
Nano-Containers: *Nano-structures/particles that possess interior space that will allow encapsulation or incarceration of smaller guest molecule (i.e., buckministerfullerenes, dendrimers, viruses and certain proteins).*
Nano-Elements: *Nanostructures and nanoparticles that are >90% monodisperse (see Mirkin, et al.)* [65] *and exhibit some degree of atom mimicry that includes;(a) robustness suitable for mass, size characterization, (b) well defined chemical valency/stoichiometries and (c) reproducible mass/molar combining ratios when allowed to react with either sub-nanoscale reagents or other nano-elements. Reactivity is determined by functional groups present on or within the nanostructures.*
Nanomaterial Categories: *Classification of nanomaterials as a function of* ***topology/shapes*** *(i.e., 0-D, 1-D, 2-D, 3-D,* ***chemical behavior*** *(i.e., metals, semi-metals, non-metals),* ***electronic behavior*** *(i.e., electron conducting, semi-conducting or insulator properties) and* ***physical properties*** *(i.e., metallic, inorganic, rigid/crystalline lattices, organic compressible, flexible, amorphous materials).*
Nano Periodic Table(s): *A proposed table(s) that expresses an overview of nano-periodic patterns associated with so-called nano-elements and nanomaterials. Such a table(s) may facilitate the categorization of nanomaterials and should allow "a prior" predictions of their chemical, physical and toxicological properties***.**
Nano Periodicity: *Periodic patterns exhibited by nanomaterials that are manifested as a function of their unique chemical, physical or toxicological behavior (properties).*
Nano Steric Effects: *Unique steric effects that occur due to nanoscale dimensions of a reagent, solvent or substrate that differentiate their behavior from classical picoscale/sub-nanoscale steric effect (i.e., neopentyl effect).*
Nanoscale Sterically Induced Stoichiometry (N-SIS): *Observed stoichiometries that are altered (i.e., reduced) versus ideal stoichiometry for nanostructure/particle reactions; generally caused by sterically congested particle surfaces, reagents or environment.*
Nano Stoichiometry: *Combining ratios of nano-entities or nano-elements based on molar mass.*
Nano Valency: *Number of reactive sites associated with a nano-entity or nano-element.*
Nano Reactivity: *Chemically active sites associated with a nano-entity or nano-element.*
Nano Surface Chemistry: *Chemical events, reactivity or chemical functionality that is presented on the surface of a nano-entity.*
Nanoscale: *Dimensional range between 1-100 nm.*
Nanoscale, Atom Mimics: *Nanoscale entities exhibiting certain properties reminiscent of atoms***.**
Nanoscale Self-Assembly: *Chemically bonded or non-bonded associations of nanoparticles to yield reproducible collections/organizations of nanoscale entities.*
Nanoscale Structure Control Parameters: *Those features manifested by nanoscale structures/particles that mimic and define traditional picoscale atom (i.e., sizes, shapes, surface chemistry or flexibility); see Critical Nanoscale Design Parameters (CNDP).*
One Dimensional (1-D) Nano-periodicity: *Periodic chemical/physical properties associated with 1-D nanostructures.*
Picoscale: *Dimensions of* 10^{-12} *meters.*
Picoscale Self assembly: *Self assembly events and entities involving picoscale particles.*
Picoscale Structure Control Parameters: *See Critical Atomic Design Parameter (CADP) definition.*
Polydisperse Nanoparticles- *A broad statistical distribution of nanoparticle sizes; usually associated with "top down" engineered nanoparticles.*
Quantum Mechanics: *A fundamental theory of matter and energy that explains phenomena associated with atoms (i.e., picoscale) entities that previous Newtonian physical theories were unable to account for. In particular, the fact that energy is absorbed and released in small, discrete quantities (quanta), that all matter displays both wavelike and particle-like properties, especially when viewed at the atomic or sub-atomic level.*

Quantized, Newtonian, Nanoscale Structures: (Dictionary definition of Quantized)*: To limit a variable or variables describing a physical system to discrete, distinct values.*[95] *This definition is applied to those entities that are large enough (i.e., nanoscale) to adhere and obey Newtonian physics.*
Quantized, Non-Newtonian Picoscale Structures: *See definition for quantum mechanics defined above.*
Quantum Confinement: *Confinement of electrons to a size regime less than an electron wavelength. The ultimate limit of such a low dimensional state is the quantum dot. Therefore, a QD is often considered to be an artificial atom.*[79]
Quantum Dots – C: *See quantum confinement.*
Soft Matter-Nanomaterials: *Nano-matter comprised of elements that manifest non-electron conducting, insulator type properties. Usually organic structures containing non-metallic elements such as: carbon, oxygen, nitrogen, hydrogen, i.e., etc.) that tends to be flexible, amorphous and non-crystalline. Many of these materials are found in biological or life supporting materials and systems.*
Semiconductors: *Any of a variety of elements (i.e., Si or Ge) or compounds (i.e., cadmium chalcogenides) that conduct electrons more easily than insulators, but less easily than conductors (i.e., metals- Cu, Au etc.).*
Statistically Defined Nanoscale Structures: *Nanomaterials that are obtained as highly polydisperse, statistically distributed structures and particle sizes (i.e., traditional colloids, polymers, top-down engineered nanoparticles such as TiO_2).*
Super Atoms: *Sub-nanoscale and larger nanoscale clusters of atoms that mimic or exhibit chemical behavior reminiscent of fundamental picoscale atoms.*
Synthetic Nanoscale Chemistry: *The synthetic methodologies involved in chemically combining simple, well-defined nanoscale modules (i.e., nanoelements/nano-polymers) to produce chemically bonded more complex nano-compounds.*
Two-Dimensional (2D) Nano-periodicity: *Periodic chemical/physical properties associated with 2-D nanostructures.*
Three-Dimensional (3-D) Nano-periodicity: *Periodic chemical/ properties associated with 3-D nanostructures.*
Unit Cell: *The smallest unit of a crystal when iterated generates the whole crystal.*
VSEPR: *Valence shell electron pair repulsion model used to predict molecular geometry/shapes. It states that electron pairs residing around a central atom tend to be as far apart as possible.*
Well-Defined Nanoscale Structures (Modules, Building Blocks): *Nano entities with at least one dimension in the 1-100 nm range; wherein, structures are controlled as a function of: (a) size, (b) shape, (c) surface chemistry and (d) flexibility (polarizability). The mass/size polydispersity should be at least 90% of ideality, as described by Mirkin, et al.*[65]
Zero-Dimensional (0-D) Nano-periodicity: *Periodic chemical/physical properties associated with 0-D nanostructures (i.e., periodic properties of dendrimers or metal nanoclusters, etc.).*

3.0 Historical Background: Old Building Block Concepts Evolving to New Concepts

3.1 The First Picoscale Building Blocks (Elements) Defined By Nature-*Traditional Chemistry:*

The "grand self assembly event" involving charge neutralization of electrons and nuclei to produce energy minimized atomic particles occurred some 13-14 billion years ago.[8] These discrete, quantized electron organizations assembled around various nuclei requiring only seven radial shells/levels to produce the core-shell like structures that define the elements of our periodic table and the picoscale building blocks (i.e., 10^{-12} meter sized) that constitute our traditional chemistry paradigm. Historically, the origin of our atomic building block chemistry began with publication of *The Elements of Chemistry* in 1789 by Antoine Lavoisier (1743-1794). At that time, the 23 building blocks were defined empirically as the *actual terms whereat chemical analysis had arrived* (Figure 3b). This new science described a completely different vision of basic matter. It was characterized by constant, homogeneous, well defined compositions (elements), as opposed to physical mixtures of indefinite compositions. The main objective of the early disciples of this "new science" was to prepare new substances, materials and to ascertain their novel properties. Most profound was the fact that these new molecular compounds exhibited unique, new properties (i.e., emerging properties) that were dramatically different than the intrinsic properties of the originating building blocks. For example, toxicology and corrosion properties observed for elemental sodium and chlorine, respectively, are dramatically different than the properties exhibited when in their compound form (e.g., NaCl).[82] These new building blocks taken two at a time might yield hundreds of new compounds, or combined three at a time would give thousands while combining the 23 known elements could literally yield millions of new compounds.

a)

The First Chemistry Set
(Based on Atomic Building Blocks)

Pervasive Patterns Supported by Experimental Observations	Discovering Scientist	Contributions
I. Atoms form chemical bonds	Antoine Lavoisier (1743 - 1794)	"Traite Elementaire de Chimie" (1789)
II. Atoms (elements) possess well defined masses relative to each other (combining weights).	Joseph L. Proust (1754 - 1844)	"Law of Definite Proportions" (1797)
III. Atoms (elements) form chemical bonds with well defined valency.	John Dalton (1766-1844)	"Law of Multiple Proportions" "New System of Chemical Philosophy" (1808)
IV. Atoms (the elements) exhibit periodicity in their reactivity and emerging properties.	Dmitri Mendeleev (1834 - 1907)	Periodic Table of the Elements (1869)
	J. Lothar Meyer (1830 - 1895)	(1870)
V. Atoms (elements) exhibit well defined directionality in the formation of chemical bonds.	Louis Pasteur (1822 - 1895)	Spatial Chemistry
	Joseph-Achille LeBel (1847 - 1930)	Tetrahedral Nature of Carbon (1874)

b)

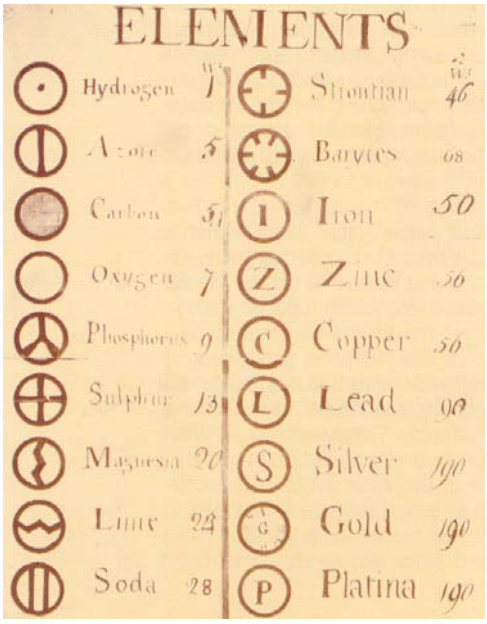


Figure 3.0. *a) Five key criteria (patterns) that were observed and analyzed by 18th-19th century scientists to define our "atomic level chemistry set" before the advent of quantum mechanics aned electronic theory. b) Dalton's quantized elemental building blocks and their combinatorial possibilities that led to his New System of Chemical Philosophy in 1808.*[5, 8]

The notion of fixed building blocks of matter that exhibit certain *pervasive patterns* was basic to the primitive atomic theory of John Dalton (1766-1844) as he published his *New System of Chemical Philosophy* in 1808.[8] This theory postulated that each chemical element is a homogeneous assembly of atoms which differ in relative weight, number per unit volume and in combining numbers from the atoms of other elements. In fact, without the benefit of understanding quantum mechanics or electronic theory, the operational parameters of this early chemistry paradigm became fairly well defined throughout the 19th century during the golden age of small molecule inorganic/organic synthesis. These parameters, derived from simple logic, were clearly based on experimental observations and generally involved the interpretation of pervasive patterns. Briefly they included at least the five critical criteria (I-V) as listed in Figure 3.0a.

3.2 Well-Defined Pico-/Sub-Nanoscale Building Blocks

3.2.1 Zero-Dimensional Picoscale Building Blocks - Atoms: Precursors to Traditional Sub-nanoscale Synthetic Chemistry

3.2.1.1 Picoscale Elemental (Atom) Core- Shell Structures and Periodicity

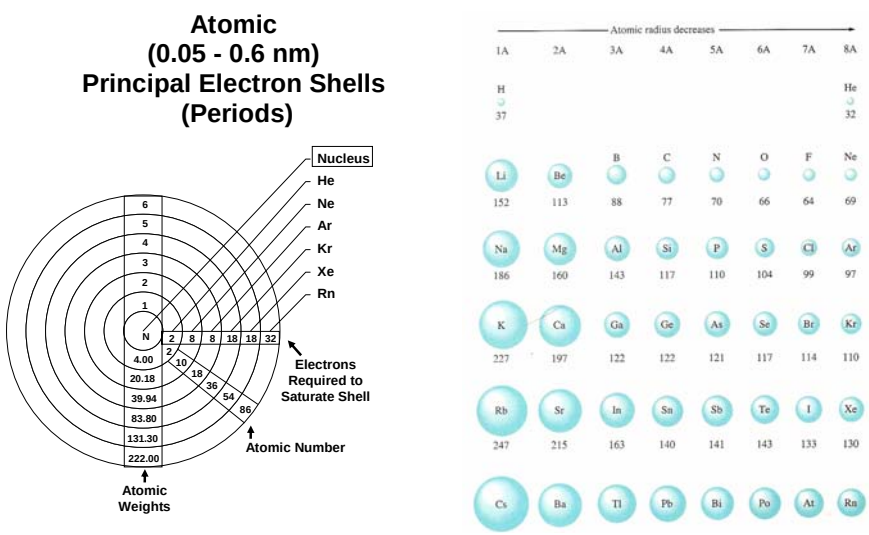


Figure 3.1. *Periodicity of picoscale elemental core-shell structures and their periodic sizes as a function of principle electron shell compared to element dimensions.*

Atom (picoscale) based periodicity is defined and controlled by *quantized charge neutralization relationships* that exist between the *nucleus* and the *electrons* occupying the respective *concentric electron shells surrounding the nucleus.* These relationships may be best visualized as core-shell structures; wherein, these discrete, quantized energy relationships are controlled by non-Newtonian physics and described with quantum mechanical mathematics. Such atom-based, core-shell architectures systematically occupy picoscale space as a function of their nuclear charge and electron occupancy/shell level (i.e., atomic number) and define discrete nuclei-electron relationships. These relationships are systematically manifested as periodic patterns (i.e., reactivity/physical property patterns) and are traditionally visualized vertically as elemental groups and horizontally as systematic electron occupation levels in Mendeleev-type Periodic Tables. Since gravitational forces interact more dramatically with the nuclear components (i.e., neutrons/protons) than with electrons in an atom, systematic weight

enhancements (i.e., atomic weights) are noted as a function of neutron/proton content which is sequentially presented left to right in a Periodic Table (Figure 3.1).

3.3 Critical Atom Design Parameters (CADPs) - Non-Newtonian Quantized: (a) Sizes, (b) Shapes, (c) Surface Chemistry and (d) Polarizability

It is apparent that the self assembly of nuclei and electrons controls "atomic space" in the elements at the picoscale level as a function of: (a) size (atomic number), (b) shape (bonding directionality), (c) surface chemistry (electron availability, unfilled shells, valency) and (d) flexibility (polarizability). These inherent properties of atoms have been referred to as *critical atomic design parameters (*CADPs) [39, 96] and may be visualized by the discrete, systematic *sizes, shapes, reactivities/valencies and polarizabilities* associated with the well defined pico-periodic patterns that are represented in Mendeelev's Periodic Table. These inherent CADP properties literally underpin and assure the dependable structural control that is observed and transferred to sub-nanoscale molecular structures by chemical bond formation or non-bonding self assembly. The endless combinations, arrangements and organization of these picoscale building blocks driven by the rules associated with their inherent CADPs, literally defined the growth and development of our traditional, sub-nanoscale, small molecule, chemical synthesis science over the past 200 years (1808-2008).

Dalton's proposal, presented nearly 200 years ago, embraced the principles of module chemical bond formation with well defined valency. Based on his naivety of atomic structure, Dalton utilized wooden spheres labeled with special icons as *heuristic atom mimics* to identify unique elemental internal structures and as yet, undefined surface interactive properties. This new vision inspired countless numbers of disciples during the 19-20th century to use these well-defined modules as a palette for the combinatorial preparation of literally millions of more complex compounds/assemblies/materials possessing a vast array of novel architectures, reactivities and physico-chemical features. Most importantly, many of these molecular complexities have manifested enormous benefits and applications that have dramatically enhanced the human condition. We now recognize the science of constructing these molecular level complexities as the basis and central dogma of our *sub-nanoscale,* "traditional synthetic chemistry" paradigm. Although the utilization of traditional *atom-based total synthesis* is a very effective strategy for constructing and controlling the critical molecular design parameters of sub-nanoscale structures, it is not broadly used for the production of nanoscale structures. Several exceptions are fullerenes and palyotoxins (i.e. ~1 nm) which are essentially at the bottom of the nanoscale range.

3.3.1 Quantized Sizes

3.3.1.1 Systematic/Periodic Picoscale Atom Size Continuum as a Function of Vertical /Horizontal Position in Periodic Table

It is well known, that systematic and periodic property patterns exist for the elements in the periodic table that produces both a vertical as well as a horizontal continuum as a function of their diameters. Comparing atomic volumes as a function of atomic numbers, clearly demonstrates very recognizable volume expansions for the alkaline metals as illustrated in Figure 3.2.

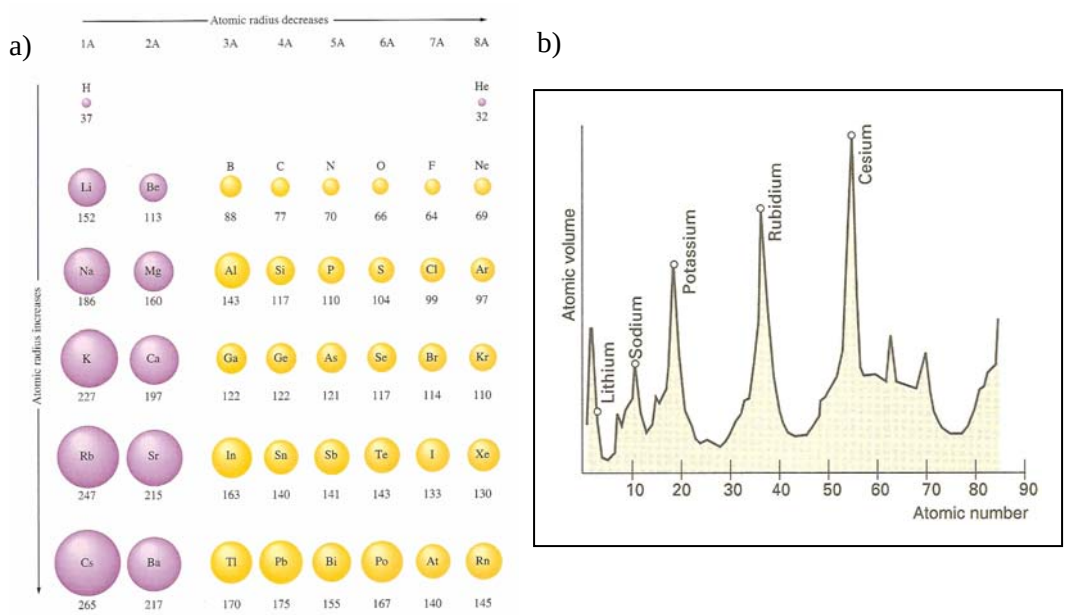


Figure 3.2. *a) The atomic radii of some atoms in picometers.*[2] *b) Periodic property pattern arising from the comparison of elemental atomic volumes vs. atomic number.*

3.3.1.2 Mass Polydispersity of 0-D Picoscale Elements Based on Isotopic Distributions

As demonstrated by Lord Rutherford and others in 1911, an atom is not homogeneous but is a core-shell type structure; wherein, the dense, positively charged core is a collection of nucleons (i.e. neutrons and protons) surrounded by electron shells to produce the charge-neutralized self assembled structures. Most impressive are its very small size, very high density (i.e. 1.6×10^{14} g/cc) and the magnitude of energy required to hold it together. The radius of a typical nucleus is 10^{-13} meters. Therein, the number of protons in a particular nucleus is the atomic number (Z) and the sum of the neutrons and protons is the atomic mass number (A). Early periodic proposals for elemental atomic weights were based on assumptions that atomic weights and numbers should be linear relative to hydrogen. Based on contemporary understanding, this assumption would have meant that the neutron/proton ratio was strictly 1:1 throughout the entire Mendeleev Periodic Table (1857). This inconsistency caused much confusion about the nature of atoms/the elements. It was questioned whether atoms were bundles of energy or could be defined systematically as bundles of mass (i.e., the Ostwald controversy). It was not until 1922 that Nobel Laureate, F.W. Aston showed with his invention of the mass spectrometer that atoms may have identical atomic numbers, but may have different atomic mass number values. Those atoms which exhibit similar chemistry, identical atomic numbers but different masses were hence forth referred to as *isotopes*. Even today, atoms are generally

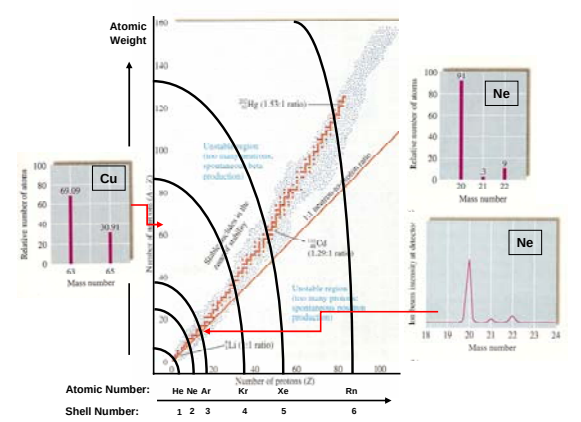


Figure 3.3: *A comparison of elemental atomic weights as a function of atomic number for atomic shell numbers 1-6. Note the PD for a light element like Li is 1.00; whereas, for heavier elements like Cu, Cd and Hg the the PDs range from 1.29-1.53.*

perceived to be very precise entities as far as size and mass. This is true for the light atoms (i.e., for Li, etc.; where A=Z); wherein, atom mass polydispersity (PD) is 1.00. However, it is remarkable to note that for common but heavier elements (i.e. Z >20), the neutron/proton ratio required for nuclear stability is greater than 1 and tends to increase with Z. This intrinsic elemental property leads to substantial atomic mass polydispersity based on isotopic distributions as illustrated in Figure 3.3; wherein, elemental mass polydispersities for common elements such as Cu, Cd and Hg can range between 1.29-1.53.[2] It is interesting to compare these polydispersity values with certain dendrimers (i.e., PD = 1.005-1.03)[4, 97] derived from light elements lacking this isotopic polydispersity.

3.3.2 Quantized Shapes/Bonding Directionality

Although many individual elemental atoms appear as 0-D, spheroid-like entities when observed by electron microscopy (TEM) or atomic force microscopy (AFM), it is understood according to quantum mechanical paradigm that each elemental atom possesses unique orbital shapes. These shapes are manifested as a function of the electron shell and saturation level (Figure 3.4). Furthermore, presentation of electrons in the outer shell defines reactivity and bonding directionality in their linear combination of atomic orbitals to form the molecular orbitals of more complex molecular structures.

(a) Orbital Shapes

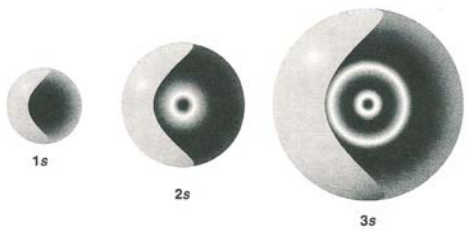
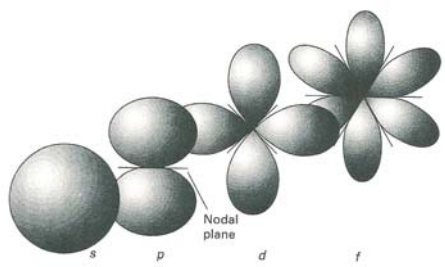


Figure 3.4. *a) A representation of the electron distributions corresponsing to 1s-, 2s-, and 3s-orbitals. Note that the orbitals are all spherically symmetric, and in each of these orbitals the single hydrogen electron may be found at the nucleus, in the center of the central cloud. The density of shading indicates the positions where the electron is likely to be found on any plane cutting through the nucleus.* [30]



b) The general form of the s-, p-, d-, and f-orbitals. There are actually three p-orbitals, five d-orbitals and seven f-orbitals of a given rank of energy, but only one representative of each kind is shown here. The two lobes of a p-orbital are on either side of an imaginary plane cutting through the nucleus; there are two such planes in a d-orbital and three in an f-orbital.[30]

(b) Bonding Directionality VESPR-(Molecular Shapes)

It is well known, that intrinsic VESPR effects which are characteristic of a particular picoscale element are uniquely presented as they enter into chemical bonding events with other elements.[2] These VESPR effects define valency and bonding directionality around that element which is imposed on the molecular orbitals of the resulting molecule. These parameters define the vast array of molecular shapes that are observed in sub-nanoscale molecules and structures (Figure 3.5).

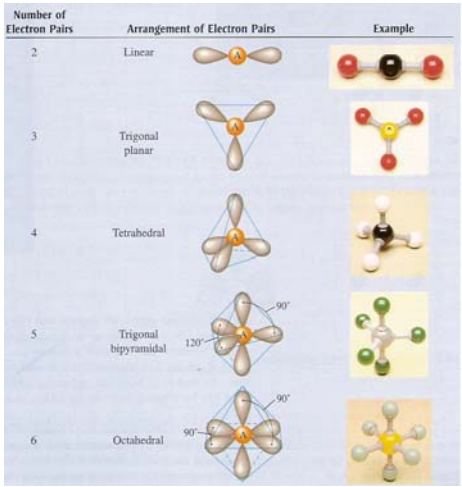


Figure 3.5: *Arrangement of electron pairs for various elements to define valency, as well as bonding directionality and hence molecular shapes resulting from chemical bond formation.*[2]

3.3.3 Quantized Atom Surface Chemistry

3.3.3.1 Surface Electron Behavior in Chemical Reactions

As such, the electrons present in the outer most atomic shells may engage in three major bonding types to form molecules, namely: (1) metallic, (2) ionic and (3) covalent. Both ionic and metallic bonding motifs tend to exhibit omni-directional bonding modes as opposed to covalent bond types which exhibit highly specified directionality. As such, these bonding types tend to be associated with metal/semi-metal type inorganic compounds, molecules and clusters exhibiting conductor/semi-conductor properties. They tend to consist of rigid, inflexible lattices/clusters that may be referred to as **hard matter**. In contrast, covalent bond types are more often associated with non-metallic organic compounds that tend to exhibit insulator type, more flexibility/compressibility and are often viewed as **soft matter.**

Essentially all traditional picoscale chemical reactivity is related to unfilled outer electron shell behavior. This critical surface chemistry property of the elements involves electron movement/placement within the elemental atomic orbitals to produce a wide variety of reactive species that may include such species as: (a) cationic, (b) anionic, (c) free radical or electron sharing entities to mention a few. It is well known, that total saturation of the outer shells produces essentially non-reactive noble gas configurations; whereas, all other unsaturated shell species may engage in molecular orbital formation to produce molecular entities. Although this is the well known central paradigm of traditional chemistry, it is important to have these basic principles in mind as we examine the mimicry/analogies that may be made with nanoscale building blocks/nano-elements that will be made later in this report (Section 4.2). Foremost, are the principles of well defined stoichiometries/mass combining ratios/bonding directionality that constituted the some of the first steps that were taken in the development of traditional picoscale/subnanoscale building block chemistry. Rigorous reproducible structural/crystallographic confirmations of resulting molecular structures, reactivity patterns, properties, etc. are the essence of traditional chemistry/physics. Such confirmation, is undoubtedly possible because of the quantized/systematic nature of the so-called *critical atomic design parameters* (CADPs) that are associated with the picoscale elements.[39, 96] These features will be examined later in the nanoscale hierarchy to define *critical nanoscale design parameters* (CNDPs) as a criterion for identifying so-called "nano-elements" (Section 4.2.5).

3.3.3.2 Surface Electron Behavior in Solids

One of the earliest elemental periodic classifications evolved from atom surface electron behavior based on the ability of an element or its compounds to conduct electrons in the solid state. As such, major elemental composition categories emerged that classified them into the three major classes, namely; (a) metals, (b) semi-metals and (c) non-metals. Experimentally, these categories were widely supported by rudimentary electron conductivity measurements. However, contemporary solid-state physics and chemistry now explain this behavior based on *band gap theory*. Whenever two or more atoms combine their orbitals to form molecular structure, new molecular orbitals arise that present and exhibit three major kinds of behavior based on this orbital mixing. The behavior of the resulting molecular elements and their compounds are thus divided into the following three categories, namely: (a) conductors, (b) semi-conductors and (c) insulators (Figure 3.6). Since nanoscale structures are, by definition, molecular level collections of atoms, these broad classifications appear to be rational descriptors that will be used later to describe similar broad categories of nanomaterials in the proposed Nanomaterials Roadmap (Section 5.0).

3.3.3.3 Classification of Hard-Soft According to Band Gap Theory

Classification of nanomaterials into *hard-soft material* categories appears to follow a pervasive conductivity property pattern that is observed in traditional molecular solids. Historically, this

classification has been based on the ability of picoscale building blocks (i.e., atoms and their assemblies) to convey the extreme intrinsic features of *electron conduction* or *insulation* properties to various molecular level, dimensional states (i.e., 1-D, 2-D or 3-D) as a function of band gaps (Figure 3.6). It is well known, that these band gaps evolve from the molecular orbitals that emerge upon chemically combining various atomic building blocks to produce molecular level products.[98] It is widely recognized, that major classifications of the atomic elements in the Mendeleev Periodic Table are based on three fundamental elemental categories, namely: (a) metals, (b) semi-metals and (c) non-metals based on these features. Since all nanoscale particles are dimensionally defined molecular level entities that arise by the assembly of atoms *via* (1) ionic, (2) metallic (3) covalent bond or some hybridized version of formation, it seems logical that this property classification should apply to all nanomaterials. It is therefore proposed, that "band gap" criteria which is used for categorizing traditional bulk materials be used as a first major classification guideline for organizing nano-materials into a property continuum.

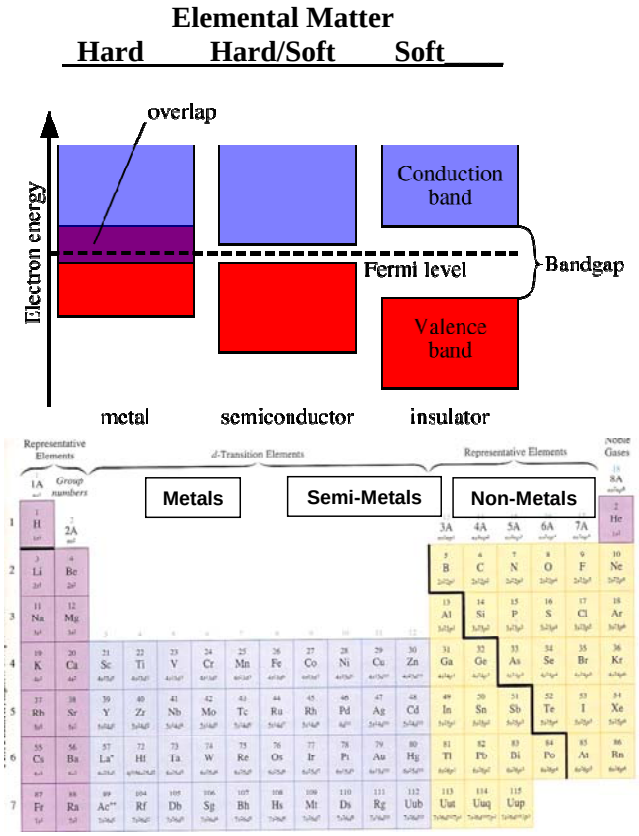


Figure 3.6. *Comparison of "band gap" properties for metals, semi-conductors and insulators and their association with representative elements in the periodic table.*

Note: this classification is made with the distinct recognition that a "quantum confinement model" is assumed for the band gap features that are observed for the nanoparticles under consideration. For example, the well known "Size Induced Metal-Insulator Transition (SIMIT) Effect" is viable and operable at some point in the size continuum.[99]

As opposed to the broad energy bands that are observed for bulk solids, nanoparticles would be expected to exhibit nanosize dependent energy levels that are higher density, and with smaller spacings than for atoms or small atom clusters. Because of these discrete energy levels, such nanostructures are referred to as *quantum dots*. As a consequence of these effects, the bandgap of a metallic quantum dot is observable only at very low temperatures. Conversely, a semi-conducting quantum dot exhibits a larger band gap that is observable at room temperature. As such, size tunable fluorescence emission for a semi-conducting quantum dot (i.e., CdSe) is observed in the visible region at room temperature and clearly illustrates the presence of a material exhibiting a nanosize dependent band gap.

3.3.3.4 Surface Chemistries that are Associated with the First Well Documented Examples of Synthetic - Traditional Colloids and Traditional Polymers

Two major scientific breakthroughs occurred in the late 19th and early 20th century that demonstrated that either 0-D, picoscale metal atom monomers[87, 100] or 1-D, sub-nanoscale organic monomers could be assembled into nanoscale, poly-atomic colloids or polymerized into macromolecular structures (polymers), respectively (Figure 3.7).[101]

(a) Metal-Metal Surface Chemistry to *Nanoscale Colloid Science:*

As early as 1857, M. Faraday reported the first synthesis of polydisperse colloidal materials including gold metal colloids [87] which involved metal-metal surface chemistry. These early examples initiated the field of colloid chemistry which was further developed by W. Ostwald[102] and many other well known contemporaries.[99, 103] As such, these methodologies have become highly refined and developed to produce a wide variety of well-defined, monodisperse metal nano-clusters and semi-conducting quantum dots that will be discussed later.

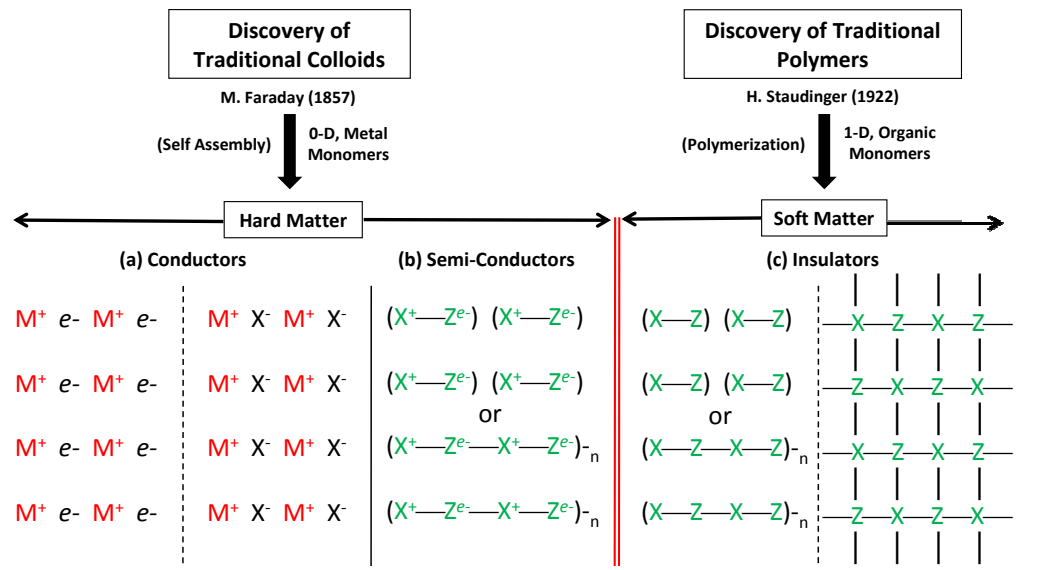


Figure 3.7. *Major discoveries by M. Faraday and H. Staudinger that provided first synthetic routes to polydisperse colloidal and polymeric materials that define hard and soft nanomaterials, respectively.*

(b) Covalent Surface Chemistry to *Nanoscale Polymer Science:*

Critical atomic design parameters (CADPs) (Section 3.3) and critical molecular design parameters (CMDPs) (Section 3.4) involved in the complexity enhancement from atomic->molecular-> macromolecular (nanoscale)-> macroscale have been described earlier.[39, 96] For the organic chemist, these CADPs may be visualized by the various molecular shapes, valencies and polarizabilities associated with carbon and its well-known *sp, sp*^{2} *or sp*^{3} hybridized orbital states. Sub-nanoscale, 1-D molecular level hydrocarbon building blocks (i.e., alkanes, alkenes and alkyenes), 0-D nanoscale (i.e., fullerenes, carbon nanotubes) and macroscale 3-D carbon allotropes (i.e., as graphite and diamond lattices) are prime examples. Furthermore, CADPs associated with other critical elements (i.e., oxygen, nitrogen, sulfur, phosphorous, silicon, etc) led to well known *organic functionality and ligands* that have provided an enormous list of reactive connectors for assembling picoscale metals, semi-metals and hydrocarbon building blocks into an endless list of sub-nanoscale molecular structures throughout the 19th and early 20th century. The traditional colloid and polymer discoveries by M. Faraday (1857) and H. Staudinger (1922), respectively, literally provided the first examples of synthetic nanoscale (a) hard matter and (b) soft matter (Figure 3.7). In fact, Faraday's earlier work on colloidal metals confused the subsequent acceptance of Staudinger's macromolecular concept.[87] Much of the resistance to Staudinger's concept focused on the opinion that polymers were actually "organic colloids" just as Faraday had observed for metals. Perhaps one of the most remarkable discoveries in the 20th century was the discovery that sub-

nanoscale 1-D molecular structures (i.e., *linear*-monomers)[104] could be catenated with chemical connectivity into macromolecular structures of nanoscale dimensions. In the context of present day nanoscale issues, Staudinger sums up the major features of "traditional polymers" in the following way:

"*There is an essential difference between a simple, uniform material and a high molecular weight substance, the neglect of which prevented application of the molecular concept. All molecules have the same size in simple uniform compounds. On the contrary, high molecular weight compounds (polymers) are mixtures of molecules of similar structure but different size. A separation into uniform products is not possible due to the small differences in their physical and chemical properties. If a molecular weight for high polymers is given, it can only be an average value."*[105] *H. Staudinger*

Therefore, traditional polymers (i.e., the plastics age) are all about "soft matter nanoscale materials;" wherein, their actual physical properties and performance in most cases depend on their molecular weight polydispersity. However, traditional polymers were not an acceptable route to precise, monodisperse macromolecules of tunable nanoscale dimensions. Access to those materials had to await the discovery of dendrimers/dendrons and related methodologies as will be described later (Section 3.6).

3.4 Critical Molecular Design Parameters (CMDPs)-Newtonian Quantized: Structural Control of (a) Sizes, (b) Shapes, (c) Surface Chemistry and (d) Flexibility

Traditional synthetic chemistry produced a wide variety of chemically bonded atom arrays (clusters) all of which are a fulfillment of Dalton's "molecular hypothesis" (1808). Such molecules consist of nuclei clusters that exhibit specific space boundaries and angular dispositions relative to each other due to the electrons that are confined in these regions of space (i.e., orbitals, usually occupied by two electrons and orbital) as described above. Each orbital is either confined exclusively to one nucleus or distributed among the nuclei defining the atom array (cluster). These electrons in their occupation of these orbitals create a distribution of electron density which are routinely observed and documented by crystallographic characterization. Considering the core-shell structures of atoms, one may consider the electrons immediately adjacent to the nucleus as chemically inert "core electrons". These core electrons manifest the prominent features of such an array in electron density maps due to their high localized electron density. On the other hand, the outer-most electrons (i.e., the valence electrons) surrounding each atom provide the reactive sites that leads to chemical bond formation. The linear combination of two or more atomic orbitals from typical organic-type elements (i.e., carbon, oxygen, nitrogen, phosphorous, sulfur) to form covalently bonded compounds generally involves two types of valence electrons, namely: (1) pi electrons or (2) sigma electrons. In each case, they reflect the space and directionality to which these electrons are confined as well as defining their chemical reactivity. This chemical reactivity is directed by the propensity for a pair of bonding electrons to form a molecular orbital involving the overlap of two or more atomic orbitals. These bonding electrons must be clearly distinguished as occupants of either pi molecular orbital, forming pi bonds or sigma molecular orbitals, forming sigma bonds. The overlap of two or more adjacent and parallel p orbitals creates a pi molecular orbital system. This has two interesting consequences; first it prevents rotation about the axes connecting the nuclei of adjacent atoms and as such rotation or flexibility is prevented and structures containing pi molecular orbitals are rigid. Secondly, extended conjugations of such pi systems can allow pi electrons occupying a pi molecular orbital system to be delocalized, such as occurs in aromatic or fullerene systems. It is this combination of rigidity and electron delocalization that confers the features of "hard nano-matter" and more recently so-called "superatom" features to buckminsterfullerene (C_{60}), which will be discussed later (Section 4.2.2.2).[34]

3.4.1 Critical Precursors to Traditional Polymer Architecture: One-Dimensional (1-D) Monomers (X-Z) - Sub-Nanoscale Building Blocks

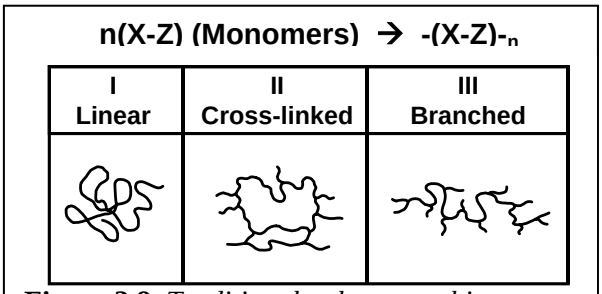


Figure 3.8. *Traditional polymer architectures.*

It was the synthesis of appropriate functionalized, 1-D molecular structures now referred to as **organic monomers** (i.e., X-Y reactive building blocks) that provided a platform for Staudinger to advance his "macromolecular hypothesis" (Figure 3.8). Over 90 years ago, H. Staudinger used these covalent monomer structures to pioneer a seminal covalent propagation strategy to produce macromolecules (polymers). It involved the catenation of reactive, 1-D (X-Y type) monomers to produce statistical distributions of single long chain molecules with high molecular weights (i.e., $>10^6$ daltons). As many as 10,000 or more covalent bonds could be induced between these monomeric building blocks. Using various initiation catalysts and techniques, three major traditional polymer architectures were developed, namely: (I) linear, single chain, random coil, (II) crosslinked or (III) branched macromolecules. Based on these traditional polymerization processes, macromolecules with nanoscale dimensions could be obtained; however, molecular level structure control of three *critical molecular design parameters (CMDPs)* such as: (a) size (b) molecular shape (c) discrete positioning of functionality was virtually impossible. As such, relatively high polydispersities (i.e., statistical distributions of molecular weight are observed for most traditional polymerization processes as described in Table 3.0. The fourth parameter (i.e., flexibility) is often controlled and routinely designed into traditional polymers. However, substantial progress has been made recently using "living polymerization" processes and the Grubbs' catalysts to control molecular weight polydispersities in some linear copolymers that have been used to produce relatively discrete, "cross-linked, polymeric micelles" that will be described later.[17]

Table 3.0. Polydispersities (**PD=M_w/M_n**) observed for traditional polymer architectures.

Architecture Type	*Process Type*	M_w/M_n
Linear	Free radical addition (low conversion)	
Linear	Terminated by coupling	1.5
Linear	Terminated by disproportionation	2.0
Linear	Condensation polymer (100% utilization of monomer)	2.0
Linear	Vinyl (high conversion)	2-5
Linear	Anionic (living type)	1.10-1.05
Branched	Branched polymers	20-50

Generally 1-D (linear) sub-nanoscale monomeric building blocks may be used as repeat units to produce the three traditional polymeric architectures (Figure 3.8 and 3.9). However, construction of dendritic macromolecules in the fourth architectural category (i.e., dendritic polymers) generally involves the intermediacy or use of 3-D (branch cell type) monomeric repeat units. It has recently been shown that dendrimers may be viewed as functionalized, spherical shaped 0-D nanoscale monomers. As such, catenation of dendrimers/dendrons may be used to produce a wide variety of well defined, multiple dendrimer topologies that are referred to as *megamers*.[21, 106]

Adapting the concepts of *critical atomic design parameters* (CADPs) and *critical molecular design parameters* (CMDPs) to the nanoscale level should provide a rational evolution to this next level of complexity (i.e., *critical nanoscale design parameters* (CNDPs)).

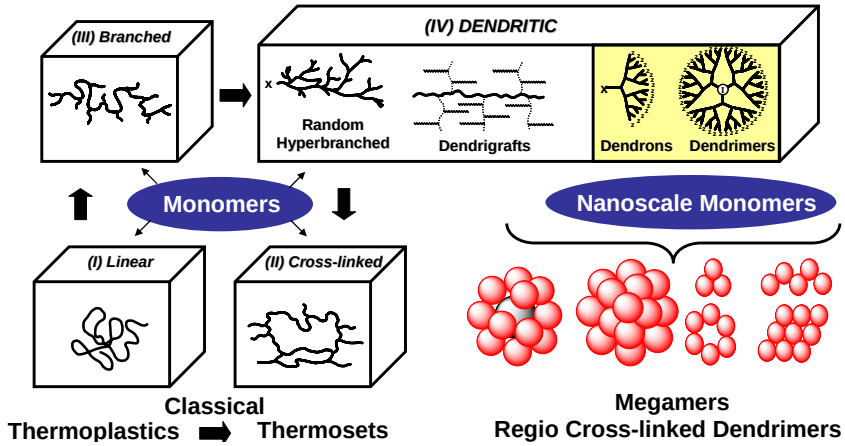


Figure 3.9. *Comparison of polymer architectures: (I) linear, (II) crosslinked, and (III) branched with (IV) dendritic, and their relationship in the transition from the thermoplastic to the thermoset state. The derivation of all architectural classes from classical monomers is noted; whereas, dendrons and dendrimers may fuction as nanoscale monomers in megamers.*[33]

3.5 The Importance of Molecular Architecture as a Strategy for Obtaining New Properties

Obtaining desirable material properties as a function of elemental composition, has been the "central dogma" of traditional chemistry since its inception in the early 19th century. Pioneering work by Berzelius on architectural isomerism/allotropes (1832)[107] provided a second significant strategy for obtaining new properties beyond the influence of chemical composition.

The importance of architectural changes imposed on carbon is dramatically illustrated by the enormous property diversity observed for its three allotropes, namely: (a) graphite, (b) diamonds and (c) fullerenes. It is interesting to note that even very subtle architectural modifications of this element can dramatically alter the electronic properties of carbon nanotubes as illustrated by the three architectural isomer forms as illustrated in Figure 3.10.[18]

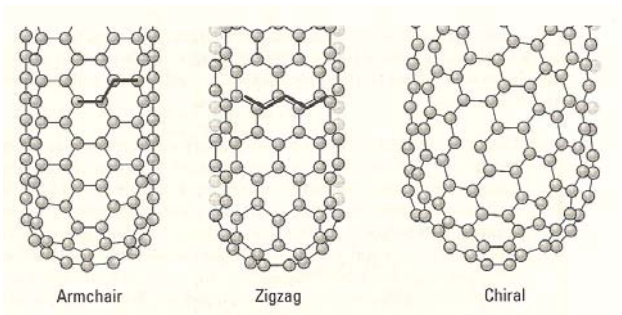


Figure 3.10. *Three architectural isomers of single walled carbon nanotubes (SWCNTs) that exhibit architecturally directed properties, namely: arm chair (metallic, conducting), (b) zigzag (metallic, conducting) and (c) chiral (semi-conducting).*[18]

In the polymer world, the dramatic influence of architecture on producing new properties, exclusive of composition, is dramatically illustrated by the diversity of properties observed for each of the four major polymer architectures[21] (Figure 3.9). In fact, the fourth major polymer architectural class, dendritic polymers are widely known to exhibit unprecedented new properties compared to the three traditional classes. Furthermore, this polymer class led to the development of new dendrimer/dendron processes/methodologies that provided complete structural control over *critical nanoscale design parameters* (CNDPs) such as: (a) size, (b) shape, (c) surface chemistry and (d) flexibility of macromolecular structure at the nanoscale level. This, in effect, presented a new molecular level strategy for controlling nanoscale structures. Many of these issues were first reported in the early 1990s[39] (Figure 3.11) and will be reviewed briefly in the next section.

3.6 A New Strategy for Structural Control of Critical Nanoscale Design Parameters (CNDP's) Based on Dendritic Polymers

Dendrimers and Dendritic Polymers

Nanoscale periodicity based on dendrimers is defined by the chemical bond connectivity relationships that exist between the core and the concentric monomer shells (i.e., branch cell monomers) surrounding the core. Dendrimers are best described as core-shell structures. Due to their nanoscale dimensions, these discrete, quantized bonding relationships are controlled by Newtonian physics. The branching and terminal group amplification of a dendrimer can be described with geometric progression mathematics. Dendrimers are constructed according to synthetic aufbau principles; wherein, monomers (branch cell monomer units) may be viewed heuristically as electron analogues relative to the core much as electrons relate to various nuclei in their charge neutralization assembly in atoms. As such, monomers may be sequentially introduced into shells (i.e., generations; Gen) until they reach a saturation limit (Z), which is mathematically defined by $Z= N_c N_b^G$, wherein: N_c= core multiplicity, N_b= branch cell multiplicity and G= generation (monomer shell level). Dendrimer synthesis involves the covalent introduction of branch cell units into concentric shells of "branch cells" according to these mathematically defined to produce discrete quantized saturation levels for each shell. These dendritic core-shell structures are systematically amplified at each shell level as a function of core connectivity/multiplicity (N_c) and monomer/branch cell multiplicity (N_b) and occupancy level (i.e., dendrimeric number).

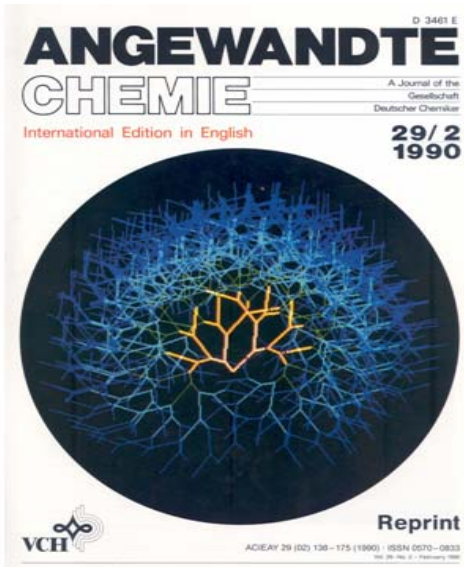


Figure 3.11. *Cover of Angew. Chem. Int. Ed. Engl. 29 (1990) 138-175. Starburst Dendrimers: Molecular-Level Control of Size, Shape, Surface Chemistry, Topology, and Flexibility from Atoms to Macroscopic Matter.*[39]

3.6.1 Critical Precursors to Dendrons/Dendrimers and Dendritic Polymers: Three-Dimensional (3-D), Sub-Nanoscale Building Blocks - Branch Cell Monomers

During the past two decades 3-D branch cell monomers, illustrated in Figure 3.12, have been used to synthesize a wide variety of dendritic polymers. Two major covalent synthesis strategies have evolved and include: (a) Tomalia/Newkome/Vögtle type divergent or (b) Fréchet/Hawker type convergent strategies as described in Sections 4.2.4.3, 6.2.1.1 and illustrated in Figures 4.9 and 6.28.

Dendritic topology is now recognized as the fourth major class of macromolecular architecture[21, 83] after the three traditional polymer architectures described above (Figure 3.9). This new macromolecular class (i.e., (IV) dendritic polymers) consists of four dendritic subclasses; namely, (IVa) *random hyperbranched polymers*, (IVb) *dendrigraft polymers*, (IVc) *dendrons and* (IVd) *dendrimers* (Figure 3.12). The order of this subset, from a to d, reflects the relative degree of structural control present in each of these dendritic architectures. Substantially different architecturally induced properties are manifested by this class of polymers[39, 108-110] compared to classical types.

All dendritic polymers are open *covalent core-shell assemblies of branch cell monomers*. They may be organized in very symmetrical, monodisperse arrays, as is the case for dendrons/dendrimers or as irregular polydisperse assemblies that are typical for random hyperbranched polymers. As such, the respective subclasses and the level of structure control are defined by the propagation methodology used to produce these assemblies, as well as by the branch cell (BC) construction parameters. The BC parameters are determined by the composition of the BC monomers, as well as the nature of the *excluded volume* defined by the BC. The excluded volume of the BC is determined by the length of the arms, the symmetry, rigidity/flexibility, as well as the branching and rotation angles involved within each of the branch cell domains. As shown in Figure 3.12, these dendritic arrays of branch cells usually manifest covalent connectivity relative to some molecular reference marker (I) or core. It should be noted, that highly controlled core-shell type structures such as dendrons and dendrimer (IVc-d) can be synthesized with very low polydispersities (i.e., Mw/Mn ≅ 1.01 – 1.0001) [4]as illustrated by Figure 3.12. Since these dendrons and dendrimers are synthesized with low atomic number elements possessing no severe isotopic distributions, it is interesting to note that dendritic structures (IVc and IV d) appear to be more monodisperse than common higher atomic weight chemical elements (i.e., Cd, Hg, etc.) as discussed earlier (Section 3.3.1.2, Figure 3.3).

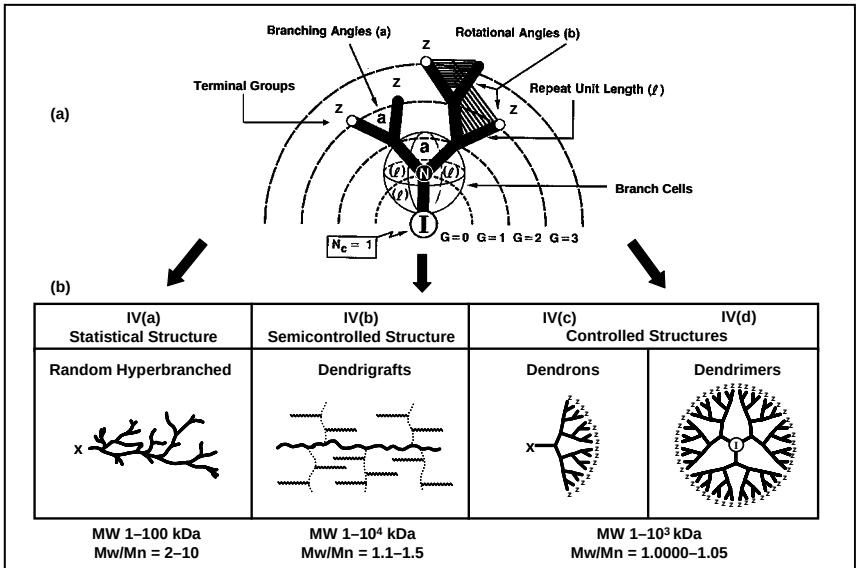


Figure 3.12. *(a) Dendritic polymers as open, covalent assemblies of branch cells. (b) Dendritic polymers: subclasses of the fourth major new class of macromolecular architecture.*

3.6.2 Critical Intermediates/Structural Control Involved in *Bottom-Up* Synthesis of Dendrimers and Other Well Defined Nano-Modules (i.e., Nano-Elements)

Throughout Sections 3.3, 3.4, and 3.6 we reviewed the importance of structural control over all key intermediates involved in the rationale synthesis of "well defined" nanostructures such as dendrimers. Control over critical design parameters was necessary at each of the intermediate hierarchical levels leading to the targeted nanostructures. This included atomic level (CADPs), molecular level branch cell monomers (CMDPs) and nanoscale intermediates (CNDPs) (i.e., dendrons/dendrimers). Similarly, the successful strategy to produce larger, well defined, nanosized (i.e., 10-50 nm) core-shell tecto(dendrimers) required such control over five key building block type intermediates; namely, (i.e., atoms (CADPs), 1-D/3-D monomers (CMDPs) and dendrons/dendrimers (CNDPs). As described in Figure 3.13, these critical building block intermediates spanned three distinct hierarchical levels, namely; picoscale, sub-nanoscale and nanoscale dimensions.

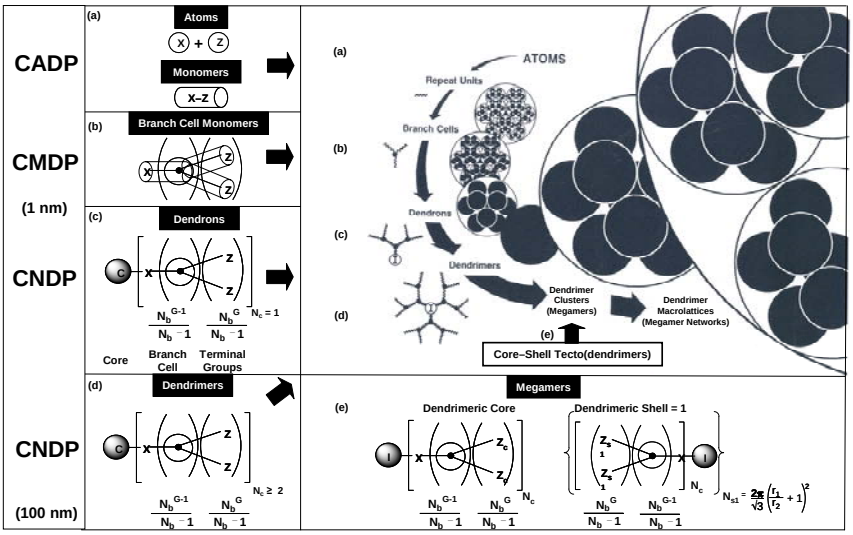


Figure 3.13. *Hierarchy of empirical construction components: monomers (a), branch cells (b), dendrons (c), and dendrimers (d) leading to core–shell tecto(dendrimers) (i.e., megamers) (e).*[38]

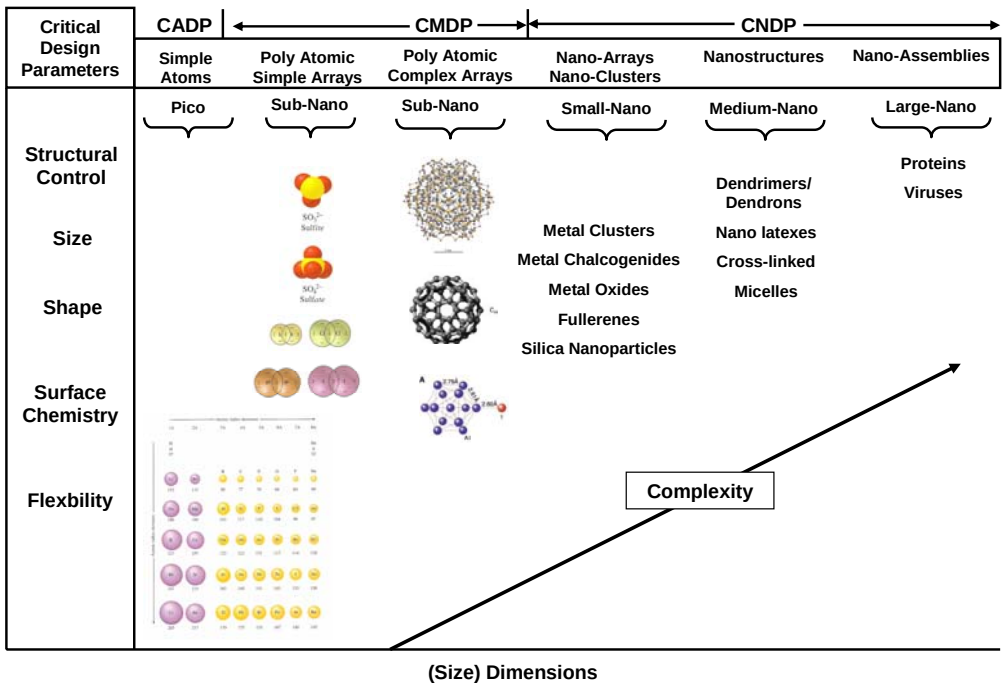


Figure 3.14. *Structural control of critical design parameters required for bottom-up synthesis of higher nano-complexity.*

Based on the experimentally demonstrated models for dendrimers, etc. it is apparent that similar control over key intermediates at these various hierarchical levels will be required as part of any other "bottom-up" strategy to other categories of well-defined nanomaterials as described in Figure 3.14.

4.0 Proposed Strategy for Defining a Comprehensive Roadmap, Nano-Elements and Nano-Compounds

4.1 General

One of the main (initial) objectives of this NSF Workshop (Section 1.0) was to use the simple logic and rationale employed by A. Lavoisier, J. Dalton and many others as a (first step) starting point for defining nanomaterials. The logic and progress promoted by those early researchers (i.e., "atom hypothesis" and "molecular hypothesis") was essential as a beginning platform for the evolutionary steps that were taken to the Periodic Table. These steps required some 61 years from Dalton's "Philosophy for a Chemical System" (1808) until Mendeleev's Periodic Table which was formalized in 1868. It was proposed that from this historical precedence, one could appraise (determine) how far these analogies to picoscale materials could be applied and used in the development and description of atom-like building blocks at the nano-level (i.e., nano-elements). Furthermore, it was hoped that demonstrated chemical bonding of such nano-elements *via* well defined surface chemistry to form more complex nanoscale molecules exhibiting reproducible stoichiometries and mass combining ratios would provide evidence for so-called, nano-compounds. Finally, observing systematic "nano-periodic property patterns" would be critical in order to complete our proposed analogy to the picoscale elements and their compounds. Experimental documentation of such periodic patterns would be essential for ultimately defining the final objective, namely; a *nano-periodic table(s)*. At the very least, it was expected that this exercise would lead to the development of a comprehensive roadmap of nanomaterial categories and classifications.

This section describes these first steps with brief examples of *soft nano-matter* (i.e., dendrimers) and *hard nano-matter* (i.e., metal nanocrystals) which we propose as extreme models in the continuum of nanomaterials. These two models were used to appraise the degree of exhibited *atom mimicry* and suitability of such "well-defined" nano-modules in the context of descriptors such as *nano-elements and nano-compounds.* This section concludes with a proposed *Nanomaterials Roadmap* which attempts to classify certain well defined nano-modules (i.e., nano-elements) into rational classifications based on historical precedence for similar tradition materials.

4.2 Atom Mimicry - *Heuristic and Proven Example*

4.2.1 Heuristic Atom Mimicry

The concept of atom mimicry was first practiced 200 years ago beginning with the naïve use of wooden spheroids bearing icons to represent the known elements at that time, as proposed by J. Dalton in his "New Philosophy of Chemistry" (1808).[8] This is perhaps the best and most profound example of macroscale *heuristic atom mimicry,* which Dalton used to explain his "molecular hypothesis." It provided the first steps for evolving the Mendeleev Periodic Table of the Elements (1869) over the next 61 years. Presently, very detailed integration of CADP's (i.e. size,

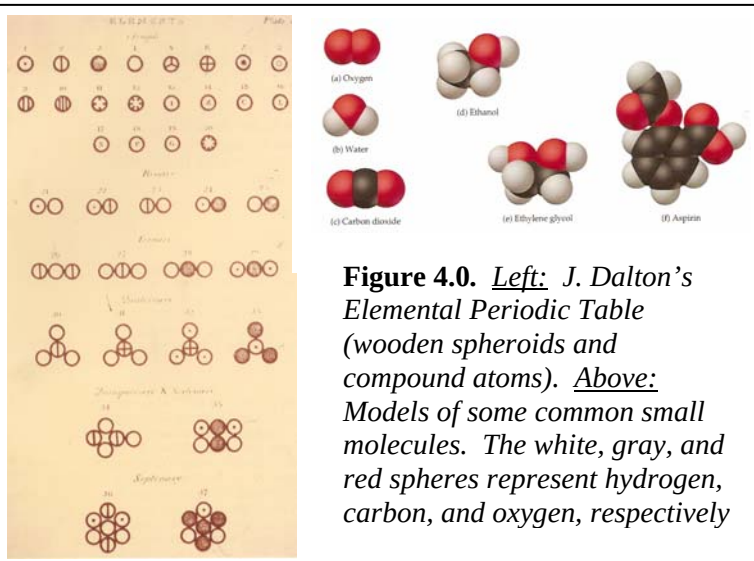


Figure 4.0. *Left: J. Dalton's Elemental Periodic Table (wooden spheroids and compound atoms). Above: Models of some common small molecules. The white, gray, and red spheres represent hydrogen, carbon, and oxygen, respectively*

shape, surface chemistry, etc.) into heuristic macroscale (i.e., cm) atom mimics is routinely practiced by the use of *Corey-Pauling-Koltun (CPK) models* for designing, constructing and analyzing molecular structures (Figure 4.0).

To our knowledge, the first use of nanoscale structures as heuristic atom mimics was introduced in the early 1990s.[39, 59] Such atom mimicry was used to describe the molecular level core-shell analogies of atoms that we noted for dendrimers. These unique architectural and reactivity analogies observed in both picoscale and nanoscale systems are compared below (Figure 4.1).

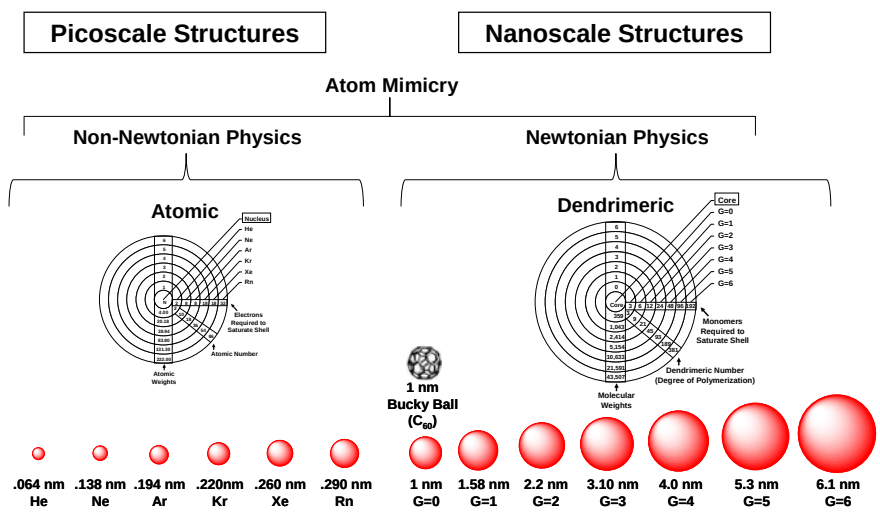


Figure 4.1. *An example of atom mimicry. A comparison of core-shell structures representing picoscale atoms and nanoscale dendrimers, as well as the continuum of sizes that prevails over the two dimensional ranges that are controlled by quantum mechanics and Newtonian physics, respectively.*

4.2.2 Proven Atom Mimicry (Super Atoms) Demonstrated With Sub-Nanoscale and Nanoscale Structures

4.2.2.1 Small Metal Clusters Behave as Super Atoms

Extensive work by Castleman, Khanna, et al.[49, 111] have shown that certain small metal atom clusters of a given element can exhibit unique chemical and electronic properties that resemble another element. As such, these metal clusters are referred to as "super atoms" and have been regarded as an extension of the traditional elemental periodic table in a third dimension. Such a sub-nanoscale aluminum cluster (i.e., $Al_{13}I^-$, Figure 4.2) was found to exhibit profound stability arising from coincidental closure of its geometric and electronic shells, as well as behaving like a *super halogen*.

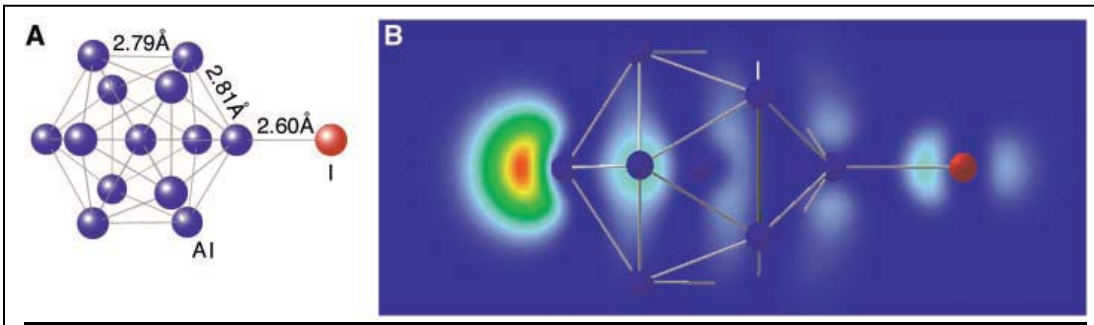


Figure 4.2. *(**A**) Lowest energy structure for $Al_{13}I^-$. (**B**) Charge density map of the HOMO for $Al_{13}I^-$. Color code: blue, aluminum; red, iodine.*[49]

4.2.2.2 Hollow Core-Pi Shell Features of C_{60} (Buckminsterfullerene) Behave as a "Super Atom"

As early as 2000, Hirsch et al.,[47] proposed that the *pi*-electron system (i.e., the spherical aromaticity) of an icosahedral fullerene can be considered as a spherical electron gas which surrounds the surface of the sphere. It was further proposed that this electron gas could be characterized by the angular momentum quantum numbers (l= 0, 1, 2, 3 ….). The s shell (l=0) is orbital. The major difference compared to a picoscale atom is that the surface of the fullerene sphere represents a nodal plane and the electron density in the hollow sphere should approach zero. Hence, the wave function characterized by (l= 1, 2, 3 …) are analogous to the atomic p, d, and f orbitals of an atom.

Recently, atom-like electron orbitals centered on spherical C_{60} molecules were simulated as illustrated in Figure 4.3. These properties have now been observed and experimentally documented by scanning tunnel microscopy and described with more detail in Section 6.1.5, as well as Figures 6.20-6.23.

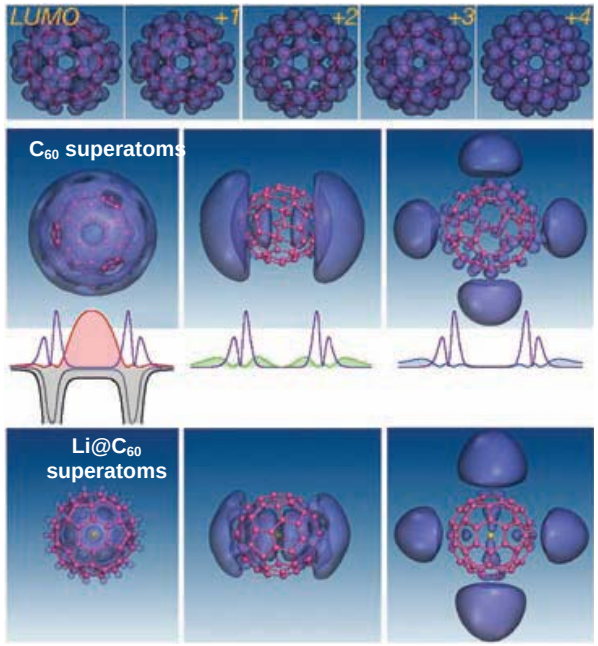


Figure 4.3. *C_{60} molecular orbitals.* (A) *Calculated LUMO to LUMO+4 and s, p, and d SAMO wave functions for isolated C_{60} and Li@C_{60} molecules.* [34]

4.2.3 Proven Atom Mimicry and Critical Nanoscale Design Parameters (CNDPs) Exhibited by Both Hard and Soft Nanoscale Matter

4.2.3.1 Core-Shell Architectures are Pervasive in Well Defined Nanoscale Building Blocks: Hard and Soft Nano-matter

Core-shell architecture best describes the nuclei/electron relationship of all the picoscale elements in the Periodic Table. At the picoscale level the core function involves charge neutralization/shielding effects imposed on both interior and surface electrons and are expressed as periodic atom expansion and contraction patterns observed in the elemental periodic table (Figure 3.1.). Of course, these nuclear influences determine the reactivity, polarizability, energy state and dynamics of both interior shell and surface shell electrons.

This structural motif also best describes both the "hard and soft matter" categories of many *well defined, nanoscale building block* classes identified in the NSF Workshop. By definition, these core-shell structures possess architecture consisting of three critical components, namely: (a) core/nucleus, (b) an interior and (c) a surface. Generally, the core component functions as a focal point in these entities that may transfer/express important informational/functional parameters externally to the interior and surface shell components of the nanostructure. Important information transfer such as: (a) shape, (b) size (c) packing/crystallization features (d) the absence/ presence of mass or (e) other functional properties (i.e., charge, electronic, magnetic, fluorescent, photochemical, redox, etc.) may be manifested by the nanostructure core. A comparison of pervasive core-shell type topologies observed in both picoscale elements and proposed *well defined nano-modules* (i.e., nano-elements as described later) are illustrated in Figure 4.4.

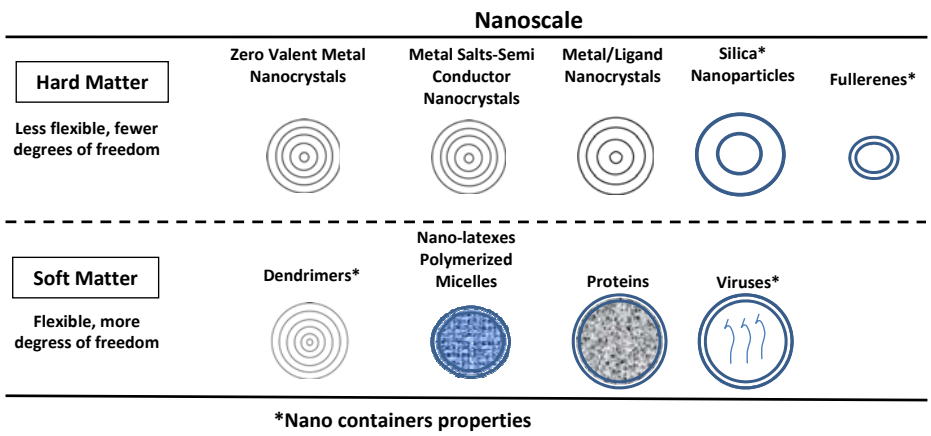


Figure 4.4. *Core-shell taxonomy of well defined, zero-dimensional (0-D), hard and soft matter nanoscale modules which are proposed later as nano-elements.*

Graphic details illustrating core-shell topologies are readily apparent in specific examples of hard and soft nano matter illustrated by metal nanocrystals and dendrimers, respectively (Figure 4.5).

Figure 4.5. *Left: Nanoparticles consisting of 2899 Cu atoms (left) and 22831 Cu atoms (right). For the sake of clarity the particles are cut along a (111) plane showing in red the surface atoms which do not have a crystalline fcc environment (OTHR), in green surface-near atoms with a crystalline fcc environment at least up to the first nearest-neighbor shell (GFCC) and in blue atoms with a crystalline fcc environment at least up to the fourth nearest-neighbor shell (PFCC); these identifications follow from a common neighbor analysis (CNA).*[57]

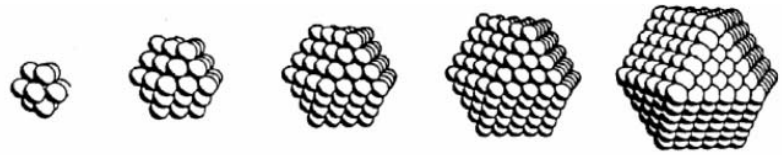
4.2.4 Nanoscale Atom Mimicry - Core-Shell Aufbau Components

In order to gain further insights into the notion of nanoscale atom mimicry, it is of value to compare the respective core and shell-type building (i.e., aufbau) components that are involved at the picoscale and nanoscale levels. Atoms utilize neutrons/protons as nuclear/core components and electrons as their shell components in their self assembly to produce picoscale core-shell structures. Mimicry of these picoscale components at the nano level to produce analogous nanoscale core-shell structures involves a variety of poly-atomic or molecular entities. These larger entities include such aufbau building entities as atoms, *linear*-monomers, *branch cell*-monomers, atom clusters, dendrons, etc. and can be used as either core or shell components in the construction of nanoscale core-shell structures. For example, the construction of *hard nano-matter* such as metal nanocrystals involves the assembly of well defined numbers of metal atoms in concentric shells around a single core atom to produce core-shell like metal clusters as shown in

Figure 4.6. On the other hand, similar construction of *soft nano-matter* such as dendrimers, may involve core component derived from atoms, small molecules or macromolecules. More specifically, the Newtonian quantized (i.e., mathematically defined) shell components for dendrimers are derived from molecular level branch cell monomers (Section 4.2.4.3; Figure 4.11).

4.2.4.1 Quantized, Aufbau Component Relationships to Produce Core-Shell, Hard Nano-Matter Metal (M^o) Nanocrystals

Using mass spectrometry, Brack, et al.[112] determined that discrete metal nanocluster masses were produced in relatively large abundance and presented a very important nano-periodic pattern. So called "magic sizes" were observed that corresponded to the closing of atomic shells. This pattern is completely consistent with (a) stable nuclear shells from nuclear chemistry[113] or (b) electronic shells which form the basis for chemical bonding and the Mendeelev Periodic Table,[2] as well as the auto-reactivity of unsaturated outer shells or inertness of saturated shells associated with dendrimers[21, 59] and core-shell tecto(dendrimers)[32] which will be described later (Section 8.3.3). Note the similarity of metal cluster shells to dendrimer generations.



Full-Shell "Magic Number" Clusters					
Number of shells	1	2	3	4	5
Number of atoms in cluster	M_{13}	M_{55}	M_{147}	M_{309}	M_{561}
Percentage surface atoms	92%	76%	63%	52%	45%

Figure 4.6. *Full-shell magic number formation showing how the number of shells relates to the number of atoms in a cluster and the percent of atoms present on the surface.*[16]

4.2.4.2 Early Examples of Periodic Patterns Based on Newtonian Quantized Aufbau Components Present in Metal Nanocrystals.

It is widely recognized, that these core-shell type, metal nanocrystals exhibit well known, size dependent absorbance spectra (Figure 4.7). These properties may be viewed as prime examples of *nano-periodic property patterns* manifested by these well defined nano-modules. Such nano-periodic patterns taken collectively for other well defined nano-modules will constitute the first steps that are required to ultimately define a comprehensive Nano-Periodic Table (Section 8.0).

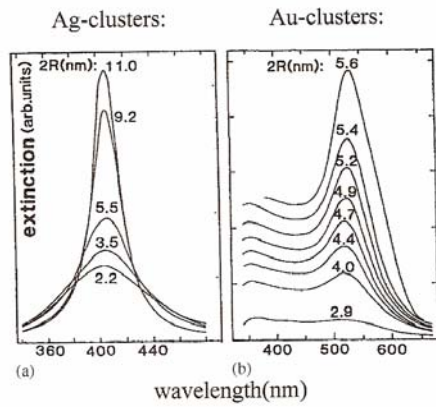


Figure 4.7. *Absorbance spectra of (a) silver and (b) gold clusters of different sizes.*[3]

Similarly, a well known picoscale periodic property observed for atoms is the fact that the electron saturation level and polarizability of the outer shell (corona) appear to determine unique crystallization patterns that are routinely observed for the elements. For example, rare gases which possess saturated outer electron shells that are non-polarizable, crystallize into *hcp* type patterns; whereas, elements possessing diffuse valence electron shells tend to crystallize into *bcc/bct* type patterns.

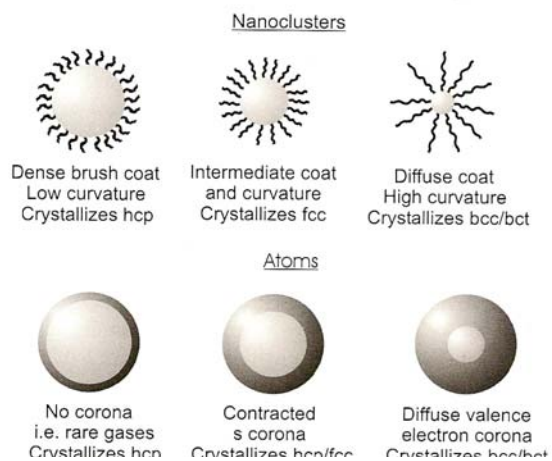


Figure 4.8. *Comparison of polarization and crystallization nano-periodic properties for picoscale (atoms) and nanoscale module.* [7]

As such, a dramatic example of atom mimicry, as well as an early nano-periodic pattern was reported by Ozin, et al.,[7] and illustrated in Figure 4.8. They noted that a nano-periodic relationship existed for a series of metal nanocrystals based on the radius of curvature and polarizability of the nanocrystal surface shell (corona). Furthermore, they noted that crystallization of various capped nanocrystals to produce superlattices yielded similar crystallization patterns at the nano level as was observed for elemental atoms.

4.2.4.3 Quantized, Aufbau Component Relationships to Produce Core-Shell, Soft Nano-Matter Dendrimer Structures

The aufbau events required to assemble dendrimers may be thought of as information driven monomer processing that is required to produce these nanoscale core-shell structures. As such, dendrimers may be viewed as nanoscale processing devices; wherein, their precise sizes and shapes are directed and can be controlled as illustrated in Figure 4.9.

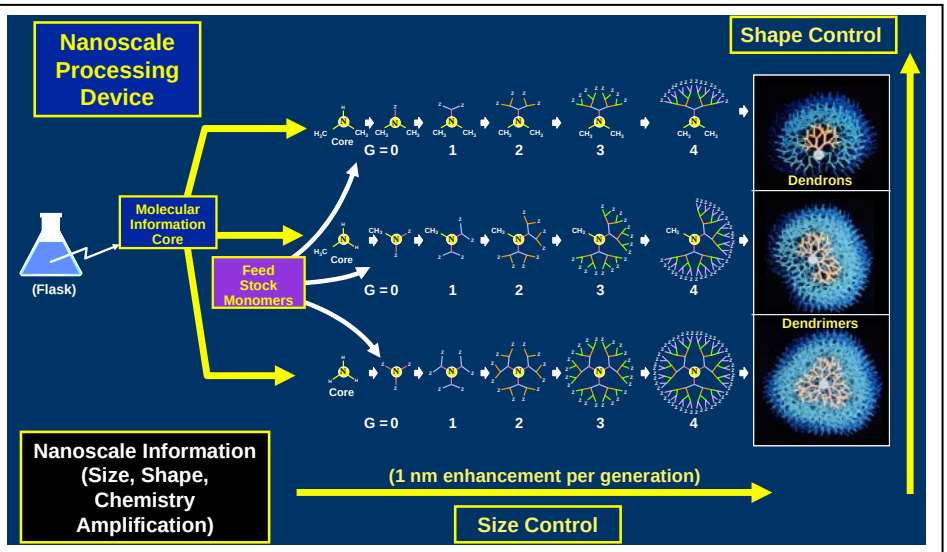


Figure 4.9. *The influence of core information and generational growth on dendrimer shape and size, respectively.*

Each architectural component manifests a specific function while at the same time defining properties for these nanostructures as they are grown generation by generation (Figure 4.9). For example, as illustrated in Figure 4.10 the *core* may be thought of as the molecular information center from which *size, shape, directionality and multiplicity* are expressed *via* the covalent connectivity to the outer shells. Within the *interior*, one finds the *branch cell amplification region* which defines the type and amount of interior void space that may be enclosed by the terminal groups as the dendrimer is grown to a surface congested level. Branch cell multiplicity (N_b) determines the density and degree of amplification as an exponential function of generation (G). The interior composition and amount of solvent filled void space determines the extent and nature of guest-host (endo-receptor) properties that are possible with a particular dendrimer family and generation. Finally, the surface consists of reactive or passive terminal groups that may perform several functions. With appropriate function, they serve as a *template polymerization region;* wherein, each generation is amplified and covalently attached to the precursor generation. Secondly, the surface groups may function as passive or reactive gates controlling entry or departure of guest molecules from the dendrimer interior. These three architectural components essentially determine the physico-chemical properties, as well as the overall sizes, shapes, reactivity and flexibility of dendrimers. It is important to note that dendrimer diameters increase linearly as a function of shells or generations added; whereas, the terminal functional groups increase exponentially as a function of generation. This dilemma enhances "tethered congestion" of the anchored dendrons, as a function of generation, due to the steric crowding of the end groups. As a consequence, lower generations are generally open, floppy structures; whereas, higher generations become robust, less deformable spheroids, ellipsoids or cylinders depending on the shape and directionality of the core.

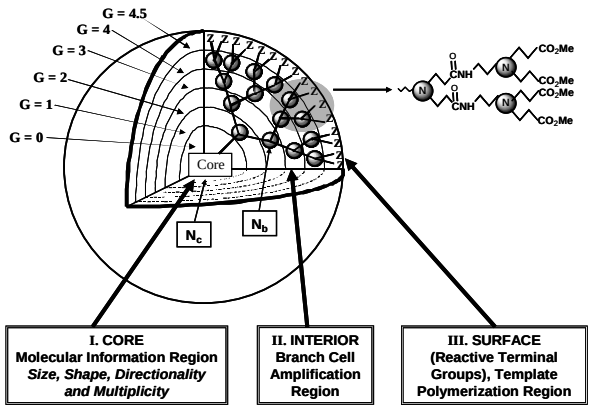


Figure 4.10. *Three-dimensional projection of dendrimer core-shell architecture for G = 4.5 poly(amidoamine) (PAMAM) dendrimer with principal architectural components (I) core, (II) interior and (III) surface.*[53]

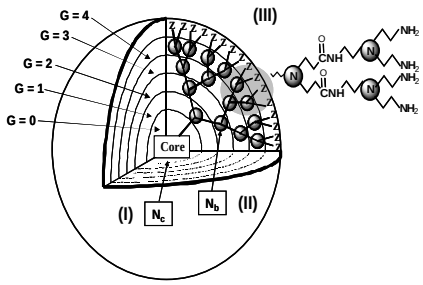
4.2.5 Proven Structural Control of Critical Nanoscale Design Parameters (CNDPs). Newtonian Quantized: (a) Sizes, (b) Shapes, (c) Surface Chemistry and (d) Flexibility of Interest to Nanoscientists

In this section we focus on experimentally proven examples that illustrate structural control of **C**ritical **N**anoscale **D**esign **P**arameters (CNDPs) using dendrons/dendrimers. This brief overview illustrates proven examples of atom mimicry based on the ability to control (a) sizes, (b) shapes, (c) surface chemistry and (d) flexibility at the nanoscale level.

It is apparent, that both the core multiplicity (N_c) and branch cell multiplicity (N_b) determines the precise number of terminal groups (Z) and mass amplification as a function of generation (G). One may view those generation sequences as quantized polymerization events. The assembly of reactive monomers,[39, 114] branch cells[39, 110, 115] or dendrons[116, 117] around atomic or molecular cores to produce dendrimers according to divergent/convergent dendritic branching principles has been well demonstrated. Such systematic filling of space around cores with branch cells, as a function of generational growth stages (branch cell shells), to give discrete, quantized bundles of mass has been shown to be mathematically predictable.[59] Predicted molecular weights have been confirmed by mass spectroscopy[118-120] and other

analytical methods.[116, 121] Predicted numbers of branch cells, terminal groups (Z) and molecular weights, as a function of generation, for [1,2-diaminoethane] cores (N_c = 4); PAMAM dendrimers are described in Figures 4.11. It should be noted, that the molecular weights approximately double as one progresses from one generation to the next. The surface groups (Z) and branch cells (BC) amplify mathematically according to a power function; thus, producing discrete, monodisperse structures with precise molecular weights as described below. These predicted values can be verified by mass spectroscopy for the earlier generations; however, with divergent dendrimers, minor mass defects are often observed for higher generations as congestion induced *de Gennes dense packing* begins to take affect.[39]

4.2.5.1 Quantized Sizes-Control of Monodisperity



Number of Surface Groups	$Z = N_c N_b^{G}$	Surface Group Amplification per Generation
Number of Branch Cells	$BC = N_c \left[\frac{N_b^{G-1}}{N_b - 1} \right] =$	Number of Covalent Bonds per Generation
Molecular Weights	$MW = M_c + N_c \left[M_{RU} \left(\frac{N_b^{G-1}}{N_b - 1} \right) + M_t N_b^{G} \right]$	

Gen	No. of NH_2 Surface Groups	Molecular Formula	MW	Hydrodynamic Diameter (nm)
0	4	$C_{24}H_{52}N_{10}O_4S_2$	609	1.5
1	8	$C_{64}H_{132}N_{26}O_{12}S_2$	1,522	2.2
2	16	$C_{144}H_{292}N_{58}O_{28}S_2$	3,348	2.9
3	32	$C_{304}H_{612}N_{122}O_{60}S_2$	7,001	3.6
4	64	$C_{624}H_{1252}N_{250}O_{124}S_2$	14,307	4.5
5	128	$C_{1264}H_{2532}N_{506}O_{252}S_2$	28,918	5.4
6	256	$C_{2544}H_{5092}N_{1018}O_{508}S_2$	58,140	6.7

Figure 4.11. *Mathematical expressions for calculating the theoretical number of surface groups (Z), branch cells (BC), and molecular weights (Mw) for [1,2-diaminoethane core]–PAMAM dendrimers as a function of generation. Approximate hydrodynamic diameters (Gen=0–7) based on gel electrophoretic comparison for the corresponding PAMAM dendrimers.*[21]

The bottom-up synthesis of dendrons/dendrimers provides one of the most precise and tunable strategies for constructing a systematic continuum of reproducible nanoscale structures. Size and structure control observed for dendron/dendrimer synthesis rivals that expected for proteins and DNA/RNA. In fact, dendrimers are often referred to as *artificial proteins*.[56, 122, 123] Based on the close mimicry of globular protein size scaling (Section 6.0; Figures 6.41 and 6.53) and their homogeneity, they are often used as protein replacements/substitutes in many nanomedicine applications.[123, 124]

Dendrimer mass and size uniformity has been exhaustively demonstrated by ESI/MALDI-TOF mass spectrometry,[120] gel electrophoresis,[121, 125] electron microscopy (TEM),[45] (Figure 4.13), atomic force microscopy (AFM)[81] and other methodologies, to mention a few. Within a specific dendrimer family, it is possible to produce a systematic, reproducible continuum of nano-sizes and precise masses as a function

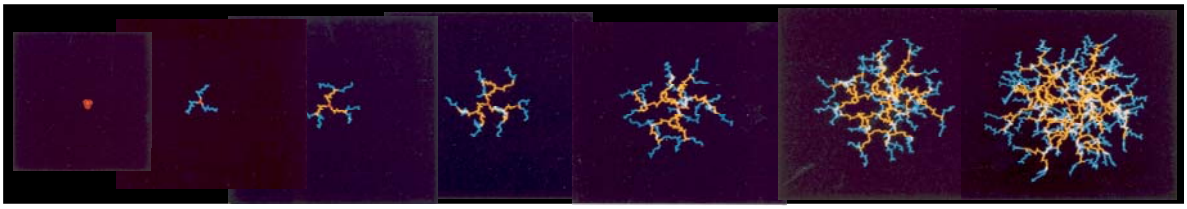


Figure 4.12. *Molecular simulations for [ammonia core]; poly(amidoamine) (PAMAM) dendrimers (GO-G5)and a generational comparison of hydrodynamic diameters.*

of generations. This is dramatically illustrated in Figure 4.9. 4.11 and 4.12. A similar continuum based on generational mass enhancements is shown in Figure 4.11. It should be noted, that dendrimer mass approximately doubles, generation to generation, with a remarkable uniformity of mass distribution over five generations exhibiting polydispersities ranging from 1.005-1.130 (Figure 4.19). These polydispersity values (PD) are substantially more narrow and uniform than values observed for common heavy elements such as Hg (PD=1.53) and Cd (PD=1.29) which are polydisperse due to naturally occurring isotopic mass distributions (Section 3.0; Figure 3.3).

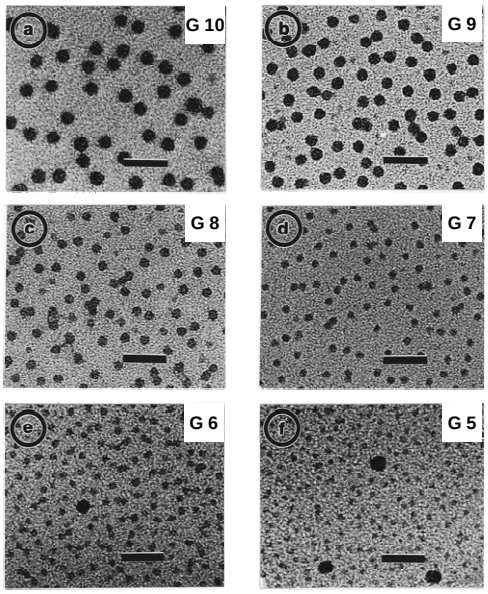


Figure 4.13. *Transmission electron micrographs (TEMs) of Gen 5–10 PAMAM dendrimers. Sample (f) contains three molecules of Gen 10 dendrimer for comparison. Bar length =50 nm.*[45]

4.2.5.2 Quantized Shapes (Dendron/Dendrimers)

Several parameters may be used to design and control dendron/dendrimer shapes. As described in Section 4.2.4.3, Figure 4.9, the multiplicity as well as the shape of the core can be selected to produce a desired shape (i.e., spheroidal, ellipsoidal, cylindrical, etc.). For example, 1-D cylindrical dendrimers are readily synthesized with shape control by dendronization or initiating dendron growth from multiple sites along the backbone of a linear polymer.[126] Iterative monomer additions to produce generational growth will then produce precise amplifications of these programmed shapes. The rigidity/flexibility of these shapes may be controlled and tuned by appropriate selection of branch cell monomer compositions and arm lengths (flexibility) (Figure 3.12.). These strategies were used extensively by Percec, et al. (Section 4.2.5.3) in the design and control of dendron shapes to produce a multitude of self-assembly motifs, as well as to demonstrate *quasi-equivalency* of dendrons in their mimicry of protein sub-units.

A second strategy can involve the combinatorial attachment of dendrons at their focal point sites as a function of generational size, interior composition (rigidity/flexibility), as well as their terminal functional groups as illustrated in Figure 4.14.[56]

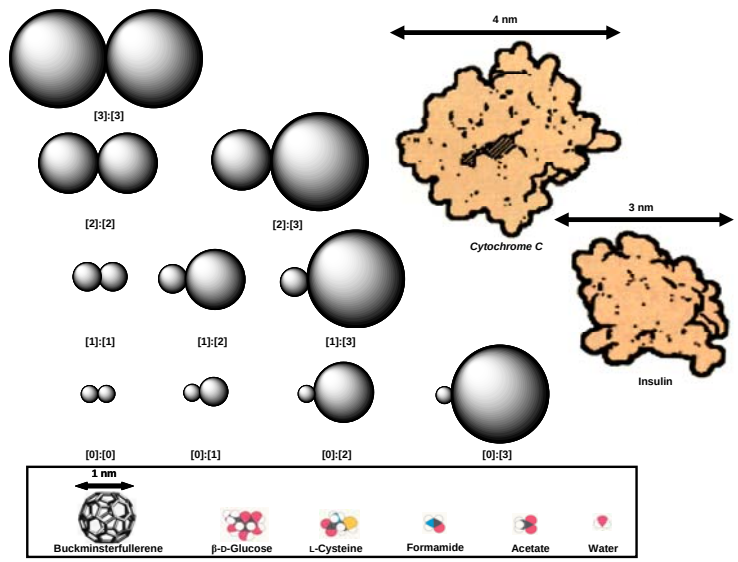
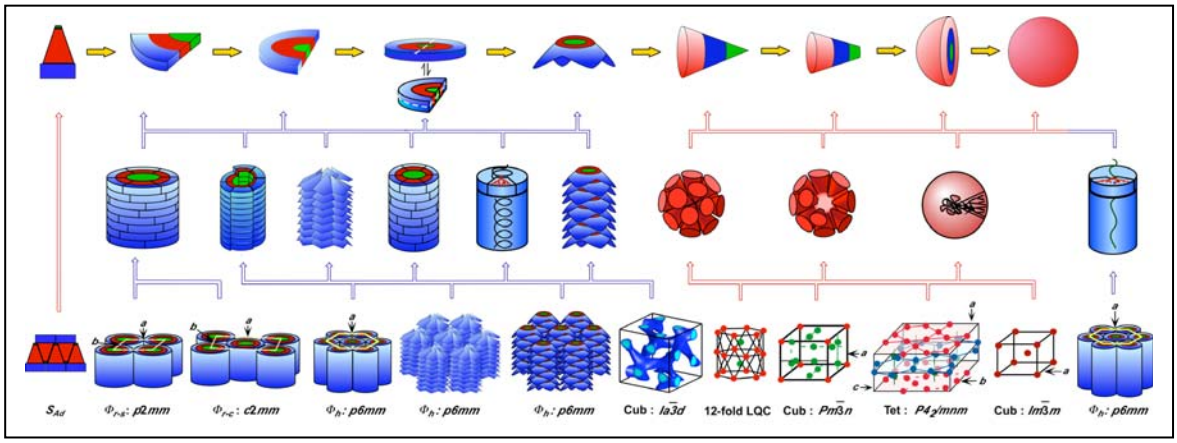


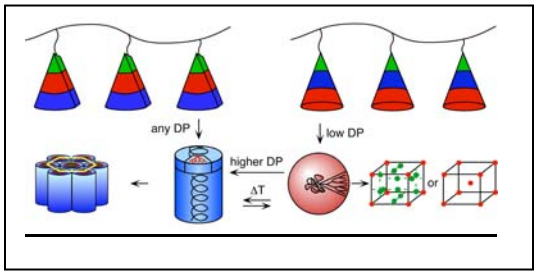
Figure 4.14. *Scaled space-filling models comparing small molecules (Corey–Pauling) to buckminsterfullerene and various [cystamine core]–PAMAM dendrimers (represented as spheres). Bold numbers in brackets indicate the generation level of the respective dendrimer hemi-ellipsoids. These size-scaled synthetic structures are compared to two globular proteins: insulin and cvtochrome C.*[56]

4.2.5.3 Designing Shape /Flexibility Aspects into Dendrons/Dendrimers

Percec, et al.[42 127] have pioneered the exploitation of two primary structural parameters; namely, the flexible and shape designing features of "soft nanomaterials" (i.e., dendrons/dendrimers). This work has led to a broad strategy for designing a wide array of self-assembling nano-systems based on anisotropically driven, periodic properties influenced by quantized shape changes in soft nano-matter such as dendrons (Figure 4.15).

The Percec group was the first to demonstrate the quasi-equivalence of dendron based, soft nanomaterials. Such quasi-equivalency features are widely observed in the self-assembly of sub-protein units to produce capsid coats that define the surfaces of viruses (i.e., soft nanomaterial category) (Section 6.2.5.2; Figure 6.46). Similar quasi-equivalency is observed for intermediates involved in the assembly of fullerenes (i.e., hard nanomaterial category) (Section 6.1.4.1; Figure 6.19).





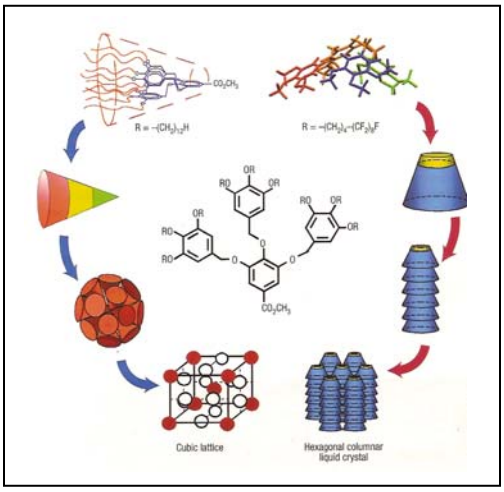


Figure 4.15. *A chain of structural consequences. From top to bottom, specific chemical structures lead to spatial conformations, to self-assembly and finally to self-organization into supramolecular architectures.*[31] *The basic dendron molecule used by Percec, et al. is shown in the middle. On the left, the non-fluorinated dendron with a conical shape leads to spherical assemblies that self-organize into a cubic lattice. On the right, the crown-like shape of the partly fluorinated dendron gives rise to columnar assemblies that self-organize into a hexagonal liquid-crystalline lattice.*[72]

4.3.5.4 Quantized Surface Chemistry

Over 1000 different surface reactions have been reported for dendrimers/dendrons. Essentially, all mechanistic reaction types (i.e., covalent, ionic, radical, etc.) have been reported. Several examples of these reactions are illustrated in Figure 4.16. Both sub-nanoscale, as well as nanoscale reagents (i.e., proposed nano-elements) has been used in these surface reactions. The surface valency and stoichiometry are mathematically quantified by relationships described in Figure 4.11 (i.e., $Z=N_cN_b^G$). Generally, these valencies and stoichiometric binding ratios are operational for all generations preceding serious de Gennes type dense packing congestion (Section 4.2.4.3 - general dendrimer features). Surface congested generations (i.e., > G=4 for poly(amidoamine) (PAMAM) dendrimers) usually exhibit lower than theoretical stoichiometries even with small sized reagents. Large sized reagents (i.e., >1 nm) may lead to

less than ideal stoichiometries even at low generations due to steric effects. These unique steric effects are referred to as *nanoscale sterically induced stoichiometries* (N-SIS).[128]

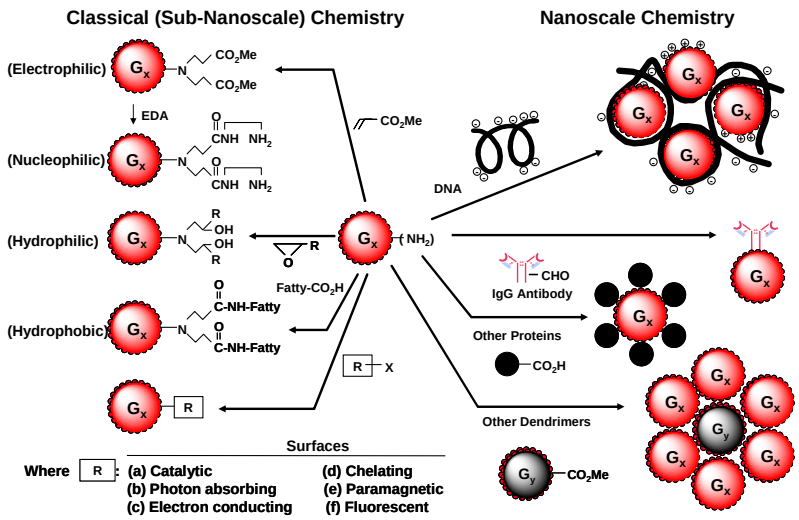


Figure 4.16. *Options for modifying amine-terminated dendrimer based nano scaffolding by utilizing classical subnanoscale and nanoscale reagents.*[21, 66]

4.2.6. Heuristic Atom Mimicry of Dendrimers: *Nano-Level Core-Shell Analogs of Atoms*

A comparison of the core–shell architecture for dendrimer-based nanoscale modules to the core–shell architecture of picoscale atoms was made as early as 1990.[39, 129] It is well recognized, that the electron orbital filling (i.e., aufbau sequencing) of atoms occurs according to discrete, well-defined principles of quantum mechanics. Electron filling of the discrete energy levels (i.e., principal quantum numbers; n = 1, 2, 3, 4) are widely recognized to follow very well-defined patterns leading to the saturated inert gas configurations (i.e., 2, 8, 8, 18, 32, etc.). Generally, the reactivity patterns observed in traditional synthetic chemistry are associated with the unsaturated electronic state of the atomic core-shell module that precedes the inert gas configurations in the respective periods. The noble gas configurations possessing saturated shells are inert and unreactive. It has been recognized since Wöhler (1828), that elements in the second period (carbon in particular) may combine with first-period elements (hydrogen), second period elements (oxygen, nitrogen, boron) and third-period elements (sulfur, silicon, etc.) to produce nearly all the compounds we classify today as organic structures. Essentially, all other combinations are referred to as inorganic. Approximately 50 years after Mendeleev published his traditional periodic table of the elements (1869), Niels Bohr introduced a non-traditional organization of the elements using a unique periodic table presentation in his Nobel lecture of 1922[130] as illustrated in Figure 4.17.

4.2.6.1 Picoscale Bohr Periodic Table Periodic Patterns Related to Reactivity

Coincidentally, in the same year, F. Aston was awarded a Nobel Prize for his invention of the mass spectrometer and his proof that the elements were precise bundles of mass that could be systematically organized and understood relative to both Mendeleev's and Bohr's periodic presentations. Bohr's representation provides the familiar electron configuration accounting system, as well as a facile visualization of several important periodic and quantized features associated with atoms (Figure 4.17).[21, 56] Bohr's unique periodic table displays the quantized electron space-filling features of atoms as a

function of their atomic number and electron shell level. This clearly illustrates the systematic electron-filling rank of the respective, reactive elements possessing unfilled electron shells in each period. Moving to the end of each period leads to the saturated shell elements (i.e., noble gas configurations). Bohr's periodic table offers a visual appreciation of atomic module reactivity as a function of electron-shell saturation and allows a very crude, but relative size comparison of the respective elements (atoms) in the picoscale and sub-nanoscale region (i.e., 0.01–1 nm).

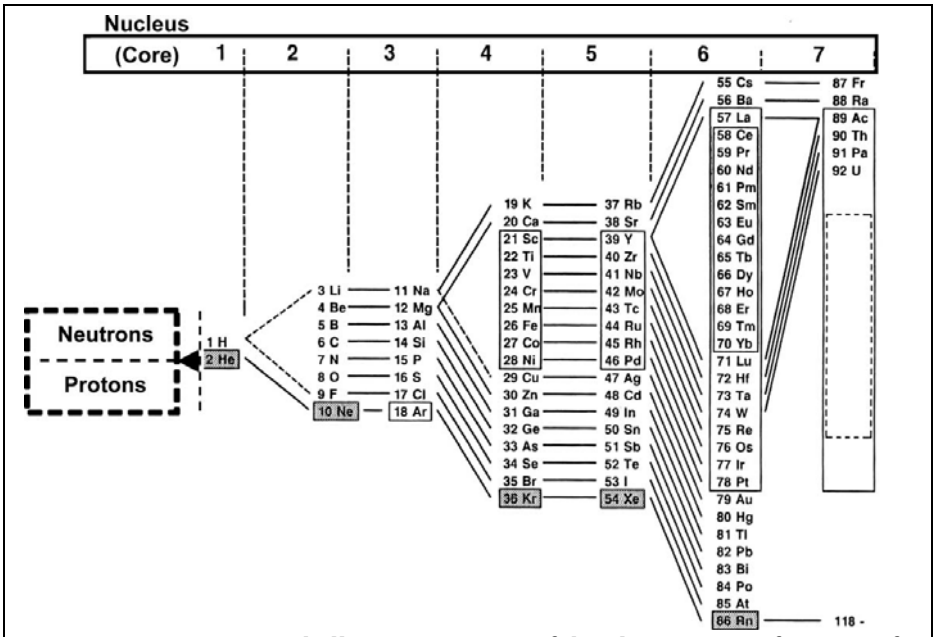


Figure 4.17. *Core–shell representation of the elements as a function of principal quantum numbers (n=107) (electron shells) according to Niels Bohr (1922).*[6]

It was from Bohr's periodic presentation of the elements that we were inspired to produce an analogous two-dimensional molecular display of the quantized, monomer-shell-filling features of dendrimers.[21] It was hoped that such a presentation would allow a crude, but nevertheless, heuristic comparison of module size/reactivity analogies that prevail in both the picoscale and the nanoscale regions (Figure 4.17 and 4.18, respectively). The mass spectrograph insert in Figure 4.18 illustrates a display of masses observed for a sample of generation=3, (PAMAM) poly(amidoamine) dendrimer described with greater detail in Figure 4.19. It should be noted that a total number of 45 monomer units is required to produce an ideal dendrimer with a saturated generation=3 monomer shell. The experimental mass expected for such a saturated species is 5154 daltons. Figure 4.18 clearly demonstrates that the appropriate theoretical mass of 5154 daltons for a saturated shell species is present, as well as several unsaturated dendrimer shell species: DP=44 (MWt.= 5040); DP=43 (MWt.= 4925) and DP=42; (MWt.= 4812). It is noteworthy that the dendrimer, saturated shell species, DP=45 (MWt.= 5154), behaves much like a saturated shell noble gas configuration normally observed for atoms. Quite remarkably, it has been shown experimentally that this species is robust and *not auto-reactive*;[38] whereas, the unsaturated species, DP=44, 43 and 42 are *auto-reactive*.[32] ***Clearly such dendrimer reactivity properties appear to be mimicking atoms.***

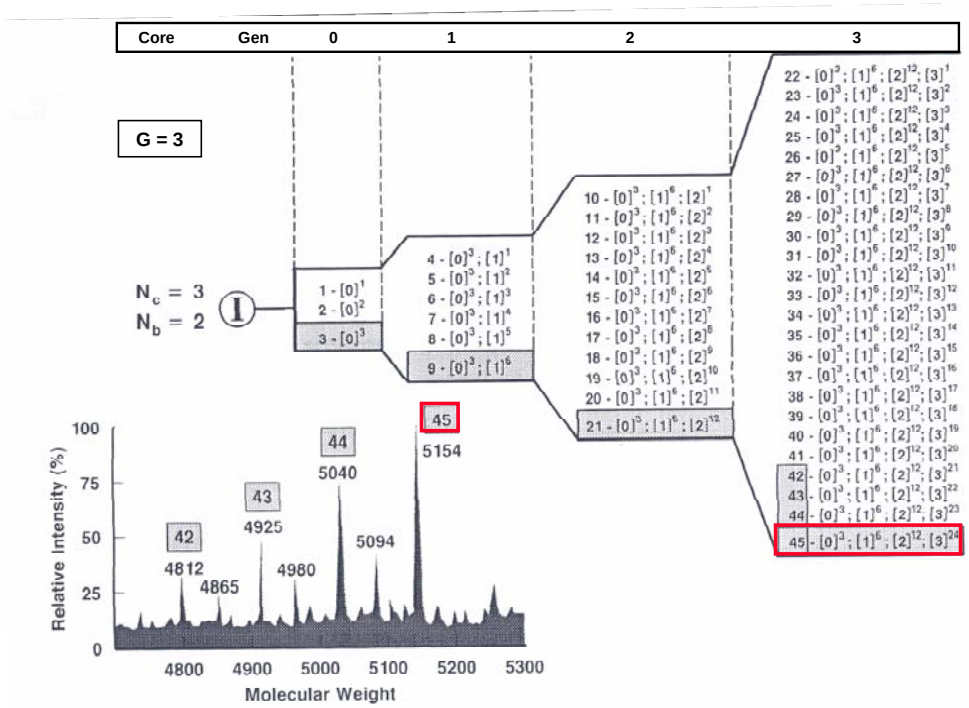
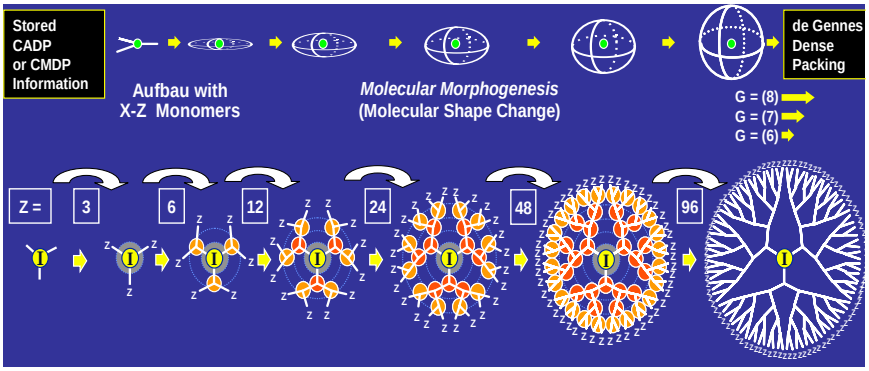


Figure 4.18. *Core–shell (Niels Bohr type representation) of [ammonia core]–dendri-PAMAM dendrimer (Gen.= 3); -$(NH_2)_{24}$ as a function of principal monomer shell levels (generations). Mass spectrometry data illustrating mass corresponding to a non-autoreactive saturated-shell structure (i.e. DP=45; MWt.=5154) (red box) accompanied by autroreactive unsaturated-shell structures (DP=44, 43, and 42; MWt's.=5040, 4295, 4812, respectively).*[21, 66]



Generations	0	1	2	3	4	5
Surface Groups (Z)	3	6	12	24	48	96
Total # of Aufbau Monomers	3	9	21	45	93	189
MW	359	1044	2414	5154	10632	21591
M_w/M_n	1.005	1.011	1.036	1.07	1.113	1.131

Figure 4.19. *A comparison of surface groups (Z), total number of aufbau monomers (DP), molecular weights (MW) and polydispersities (PD=Mw/Mn) as a function of generation for an [ammonia core]; poly(amidoamine) (PAMAM) dendrimer series.*

4.2.6.2 Atom Mimicry of Inert Noble Gas Configurations at the Nanoscale Level-Nanoscale Periodic Table

By analogy to electron-saturation levels found in elemental atoms, dendrimers possessing unfilled monomer shells are very reactive at the molecular level *via* their terminal functional groups. *They have been demonstrated to auto-react by interdendrimer surface reactions to form covalently linked dendrimer multiples (i.e., dimers, trimers, etc.) or* ***in essence, nanoscale compounds****. These dendrimeric oligomers are called* ***megamers.*** Alternatively, they may simply undergo intramolecular reactions to produce macrocyclic sites.[118-120] *In sharp contrast, dendrimer species possessing saturated monomer shells, mathematically defined by* $Z = N_c N_b^G$ (Figure 4.11) *are not autoreactive* nor do they react with reagents possessing a compatible surface functionality (i.e., either nucleophilic or electrophilic moieties, respectively). A similar reactivity pattern was also observed in the larger core-shell tecto(dendrimer) series as illustrated in Figure 4.19[21, 32, 38] and will be described later (Section 7.5.1.).

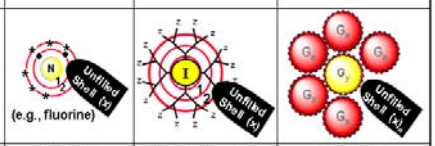
	Atoms	Dendrimers	Core-Shell Tecto(dendrimers)
Dimensions	0.5-0.6 nm	1-15 nm	5.0 ≥ 100 nm
Valency (Reactivity)	Unfilled Outer Electron Shells	Unfilled Outer Branch Cell Shells	Unfilled Outside Dendrimer Shells
Architecture Induced Reactivity (Unfilled Shells)			
Functional Components Directing Valency	Missing Electron (x)	Missing Terminal Branch Cell Functionality Exposed (x)	Missing Dendrimer Shell Reagent Exposed (x)

Figure 4.19. *Quantized module (building block) reactivity patterns at the subnanoscale (atoms), lower nanoscale (dendrimers), and higher nanoscale (core–shell tecto(dendrimers)) levels involving unsaturated electron, monomer or dendrimer shells.*

4.2.6.3 A Proposed Dendrimer-Based Nanoscale Periodic Table

It is noteworthy, that reactivity patterns/properties as observed with unsaturated electron shells (i.e., atoms) are also observed when compared to analogous unsaturated monomer shells in dendrimers. On the other hand, robust, non-reactivity patterns associated with noble gas configurations in atoms is also observed with dendrimers. As such, it was compelling to model a proposed dendrimer periodic table after the traditional Mendeleev table as shown in Figure 4.20. As illustrated, the generational monomer aufau as a function of shell level is compared to the respective horizontal electron shells in the atom-based periodic table.[58, 59]

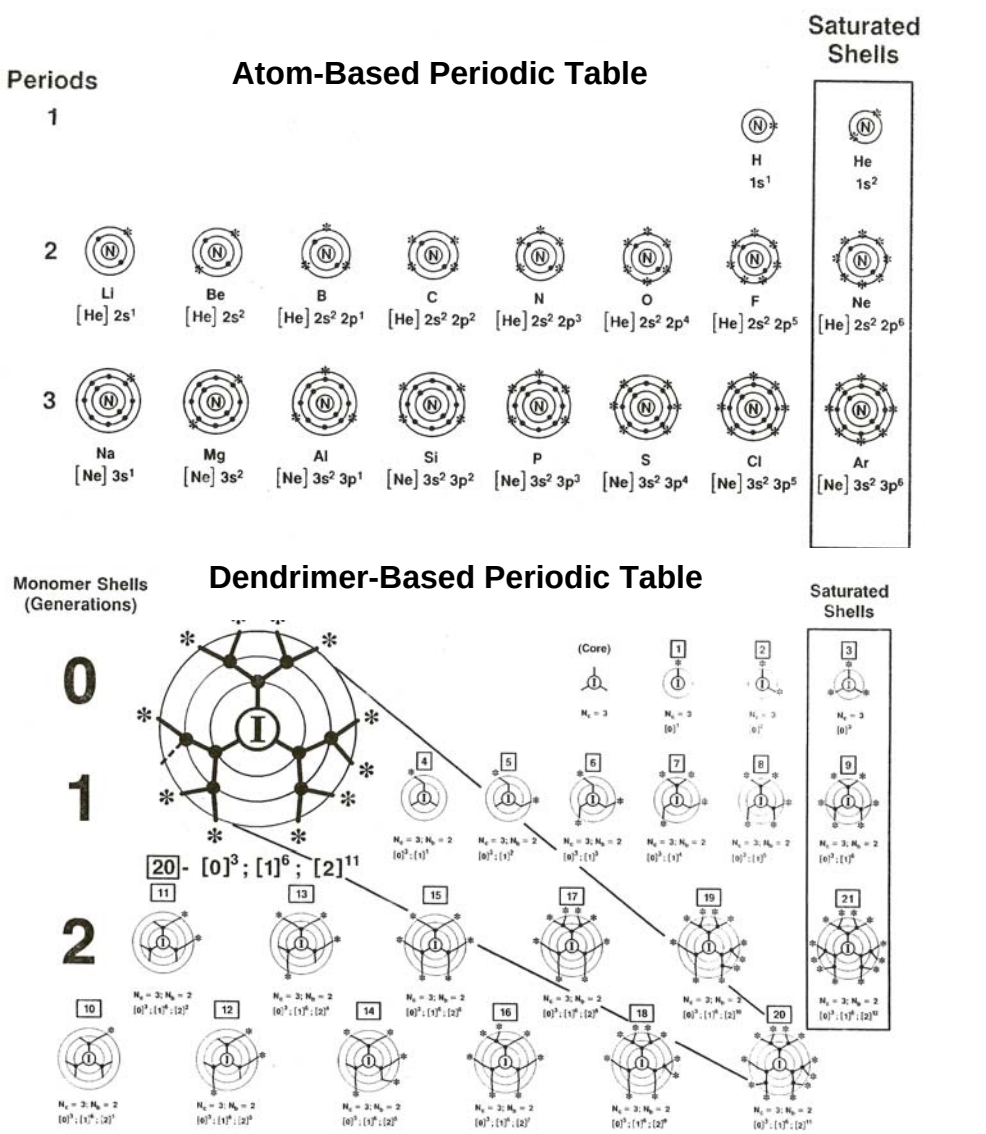


Figure 4.20. *A comparison of atom and dendrimer based periodic tables.*[58, 59]

5.0 A Proposed Nanomaterials Classification Roadmap

A proposed classification and categorization roadmap for all nano-matter is described in this section. This classification exercise was based on the following considerations:

- Consider all substances that possess at least one dimension residing in the nanoscale definition range of 1-100 nm as nanomaterials.
- Based on atom size scaling, these materials will be molecular level compounds, clusters, assemblies, etc. containing from 10^3 to 10^9 atoms and exhibit molecular weights ranging from 10^4 to 10^{10} Daltons.
- These nanomaterials are then divided into two major categories based on homogeneity/uniformity as a function of: (a) composition, (b) size, (c) shape and (c) mass, namely;
- **Category (1): Well Defined Nano-Modules:** those materials must be available in > 90% homogeneous form as a function of composition, size, shape and mass distribution. ***This > 90% monodispersity level is imposed based on the module monodispersity level that was required in order to observe nano-super lattice crystallinity as reported by Mirkin, et al.***[65]
- *****We will consider only this group of nanomaterials in this report*.**
- **Category (2)**: **Undefined, Statistically Polydispersed;** those materials are available only in polydisperse form as a function of composition, size, shape and mass.
- Since all homogeneous nano-compositions (i.e., elemental and molecular level) are derived from the periodic table, the first classification was based on the traditional horizontal periodic elemental features associated with (a) metals, (b) semi-metals and (c) non-metals.
- Placed in the context of contemporary "band gap theory", which provides criteria for separating nanomaterials according to outer shell electron mobility, allows one to further classify into the categories of (a) conductors, (b) semi-conductors and (c) insulators.
- Next, these three categories appeared to embrace two major descriptive features, namely: (a) *conducting/semi-conducting materials*. Such materials are usually associated with more rigid, lattice like, inflexible, metallic/ inorganic type structures/assemblies. As such, they are referred to as ***hard nano-matter.*** In contrast, a second category, (b) consists of *insulator-type* nanomaterials and are associated with covalent, organic like structures/assemblies and thus referred to as ***soft nano-matter***.
- Based on "atom mimicry" criteria described earlier, selected ***nano-element*** categories are proposed for both hard and soft nanomaterial classifications. These candidates were selected based on features such as core-shell architectures that exhibited nanoscale structure control properties. Specifically, such *critical nanoscale design parameters (CNDPs)* included well-defined: (a) sizes (b) shapes and (c) surface chemistries and (d) flexibility.
- Subsequently, these CNDP features had to be articulated within each category to such a level that they fulfilled a proposed criteria for "nano-elements" (Sections 5.1 and 5.2). Furthermore these candidates had to behave as chemically reactive/functional entities exhibiting well defined, reproducible stoichiometries and combining ratios/masses to yield products that fulfilled the criteria for ***nano-compounds*** as described in Section 7.2 of this report.
- Finally, well documented literature examples describing these features as well as associated **nano-periodic property patterns** were sought to provide additional scientific evidence for these proposed nano-elements, nano-compounds and nano-periodic function. These key features are suggested to underpin the "central dogma" for this proposed ***nano-chemistry hypothesis*** (Section 8.0) and provide additional rationale for this proposed **Nanomaterials Roadmap**.

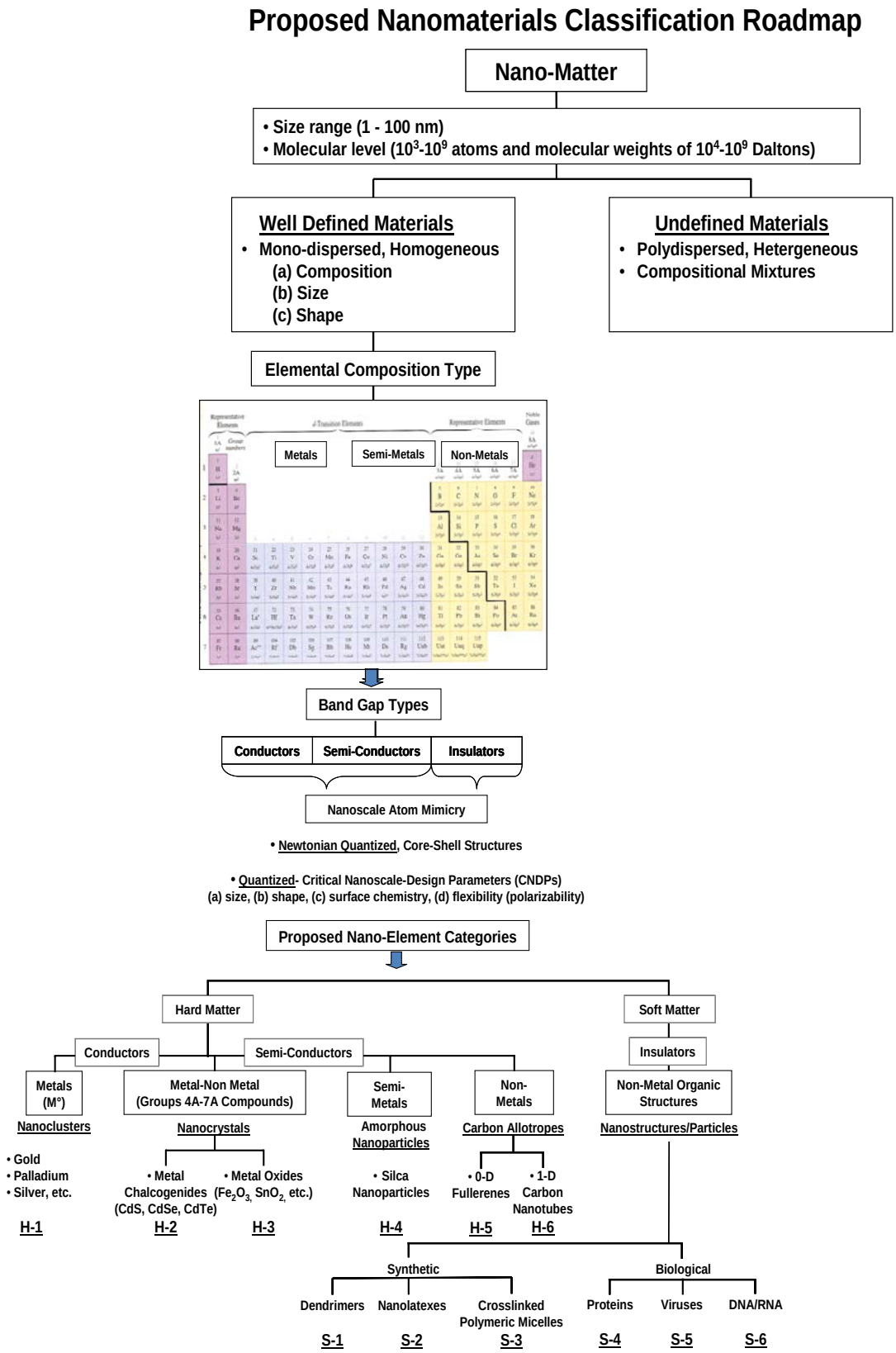


Figure 5.0. *Proposed nanomaterials classification roadmap.*

5.1 Proposed Nanomaterial Categories for Consideration as Well Defined Nano-Building Blocks (i.e., Nano-Element Categories).

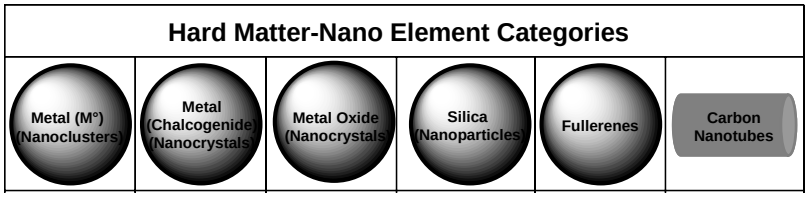


Figure 5.1. *Proposed hard matter: 0-D and 1-D nano-elements.*

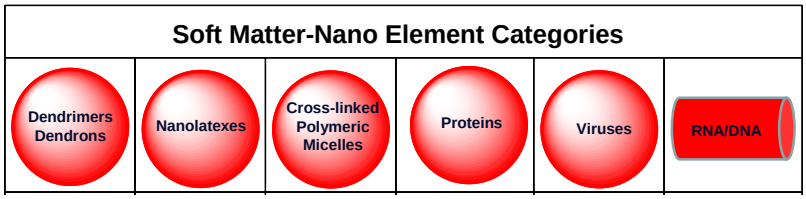


Figure 5.2. *Proposed soft matter: 0-D and 1-D nano-elements.*

5.2 Criteria for Defining Nano-Elements

5.2.1 Profile of an Ideal Nano-Element:

(1) Nanoscale objects with any elemental composition that possesses at least one nanoscale dimension (i.e., 1-100 nm) and exhibit multiple reproducible *atom mimicry* features at the nanoscale level. Most notable, are features such as 0-D/1-D core-shell type architectures that may be "structure controlled" (Newtonian quantized) as a functions of *(a) size, (b) shape, (c) surface chemistry, (d) topology and (e) flexibility.* Such entities would be expected to exhibit nano-periodic patterns (i.e., a systematic size continuum), nano behavior patterns (i.e., reactivity/self-assembly profiles, anisotropy, physical properties, etc.) derived from discrete interactive relationships of the core with interior shell components and most importantly with the surface shell component. The surface shell may be passive or reactive. If reactive, it should exhibit well defined valency (i.e., reactive nano-elements) and stoichiometries. If passive or non-reactive (i.e., inert nano-elements), they may possess surface features that are suitable for non-bonding, self-assembly or aggregation. Reactive features of the surface shell may involve electron active moieties such as: reactive chemical functionality, reactive atoms, etc.) or non-bonding, interactive self-assembly type moieties such as: hydrogen bonding, dipolar, ionic, hydrophobic/hydrophilic or shape selective functions.

(2) Homogeneous 0-D or 1-D nanoscale objects, that by definition, are molecular level entities and consist of 10^3 - 10^9 atoms with molecular weights of 10^4 – 10^{10} da. They are monodisperse as a function of size and/or mass (molecular weight). A ***monodispersity level of > 90% is imposed based on the module monodispersity level that was required in order to observe nano-super lattice crystallinity as reported by Mirkin, et al.***[65] Alternatively, mass polydispersities should not exceed values observed for isotopic distributions observed for traditional heavier picoscale elements (i.e., Hg=1.50, Cd=1.29).[2] In the case of 1-D nanostructures, it is desirable for both the cross sectional diameters, as well as the lengths to be homogeneous and monodisperse.

(3) A nano-element should be appropriately robust to be reproducibly characterized as a function of: (a) composition, (b) size, (c) mass (c) shape or (c) surface functionality using traditional analytical methodologies such as: compositional elemental analysis, mass spectroscopy, chromatography, electrophoresis, TEM, AFM, X-ray crystallography, etc.

(4) Reactive nano-elements will exhibit reproducible, well defined stoichiometries and mass combining ratios in chemical reactions or /self-assembly events involving traditional pico/sub-nanoscale reagents and/or other nanoscale elements.

(5) The “aufbau” components for the construction of nano-elements may be individual atoms or discrete clusters (groups) of atoms, inorganic compounds (i.e., metal salts) or organic compounds (i.e., linear/branched monomers, oligomers or polymers, polypeptides, polynucleotides). Usually aufbau construction approaches for nano-elements, will require unique templating/quantizing strategies (i.e., micellar compartments, divergent/convergent-dendritic branching rules, designed self-assembly, etc.) as critical precursor steps/intermediates in order to attain precise control of sizes, shapes and surface chemistries.

6.0 Brief Overview of Synthesis and Key Features of Proposed Nano-Element Categories

This objective of this section is to provide a brief overview of key features and leading references to synthetic routes for proposed hard and soft nano-element categories. In some instances, selected *nano-periodic property patterns* are included in an effort to illustrate those features of these proposed nano-elements that appear to be reminiscent of traditional picoscale elements.

6.1 Hard Matter: Proposed 0-D and 1-D Nano Element Categories

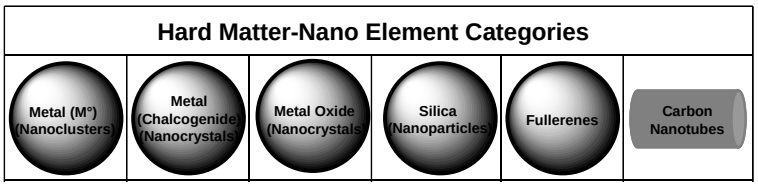


Figure 6.0. *Proposed 0-D and 1-D nano-element categories.*

6.1.2 Metals

6.1.2.1 Metal (M^o) Nanoclusters

At least four major synthetic strategies are commonly used for the construction of zero valent metal nano-clusters, namely: (1) metal reductions in inverse micelles (non-polar solvents), (2) reduction of metal salts encapsulated within dendrimers (i.e., covalently fixed micelles), (3) metal reductions in the presence of stabilizers (polar solvents) and (4) thermal decomposition of organo-metallics in the presence of stabilizers. Ligand exchange reactions can often be performed on surfactant stabilized/protected metal nano-clusters to introduce a wide variety of surface reactive chemical functionality.[22] An extensive review of these issues and this nanomaterial category has been reported recently.[37] Although these nanoclusters are treated as 0-D particles in our classification, the subtle 3-D features of these metal nanoclusters are still controversial and the subject of extensive research by physicists.[131]

(1) *Metal Reductions within an Inverse Micelle (Non-polar Media)*

The key feature of this method is that the metal cluster growth is controlled by the nano-heterogeneous environment of the nano-droplet-like inverse micelles. This approach has been intensively investigated[16, 132-135] and is especially popular since the metal atom source may be derived from simple salts. Most metal salts are used at such a low concentration that approximately 1-4 precursor ions are available per micelle. As a result, cluster growth to the final observed sizes (i.e., 10-10,000 atoms) is controlled *via* micellar diffusion, micelle collision, temporary interface fusion and atom interchange. As a consequence, thermodynamically favored cluster structures with narrow size dispersion are usually obtained. Generally, cationic surfactants (i.e., tetraoctylammonium bromide, (TOAB)) in concert with either strong reducing agents (i.e., $LiBH_4$, $LiAlH_4$) or weak reducing agents (i.e., $NaBH_4$) are used in non-polar solvents such as THF or toluene. Although weak reducing agents may be used for synthesizing Au or Ag nanoclusters, one may have to resort to stronger agents for the reduction of Pt, Pd, Fe, Ni, Co, Si, or Ge salts (Figs. 6.1-6.2).

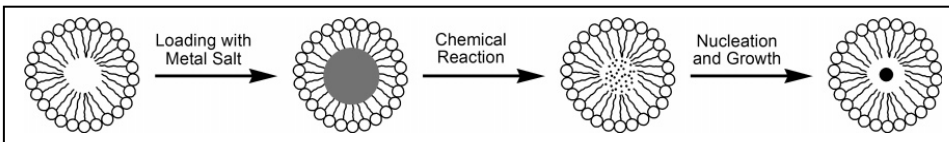


Figure 6.1. *Steps involved in the preparation of a metal nanoparticle inside a classical micelle.*[27]

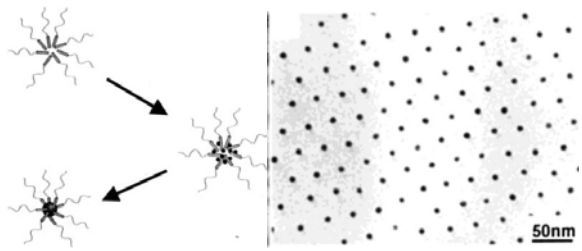


Figure 6.2. *(a) Formation of nanoparticles in a block copolymer micelle: 1) micelle formation; 2) loading with precursor; 3) reduction to form a single gold particle. (b) TEM of gold particles with a diameter of 9 nm in each block copolymer micelle.*

(2) *Reduction of Metal Salts Encapsulated within Dendrimers (i.e., covalently fixed regular micelles).*

Dendrimers have been recognized as *covalently fixed mimics* of classical regular/inverse micelles[14, 136] and as such, have been utilized for that purpose in a variety of ways.[137] Most notable, has been their use as nano-reactors for encapsulating a wide variety of metal salts either in water or in non-polar solvents (i.e., toluene). Subsequent reduction of these templated metal salts with a variety of reducing agents (i.e., ascorbic acid, sodium borohydride) has been shown to be a versatile and effective strategy for producing zero valent metal nano-clusters as shown in Figure 6.3.[14]

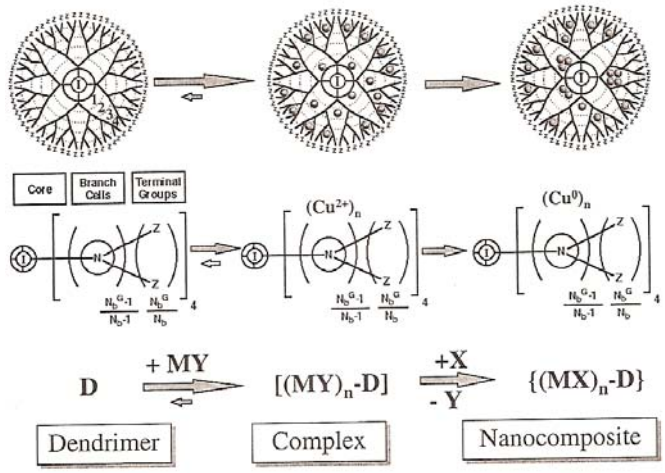


Figure 6.3. *Construction of dendrimer-metal nanocomposites.*[14]

(3*) Metal Reductions in the Presence of Stabilizers (Polar Media):*

The synthesis of ligand stabilized metal nanoparticles using aqueous alcohol reduction of a metal salt was first reported by Hirai, et al.[138] This method produces metal cluster formation by chemical reduction of an organic soluble metal salt precursor in the presence of a polymer stabilizer (i.e., usually poly(vinyl alcohol) (PVA) or poly(vinylpyrolidone) (PVP)). It is interesting to note, the PVP is widely used as the ligand stabilizer in many of the reported examples. It is presumed, that the metal surfaces readily ligate with both the adjacent nitrogen and oxygen functionality of the polymer to provide superior steric stabilization against aggregation. This approach is best described by Schmid[99] and is exemplified as a preferred method for producing Au_{55} nanoclusters as shown below in Figure 6.4.

This category of nano-elements exhibits many examples of atom mimicry, as well as widely documented nano-periodic patterns. For example, so called *full-shell magic number clusters* clearly illustrate core-shell structures derived from metal atoms. These shells are similar to dendrimer monomer shells and clearly mimic electron shells in atom scale elements. These shells are clearly quantized and represent very high percentages of the surface atoms in the smaller nanoclusters as shown in Figure 6.4. 6.5 and 6.6.

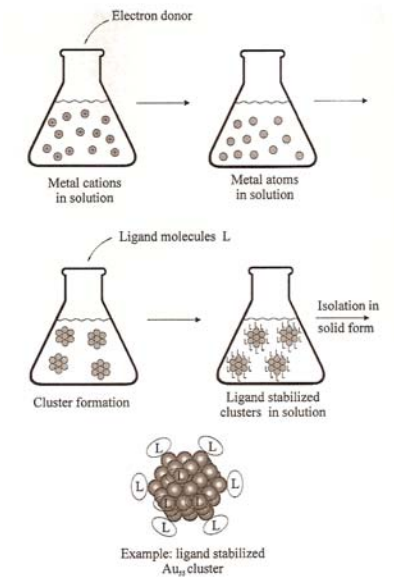


Figure 6.4. *Schematic procedure for metal cluster synthesis.*[1]

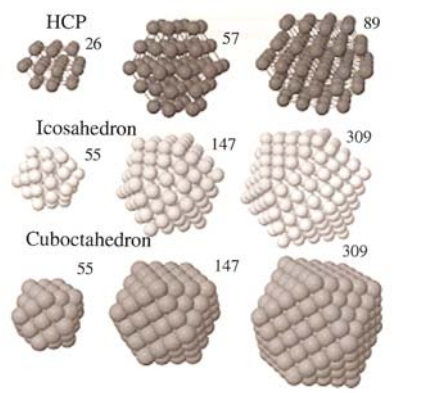
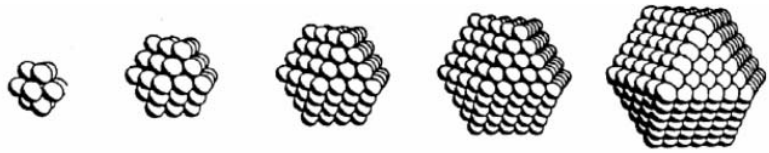


Figure 6.5. *Atomic configurations and magic numbers for several representative clusters.*[10]



Full-Shell "Magic Number" Clusters					
Number of shells	1	2	3	4	5
Number of atoms in cluster	M_{13}	M_{55}	M_{147}	M_{309}	M_{561}
Percentage surface atoms	92%	76%	63%	52%	45%

Figure 6.6. *Full-shell magic number formation showing how the number of shells relate to the number of atoms in a cluster and the percent of atoms present on the surface.*[16]

Work by Stellaci, et al.[139-141] has shown that one can introduce anisotropic, divalent chemical reactivity into certain M^o nanocrystals based on their unique surface features. More recently Greiner, et al.[22] have reported a clever strategy for functionalizing gold nano-clusters to provide monovalent clusters.[22]

A unique nano-periodic property pattern reminiscent of atomic elements is the size dependent relationship exhibited by metal nano-clusters relative to their melting points (see Section 8.3.1; Figures 6.7, 8.0 and 8.1.). Many of these issues have been extensively reviewed elsewhere.[7, 16, 99]

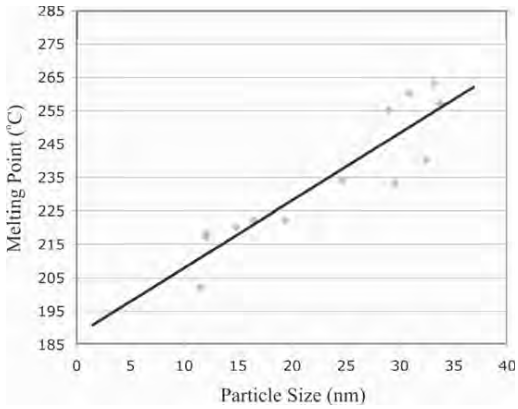


Figure 6.7. *Illustrating periodic increase in Mp vs. nanoscale size.*

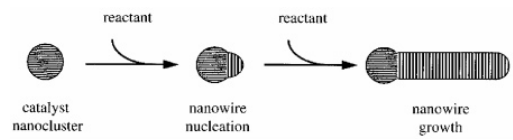


Figure 6.8. *Schematic diagram illustrating the catalytic synthesis of nanowires. Reactant material, which is preferentially absorbed on the catalyst cluster, is added to the growing nanowire at the catalyst-nanowire interface.*[37]

6.1.2.2 One Dimensional (1-D) Metal Nanoclusters (Wires)

Nanowire growth/propagation to produce 1-D hard matter-nanostructures is analogous to the traditional polymerization of organic monomers from a catalytic initiation site to produce classical 1-D soft nano-matter linear-polymers (Figure 6.8). In the case of 1-D metal nanowires, the respective metal atoms used for the 1-D nano-constructions are viewed as monomers. The resulting 1-D structures generally possess homogeneous nanoscale diameters, however, they may have polydispersed lengths (aspect ratios) which may be controlled to some extent by process methodology and reactant concentrations (Section 6.1.2) .[28, 37] Other established strategies to these 1-D structures are as illustrated in Figure 6.9.[9]

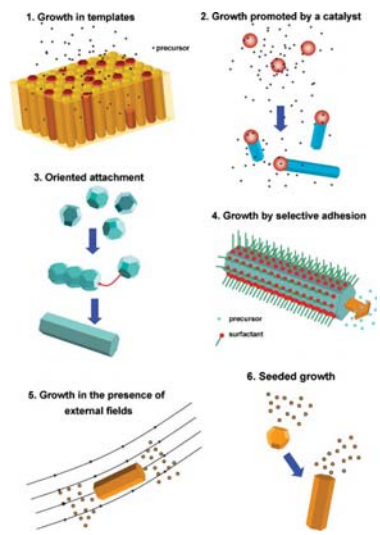


Figure 6.9. *Established approaches to grow NCs with anisotropic shapes.*[9]

6.1.3 Metal (Group 8-10 Transition Metal)-Non Metal (Group 6A) Structured Nanocrystals

6.1.3.1 Metal-Ligand Nanocrystals

A number of larger core-shell type palladium and platinum clusters stabilized by N/O-ligation were reported as early as the mid 1980s by Moiseev, et al.[142] and Schmid, et al.[99] These "full" *n*-shell, core-shell structures involved normal vertex-(edge-shared) shell growth with the total number of atoms in a complete n^{th} shell being ($10\,n^2 + 2$). Core-shell nanostructures possessing four shell (i.e., Pt_{309}),[143] five shell (i.e., Pd_{561}),[142] seven shell (i.e., Pd_{1451})[144] and eight shell (i.e., Pd_{2057})[144] architectures have been

isolated as giant sized nanoclusters. Although they have not been isolated in single-crystal form suitable for x-ray crystallographic studies, they have been characterized by indirect methods including TEM, SAXS, EXAFS, ED, HREM and elemental analysis. All of these nanoclusters contain anionic ligands at their surfaces, suggesting the metal surface layer may be partially oxidized. The five shell Pd_{561} cluster was shown to perform under mild conditions as a catalyst in oxidation, redox disproportionation and in chain termination reactions.[74, 99] Since that time, a wide variety of nano-sized palladium carbonyl/ phosphine clusters (i.e., possessing at least 18 distinctly different Pd_n core-geometries) have been isolated and characterized.[145]

Very recently, Mednikov/Dahl, et al.[74] have reported the synthesis, isolation and complete structural characterization of Pt-centered, four-shell 165 atom Pd-Pt nanoclusters as shown below (Figure 6.10). These nanoscale core-shell type structures truly fulfill the *well defined* nanoscale-atom mimicry criterion with mathematically defined core and shell components that can be unambiguously characterized both spectroscopically and crystallographically.

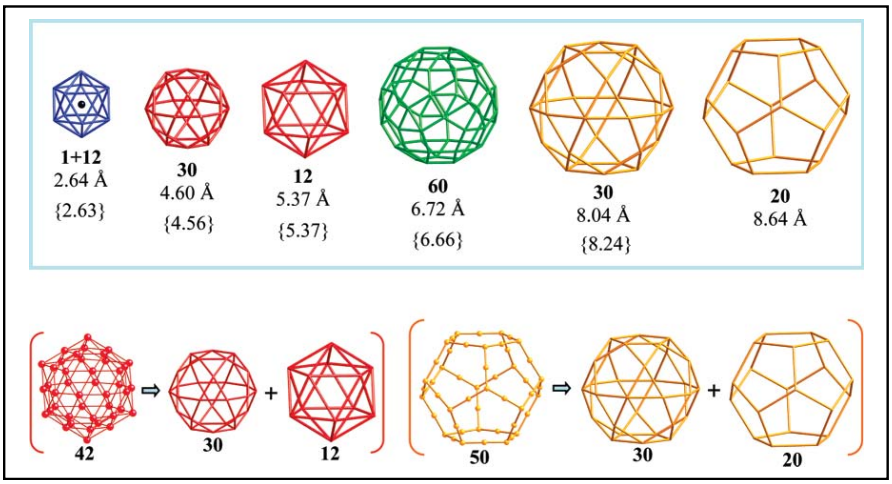
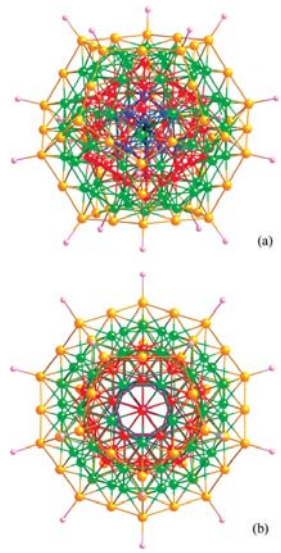


Figure 6.10. *Complementary Pt-centered six-shell successive polyhedral description of (μ_{12}-Pt)M_{164} core-geometry of **1** having only equivalent Vertex atoms under pseudo-icosahedral I_h symmetry:*
*Pt@M_{12}(icosahedron)@M_{30}(icosidodecahedron)@M_{12}(icosahedron)@M_{60}(rhombicosidodecahedron)@M_{30}(icosidodecahedron)@ M_{20}(pentagonal dodecahedron). Six successive concentric Platonic/Archimedean polyhedra encapsulate the central Pt atom. Radial shell distances between the central Pt atom and equivalent vertices are given below the number of atoms in each shell. Corresponding radial shell distances for **2** are given in brackets. An Archimedean M30 icosidodecahedron (3.5.3.5) is generated via midpoint truncation of either an icosahedron (35) or pentagonal dodecahedron (5^3); consequently, a v_2 M_{42}(icosahedron) is transformed into M_{30}(icosidodecahedron) + M_{12}(icosahedron), and likewise a î2 M_{50}(pentagonal dodecahedron) is transformed into M_{30}(icosidodecahedron) + M_{20}(pentagonal dodecahedron).*[9, 74]

Side/top views of (μ12-Pt)$Pd_{164-x}Pt_x(CO)_{72}P_{20}$ fragment in Ptcentered four-shell 165-atom Pd-Pt cluster, (μ12-Pt)$Pd_{164-x}Pt_x(CO)_{72}(PPh_3)$20 ($x \approx 7$), of pseudo icosahedral I_h (2/m35) and cubic crystallographic T_h(2/m3) site symmetry. (a) Side view showing four-shell geometry; (b) top view along one of six noncrystallographic 5(S_{10}) icosahedral axes passing through central (μ_{12}-Pt) atom, two centrosymmetrically opposite Pd(Pt) atoms in both shells 1 and 2, and midpoints of two centrosymmetrically opposite pairs of 12 pentagons within each shell 1, 2, 3, and 4.[74]



6.1.3.2 Metal Chalcogenide Nanocrystals

The self assembly of metal chalcogenides (i.e., S, Se, Te) into monodisperse 0-D nanocrystals was pioneered by Steigerwald/Brus, et al. as early as 1988.[133, 146] They developed methodologies for nanocluster nucleation, growth and stabilization by capping with various organic ligands, surfactants and polymers. Especially significant, was their use of reverse micelles in the presence of organic thiolates. This work set the stage for seminal work by Alivisatos/Bawendi;[147] wherein, they developed controlled nucleation and growth conditions for producing mono-disperse Zn and Cd chalcogenides nanoclusters in the presence of phosphine oxide surfactants; wherein, these agents functioned as both a solvent and capping agent. Modifications of their original methodologies allowed fractionations into extremely narrow, mono-disperse size distributions that clearly demonstrated the ability to size tune these semi-conducting nanocrystals. These entities are referred to as quantum dots (QDs) and are widely recognized for exhibiting size-dependent light emission properties that are used for a wide range of *in vitro* biological applications. Note these nanostructures exhibit experimentally well documented nano-periodic property patterns (Section 8.3.1; Figure 8.2).

Considerable progress concerning the control of nanoscale shapes, utilizing process control strategies (i.e., monomer concentrations) associated with sized nuclei have been reported as shown in Figure 6.11.[28, 37, 148, 149]

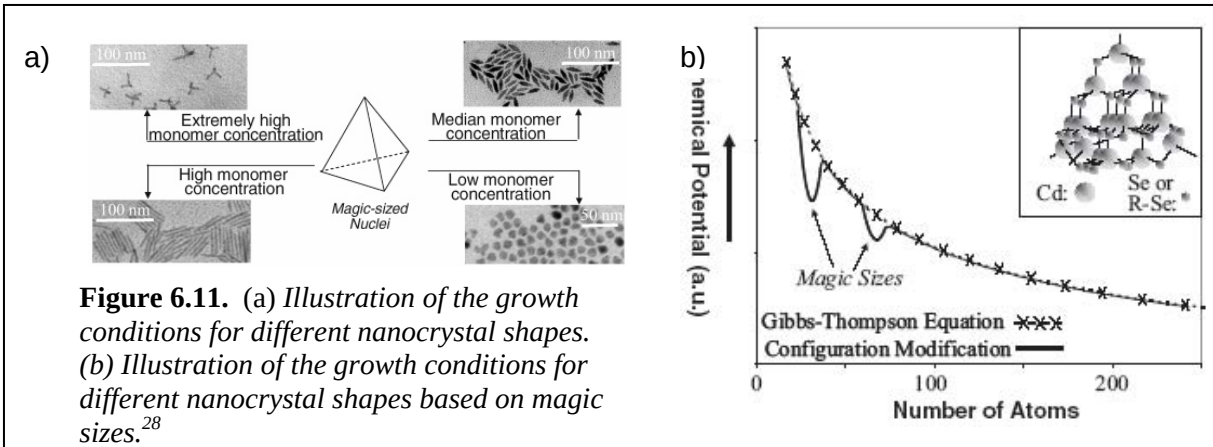


Figure 6.11. (a) *Illustration of the growth conditions for different nanocrystal shapes. (b) Illustration of the growth conditions for different nanocrystal shapes based on magic sizes.*[28]

Very recently, Anson et al.,[75] have reported the synthesis of small nano-sized silver chalcogenides as illustrated in Figure 6.12. It should be noted, that this nano-element category was extensively characterized by MALDI-TOF mass spectrometry.

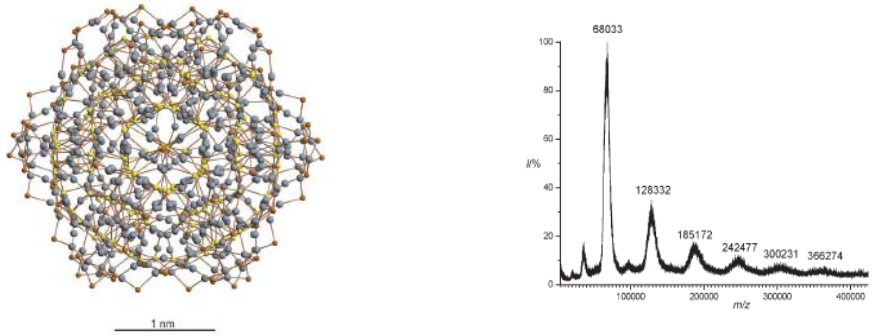


Figure 6.12. *Silver chalcogenide nanostructures reported by Anson, et al.*[75] *MALDI-TOF spectrum of (a).*

6.1.3.3 Metal Oxide Nanocrystals

Recent developments in inorganic chemistry have led to the emergence of a large class of nanoscale metal –oxide-based polyoxometalate (POM) nanocrystals. These well-defined inorganic nanostructures exhibit unparalleled structural, magnetic and electronic properties compared to traditional inorganic compounds.[150-158] A typical example of this category of nano-building blocks is the (Mo_{132}) "Kleplerate" giant cluster as illustrated in Figure 6.13.[47]

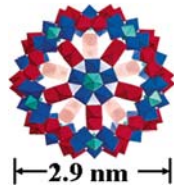


Figure 6.13. Structure of [Mo_{132}] "Keplerate" giant cluster (full formula $(NH_4)_{42}[Mo_{132}O_{372}(CH_3COO)_{30}(H_2O)_{72}]$ ca.$300H_2O$ ca.$10CH_3COONH_4$).[50]

Quite remarkably, these nanoscale building blocks readily self-assemble into "giant clusters" referred to as "blackberry structures" by simply adjusting the solvent quality of a (Mo_{132})/H_20/acetone system to produce a *nano-periodic aggregation pattern* as described in Figure 6.14 below.[50]

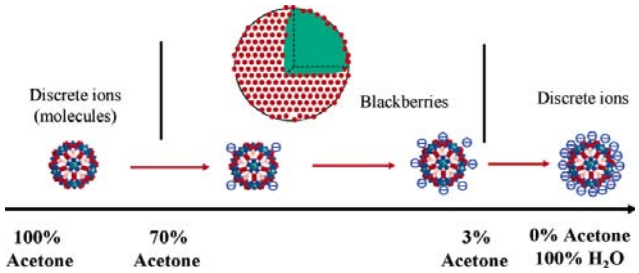


Figure 6.14. *Complete transition of single macroanions-blackberry structures-macroanions is achieved by simply adjusting the solvent quality of the [Mo_{132}]/H_2O/acetone system.*[50]

This self-assembly behavior to produce giant soluble, hydrophilic molybdenum/oxide based spherical/wheel-shaped species has been reported by a number of groups.[159-169]

The Fahlman group[170] has shown that dendrimers (i.e., PAMAM/PPI-type dendrimers) can be used as host templates for the controlled synthesis of 0-D semi-conducting metal oxide nanocrystals such as tin oxide.

Extensive work by O'Brien, et al.[51] have demonstrated unique nano-periodic property patterns that are possible by self-assembling (6 nm) PbSe nanocrystals with (11 nm) Fe_2O_3 nanocrystals to form superlattices consisting of AB_{13} unit cells as illustrated in Figure 6.15 (Section 7.4.2 for more examples).

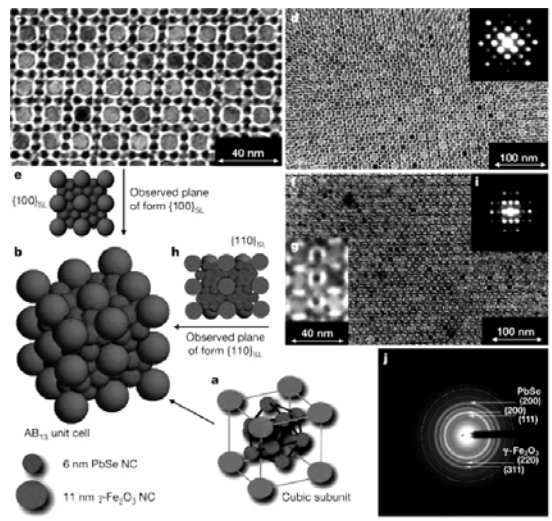


Figure 6.15. *TEM micrographs and sketches of AB_{13} superlattices of 11-nm -Fe_2O_3 and 6-nm PbSe NCs: (a) cubic subunit of the AB_{13} unit cell; (b) AB_{13} unit cell built up of eight cubic subunits; (c) projection of a $[100]_{SL}$ plane at high magnification; (d) same as (c) but at low magnification [(inset) small-angle electron diffraction pattern from a corresponding 6-μm^2 area]; (e) depiction of a [100] plane; (f) projection of a $[110]_{SL}$ plane; (g) same as (f) but at high magnification; (h) depiction of the projection of the [110] plane; (i) small-angle electron diffraction pattern from a 6-μm^2 $[110]_{SL}$ area; (j) wide-angle electron diffraction pattern of an AB_{13}-superlattice (SAED of a 6-μm^2 area) with indexing of the main diffraction rings for PbSe and -Fe_2O_3.*[51]

6.1.4 Semi-Metals

6.1.4.1 Silica Nanoparticles

The Stober synthesis (1968) is the first method reported for making highly spherical, 0-D, monodisperse silica nanoparticles of high enough quality to be of interest as building blocks for nano-synthesis.[171] Typically, tetraethylorthosilicate (i.e., tetraethoxysilane, TEOS) is combined and stirred with appropriate condensation reagents (i.e., ethanol, ammonium hydroxide and water) to initiate the condensation of –OH groups to produce a Si-O-Si network accompanied by the formation of water. Appropriate handling of the TEOS in an inert environment is essential to avoid indiscrete polymerization events that may provide nucleation sites leading to significant size distributions and polydispersity. Since these early reports, many substantial improvements have been made to give enhanced control of size, monodispersity, as well as both surface and interior functionality.[172, 173] By simply controlling the concentration of critical synthesis reactants, one can tailor the core and outer shell sizes from nm to microns dimensions as illustrated in Figure 6.16.[174] More recent work by Wiesner and co-workers,[29, 68] has shown that unique monodisperse core-shell silica nanoparticles possessing a variety of fluorescent dyes can be produced in the size range of 20-30 nm as shown in Figure 6.17 (A-B.)

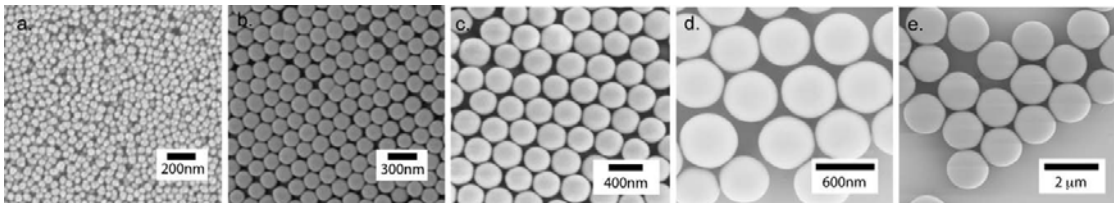


Figure 6.16. *Representative scanning electron micrographs of core–shell fluorescent silica nanoparticles-microparticles of different diameters: (a) 50 nm, (b) 150 nm, (c) 250 nm, (d) 500 nm, (e) 1.5 mm.*[29]

The Wiesner group[175] has developed a new class of well defined, highly monodisperse core-shell silica nanoparticles that possess three types of architecture, namely: (1) a compact core containing dye surrounded by a silica shell, (2) an expanded core containing dye surrounded by a thinner shell and (3) a homogeneous nanoparticle with dye molecules sparsely embedded within. All three particle types are of approximately the same size and composition; however, they exhibit substantially different photo-physical properties (Figure 6.17).

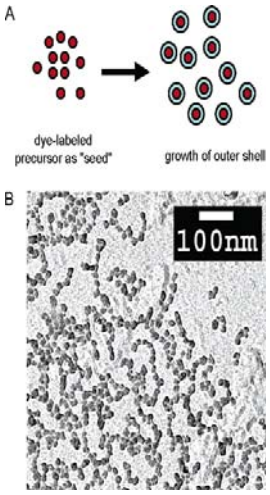


Figure 6.17. *Fluorescent core-shell silica nanoparticles. (A) Schematic representation of the synthesis of core-shell fluorescent silica nanoparticles. (B) The resultant 30 nm particles as characterized by transmission electron microscopy (TEM).* [29, 68]

It has recently been reported,[19] that silica nanoparticles may be chemically modified to be used as a nano-scaffolding for the attachment of a variety of biological moieties by means of standard bioconjugation schemes such as illustrated in Figure 6.18. These strategies provide a wide range of surface chemistries and hard-soft type nano-compounds (Section 7.6).

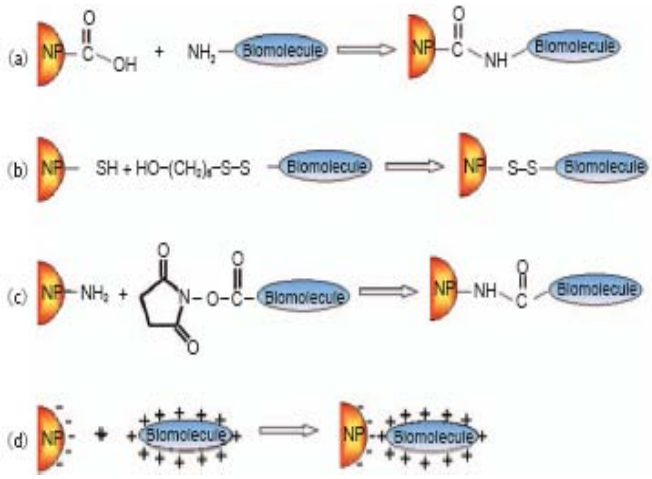


Figure 6.18. *Representative bioconjugation schemes for the attachment of biomolecules onto the surface of silica NPs.*[19]

6.1.5 Non Metals-Carbon Allotropes

6.1.5.1 Fullerenes; 0-D Buckministerfullerenes

Since the discovery of fullerenes in 1985,[176] a subsequent report by Caspar[177] revealed that fullerenes and icosahedral virus particles shared fundamental quasi-equivalence geometry principals applied by Buckmininster Fuller in his geodesic dome designs. The basic concept for fullerene formation involved the construction of polyhedra from 12 pentagons together with some number of hexagons or the symmetrically equivalent construction of triangular faceted surface lattices (deltahedra), as shown below, with 12 five-fold vertices and some number of six-fold vertices. Under appropriate synthesis conditions, certain surface lattice symmetry and geometrical relationships between critical polycyclic precursors can lead to a variety of close caged fullerenes (i.e., C_{20}, C_{60}, C_{70}, C_{80}); wherein, it is well known that C_{60} is one of the most stable and preferred (Figure 6.19). Similarly, earlier quasi-equivalence principals were utilized by Caspar and Klug[178] to describe the ways in which large numbers of identical protein subunits could self assemble to build closed containers (i.e., virus capsids) of predetermined nanoscale dimensions that define the closed surfaces of icosahedral viruses. *Such quasi-equivalence observed in both soft and hard nanomaterial categories represents a very pervasive "nano-periodic pattern" of behavior in the nanoscale realm.* (See Percec examples using soft nano-matter dendrons, Section 4.2.5.2.) Recent work reported by a Spanish research group describes a very versatile and highly efficient process for synthesizing fullerenes based on surface catalyzed cyclodehydrogenation of aromatic precursors.[179]

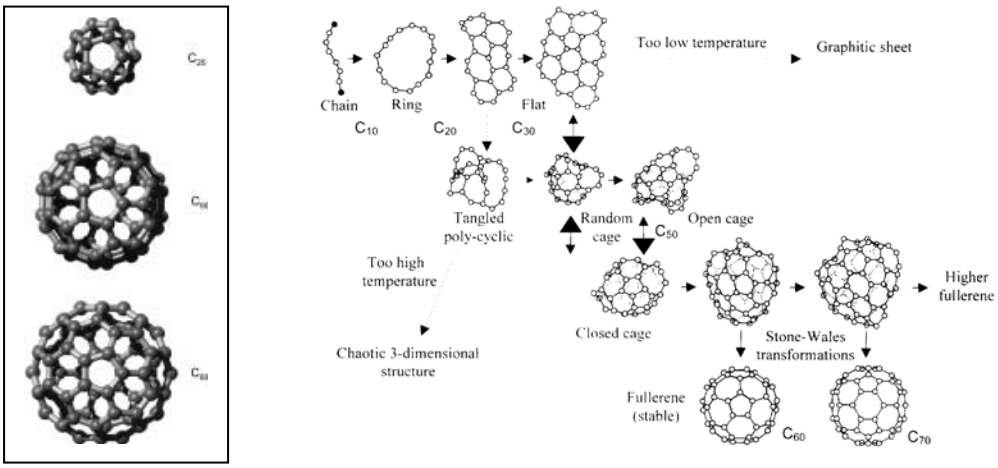


Figure 6.19. *Proposed fullerene formation model.*[13]

Several key chemical features of fullerenes include the dramatic reduction in cytoxicity properties by simply functionalizing the fullerene surface with water solubilizing functionality as shown in Figure 6.20, as well as the demonstration that fullerenes may function as nano-containers.[46] Encapsulation of metal atoms, within the interior of fullerenes, produces *endohedral metallofullerene.* As such, these fullerene based nano-containers provides a metallic core and a covalent outer shell much as is observed for dendrimers.

As early as 2000, Hirsch, et al.[47] proposed that the *pi*-electron system (i.e., the spherical aromaticity) of an icosahedral fullerene can be considered as a spherical electron gas which surrounds the surface of the sphere. It was further proposed, that this electron gas could be characterized by the angular momentum quantum numbers (l= 0, 1, 2, 3, ...). The s shell (l=0) is orbital. The major difference compared to a picoscale atom is that the surface of the fullerene sphere represents a nodal plane and the electron density

in the hollow sphere should approach zero. Hence, the wave function characterized by (l= 1, 2, 3,…) are analogous to the atomic p, d and f orbitals of an atom as illustrated in Figure 6.21.

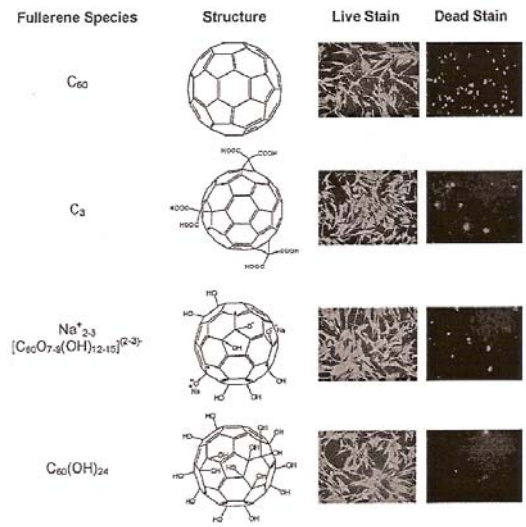


Figure 6.20. *Structures and human dermal fibroblast live/dead cell viability assay results for C_{60} and derivatives.*[46]

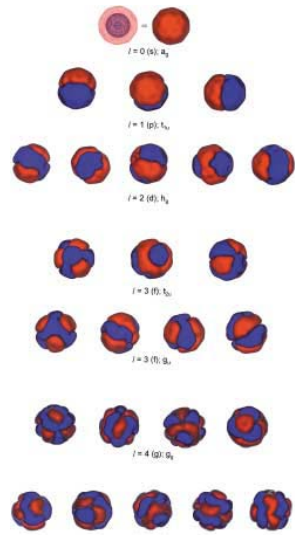


Figure 6.21. *Simulated spherically aromaticity of fullerenes.*[47]

Quite remarkably, this hypothesis was experimentally demonstrated recently by Petek, et al.[34] Using scanning tunnel microscopy and density functional theory, the unoccupied electronic structure of C_{60} was shown to manifest *superatom*-type properties. These superatom states hybridize much like the *s* and *p* orbitals of hydrogen and alkali atoms into diatomic molecular-like dimers and free electron bands of 1-D wires and 2-D quantum wells in their respective C_{60} aggregate states (Figures 6.22 and 6.23).

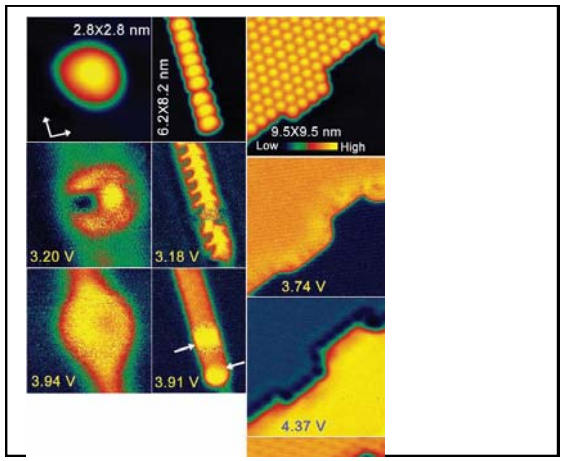


Figure 6.22. *Topographic (Ato C) and dI/dV (D to J) images of LDOS of a single C60 molecule, 1D quantum wire, and 2D quantum well. The quantum well is on a Cu(111) substrate, whereas all other images are for C60 molecules on 7.6 Å–wide bare Cu lines between oxide domains on an O/Cu(110) substrate (6). (K) dz/dV spectra identifying specific tunneling resonances in a single C60molecule, a molecular dimer, and a C_{60} island. For potentials up to 3.2 V [(D) and (E)], the LDOS images show intramolecular structure characteristics of the p* orbitals localized on the C atom framework. The complete absence of molecular contrast in the LDOS images taken above 3.5 V for closepacked C60 aggregates is indicative of intermolecular wave function delocalization. The quantum-wire images show the transition from the localized molecular orbital LDOS of LUMO+2 at 2.8 to 3.2 V (E) to the delocalized one of s SAMO at 3.91 V (G). The complementary smooth contrast over both the C_{60} island (H) and the bare Cu(111) surface (I) regions reflects the NFE properties of SAMOs and IP states. The arrows indicate the bright contrast at the edges and gaps of the quantum-wire antibonding band (G) and the dark contrast at the edge of the quantum-well bonding band (J).*[34]

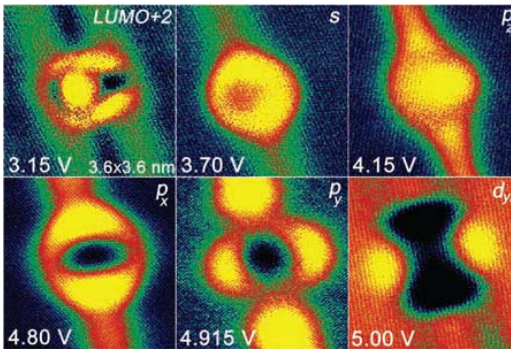


Figure 6.23. *dI/dV mapping of an individual C_{60} molecule's SAMOs. As the measurement voltage is increased, the dI/dV images of a single C60 molecule evolve from the p* molecular orbital character of LUMO+2 to the core-centered s, pz, px, py, and dyz SAMO character. The characteristic dark spot on the SAMO occurs above the top C_{60} pentagon. Tunneling through the image potential states of the substrate is responsible for the bright contrast above the metal and the oxide domains.*[34]

6.1.5.2 Fullerenes: 1-D Carbon Nanotubes

Single-walled carbon nanotubes (SWNTs), as opposed to multi-walled carbon nanotubes (MWCNTs), (Figure 6.24) are hollow cylinders of carbon with diameters approximately 1 nm lengths ranging from tens of nm to cms and walls that are one carbon atom thick. SWNTs are thermodynamically stable forms of carbon that are produced when a carbonaneous feedstock is exposed to a metal catalyst at high temperatures. The most common means of synthesizing SWNTs include: (1) arc discharge,[180] (2) laser ablation[181] and (3) chemical vapor deposition.[182] Although some progress has been made on synthetic techniques that will produce uniform populations, lack of uniformity is still a problem. In an effort to overcome that problem, considerable effort is being placed on post-synthetic sorting schemes and selective growth methods for the production of bulk samples of monodisperse SWNTs.[183-185] Size and architectural sorting of SWNTs according to conductivity properties has recently been reported and is illustrated in Figure 6.25. These issues have been examined extensively in a recent review.[186]

Figure 6.24. *Single walled and multi-called carbon nanotubes***.**

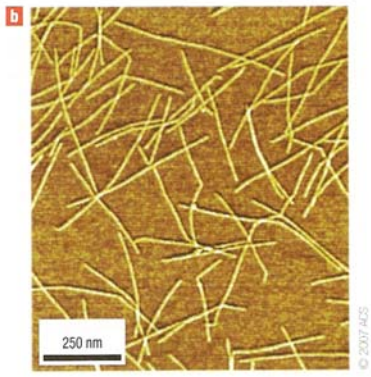


Figure 6.25. *Sequential sorting by size exclusion chromatography and ion exchange chromatography results in SWNTs of uniform diameter and length as observed in this atomic force microscopy image.*[25]

In an effort to amplify differences between various SWNT species in a polydisperse mixture, many researchers have explored chemistries that vary as a function of SWNT electronic type, diameters and/or chirality handedness as a means for fractionating homogeneous populations of SWNTs. Wong, et al.[61] have published an extensive review covering a wide range of covalent surface chemistry at the ends, as well as at defect sites along the side wall as illustrated in (Figure 6.26). Solution of this problem will be necessary before this class of nano-modules can be considered to be a *well defined* nano-element with controlled length.

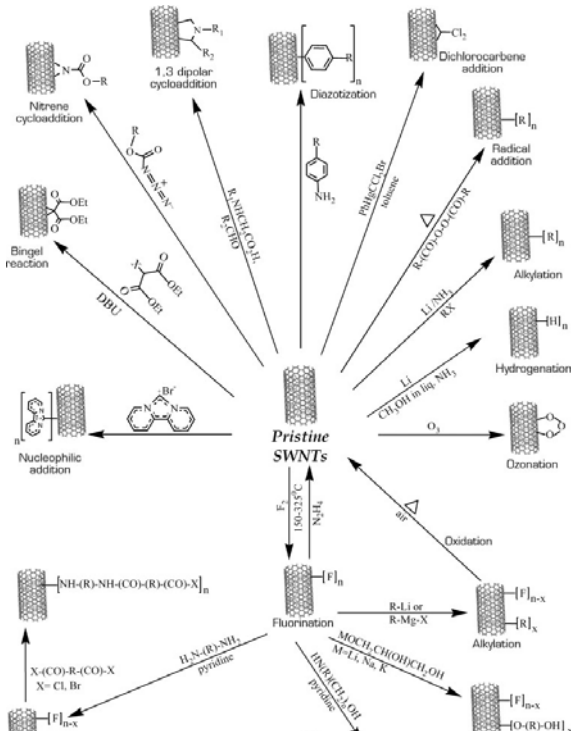


Figure 6.26. *Schematic of the various methods to perform sidewall functionalization of SWNTs.*[61, 62]

6.2 Soft Matter (Synthetic/Biological): Proposed Zero Dimensional (0-D) Nano-Element Categories

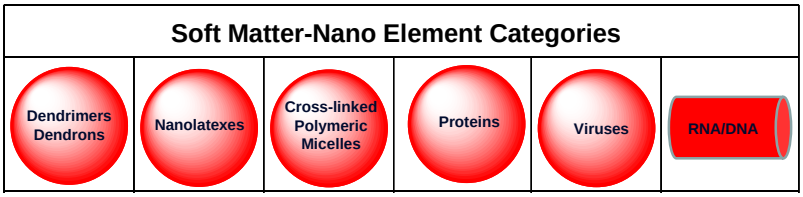


Figure 6.27. *Proposed soft matter: 0-D and 1-D nano-element categories.*

6.2.1 Dendrons/Dendrimers

6.2.1.1 Dendrimer Synthesis: Divergent and Convergent Methods

In contrast to traditional polymers, dendrimers are unique core–shell structures that possess three basic architectural components**,** namely; (I) a core, (II) an interior of shells (generations) consisting of repeating branch-cell units, and (III) terminal functional groups (the outer shell or periphery). In general, dendrimer

synthesis involves *divergent* or *convergent* hierarchical assembly strategies that require the construction components shown in Figure 6.28. Within each of these major approaches, there may be variations in methodology for branch-cell construction or dendron construction. Many of these issues, together with experimental laboratory procedures, have been reviewed elsewhere.[187-189]

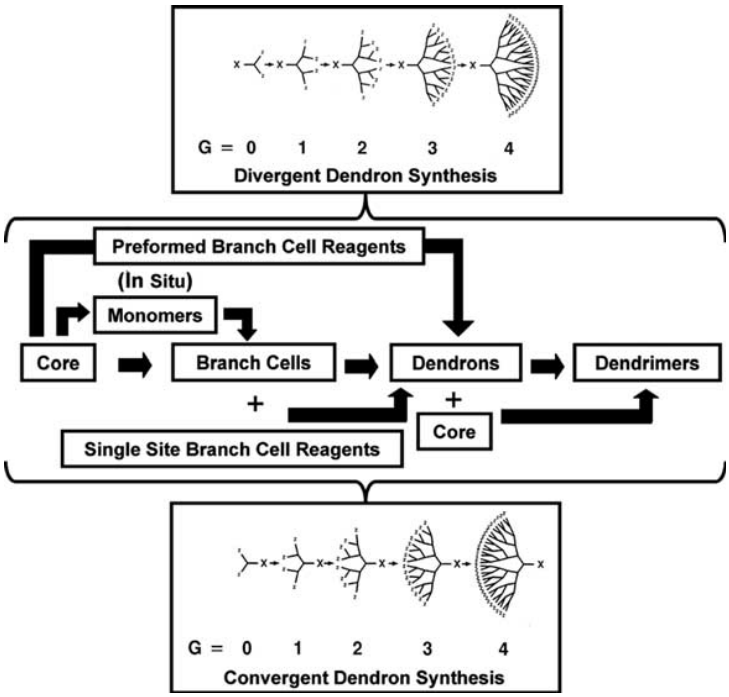


Figure 6.28. *Hierarchical assembly scheme illustrating the options for constructing dendrimers by either divergent (Tomalia-type) or convergent (Frechet-type) synthetic strategies.*[21]

Dendrimers may be viewed as unique, information-processing, *nanoscale devices*. Each architectural component manifests a specific function, while at the same time, defining properties for these nanostructures as they are grown generation by generation. For example, the *core* may be thought of as the molecular information center from which size, shape, directionality, and multiplicity are expressed *via* the covalent connectivity to the outer shells. Within the *interior*, one finds the branch-cell amplification region which defines the type and volume of interior void space that may be enclosed by the terminal groups as the dendrimer is grown. This interior defines the nano-container properties that are observed in dendrimers (Figure 6.29). Branch-cell multiplicity (N_b) determines the density and degree of amplification as an exponential function of generation (G). The interior composition and volume of solvent-filled void space determines the extent and nature of guest-host (endo-receptor) properties that are possible within a particular dendrimer family and generation. Finally, the *surface* consists of reactive or passive terminal groups that may perform several functions. [58, 59] With appropriate functionalization, they serve as a template polymerization region as each generation is amplified and covalently attached to the precursor generation. The surface groups may also function as passive or reactive gates controlling entry or departure of guest molecules from the dendrimer interior. These three architectural components (core, interior, and periphery) essentially determine the physical and chemical properties, as well as the overall size, shape, and flexibility of a dendrimer. It is important to note that dendrimer diameters increase linearly as a function of shells or generations added; whereas, the terminal functional groups increase exponentially as a function of generation. This dilemma enhances the “tethered congestion” of the anchored dendrons as a function of generation due to the steric crowding of the end groups. As a

consequence, lower generations are generally open, floppy structures; whereas, higher generations become robust, less deformable spheroids, ellipsoids, or cylinders—depending on the shape and directionality of the core (Figure 6.29).

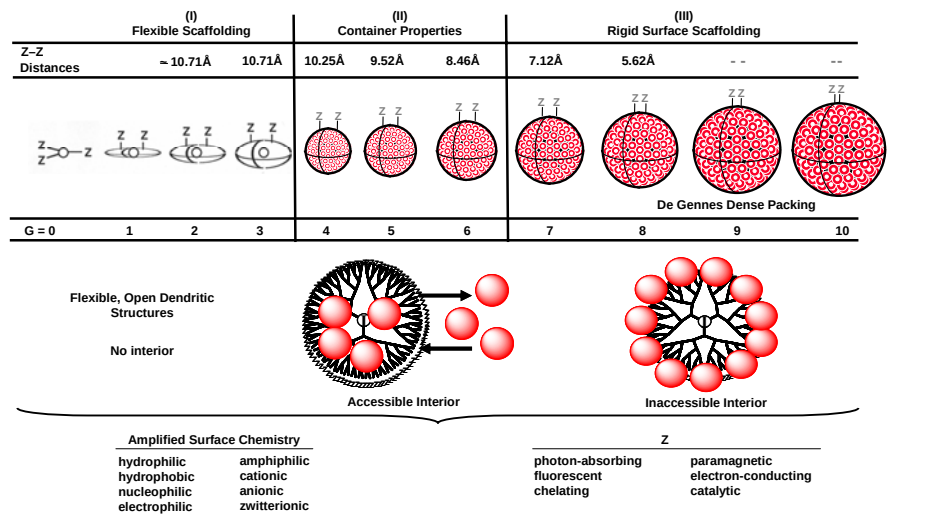


Figure 6.29. *Control of dendrimer flexibility and nano-container properties as a fuction of generation.*[21]

An overview of other critical structurally controlled dendrimer features such as: size, shape and surface chemistry may be found in Section 4.2.4.3.

6.2.2 Nano-latexes

Subtle modifications of classical microemulsion polymerization methodology [190] have been used to access this soft nanomaterial category. As early as the 1990s, traditional oil-water microemulsion polymerization strategies have been reported to produce polymeric nanoparticles with diameters smaller than 30 nm.[191] Use of this approach to produce well defined core-shell type nanoparticles with functionality, presented on the outer shell did not occur until more recently.[192] This pioneering work by Larpent, et al.[193] clearly demonstrated that nano-latexes with average diameters ranging from 12 to 20 nm could be readily obtained by copolymerizing the monomers: styrene, divinyl benzene and vinyl benzyl. Subsequent reaction with cyclam produced stable, translucent aqueous suspensions of the nanoparticles. These nano-latexes were determined to have average diameters of 12-22 nm by quasi-elastic light scattering and electron microscopy. Specific runs exhibited narrow polydispersity features with particle size distributions of 12-15 nm. These nano-latexes were determined to possess core-shell type structures wherein the interior core consisted of primarily hydrophobic components derived from the styrene/divinyl benzene monomers and the outer shell contained a predominance of the hydrophilic cyclam monomer, thus presenting the macrocyclic ligand to the aqueous medium for subsequent reactions or metal chelation functionality. Subsequent metal chelation with copper salts demonstrated that these 12-13 nm nanoparticles could chelate as many as 400-450 Cu(II) per particle with high surface to volume ratios (i.e., 350-450 mmol. Cu(II) per nm^3) (Figure 6.31).

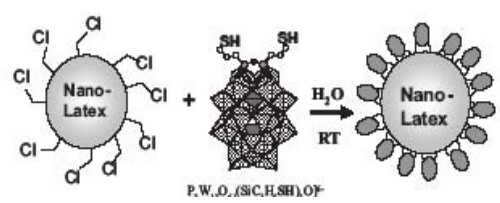


Figure 6.30. *Synthesis of nanocomposite material at room temperature.*[20]

Subsequent work by Larpent, et al.[20, 41] demonstrated that a variety of reactive surface functionality (i.e., benzyl halides, etc.) could be introduced on the surface of these nano-latexes. This surface functionality could then be used as a reactive core to covalently attach both inorganic (i.e., Dawson polyoxometalate shells), as well as nanoscale organic shells (i.e., dendron type shells) to produce novel core-shell nanostructure hybrids as illustrated in Figure 6.31.

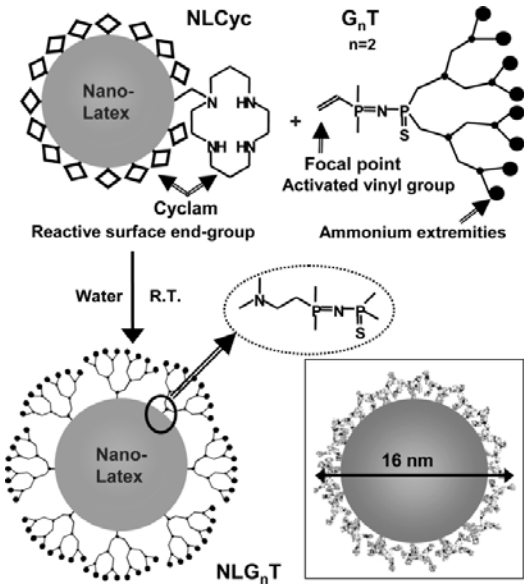


Figure 6.31. *Synthesis of dendronized nanolatexes* ***NLG_nT****. Insert: scaled cross-section of a dendronized nanoparticle* ***NLG_1T*** *showing the thin* ***G_1T*** *shell as CPK space filling molecular models.*[41]

6.2.3 Cross-linked Polymeric Micelles

This category of well defined soft matter nanoparticles pioneered by Wooley, et al.[17] were readily accessible *via* a three-step synthesis strategy. This strategy involved the following steps: (1) controlled free radical or living anionic polymerization methodologies to produce monodisperse amphiphilic-(hydrophilic(A)/hydrophobic (B))-AB diblock copolymers possessing cross-linkable groups in either the A or B segment (Figure 6.32), (2) self assembly of the copolymer in an aqueous solvent to produce a polymeric micelle (Figure 6.33); wherein, the hydrophobic (B) segments reside at the core and the hydrophilic (A) segments define the outer corona/shell and (3) subsequent regio-specific crosslinking of reactive groups residing in either the core or shell of the polymeric micellar assemblies (Figure 6.34) to produce a broad diversity of covalently fixed polymeric micelles/robust nano-objects with dimensions ranging from 10-100 nm.[7]

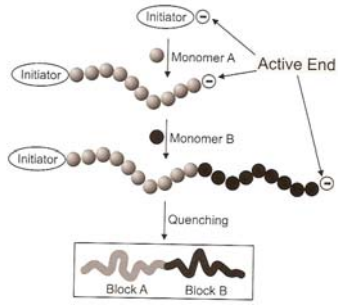


Figure 6.32. *Standard method for copolymerizing monomer A with monomer B to produce diblock AB copolymer.*[7]

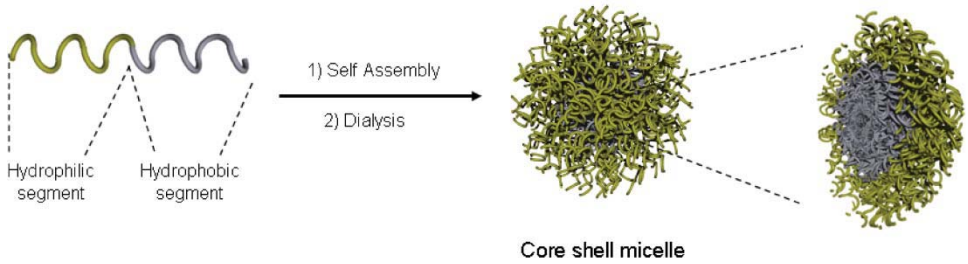


Figure 6.33. *Solution state self assembly of amphiphilic diblock copolymers into spherical micelles.*[17]

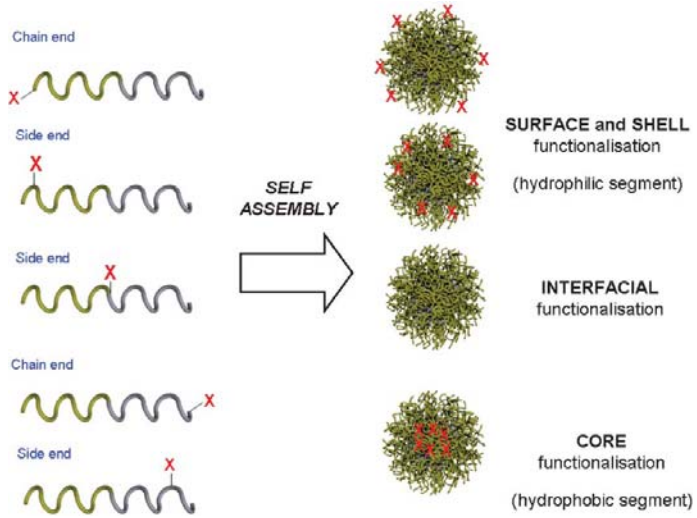


Figure 6.34. *Schematic to illustrate the possible locations of functionalization within a spherical diblock polymer micelle.*[17]

6.2.4 Proteins: Proposed 0-D and 1-D Nano-Elements

6.2.4.1 The Importance of Controlled Organic Nanostructures in Biology

All critical biological structures required for life have been based on the evolutionary development of quantized building blocks derived from controlled organic nanostructures. This evolutionary development occurred in two significant phases and involved *bottom-up synthesis*. Clearly, critical parameters such as mass and dimensions had to increase in size to define the appropriate building modules. The first phase was abiotic and involved molecular evolution from atoms to small molecules. Nature dealt with this problem several billion years ago and shattered this nanoscale synthesis barrier with its evolutionary biological strategy for producing precise nanoscale modules such as DNA, RNA and proteins. These modules were generally collections of precisely bonded atoms that occupied space with dimensions ranging from 1 to 10^2 nm. These building blocks set the stage for the synthesis of more complex

nanostructures and defined the dimensional scaling that determines essentially all significant molecular level factors required for initiating and sustaining life. These critical parameters included: *nanoscale sizes, nano-surfaces/interfaces, nano-containment, nanoscale-transduction/amplification* and *information storage*.[194] They have important implications, not only in biology, but also in significant abiotic areas such as: catalysis, computer miniaturization, nanotribology, sensors and new materials. Bottom-up synthetic strategies that produce size-monodisperse, well-defined organic and inorganic nanostructures with dimensions ranging from 1-100 nm will be of utmost importance. It will be essential that these strategies allow the systematic construction of nanoscale structures and devices with precise atom-by-atom control as a function of *size, shape, surface chemistry and flexibility.*

6.2.4.2 Synthetic Strategies to Precise Bio-Nanostructures

In the past 30 years, several major scientific breakthroughs in the synthesis and characterization of proteins, DNA/RNA and viruses have now made these nano-modules available from other than biological sources. Nobel Laureate, B. Merrifield's pioneering work (1984)[12] using solid phase synthesis has provided a very versatile strategy for the *bottom-up* synthesis of a wide range of precise 1-D polypeptides and polynucleic acids. Utilizing 1-D monomer units (i.e., amino acids or nucleic acids), as illustrated in Figure 6.35, it was possible to both sequence as well as precisely control the total length of the 1-D macromolecular precursors (i.e., polypeptides or polynucleic acids) (Figure 6.36) that are required for final self-assembly to protein and DNA/RNA structures, respectively. Presently these sequencing strategies represent the most viable routes for macromolecular, length (aspect ratio) control to produce 1-D nanostructures. Synthetic strategies to macromolecular length control in other 1-D nanostructures such as: carbon, metal, and metal chalcogenide /oxide nanotubes still remain elusive.

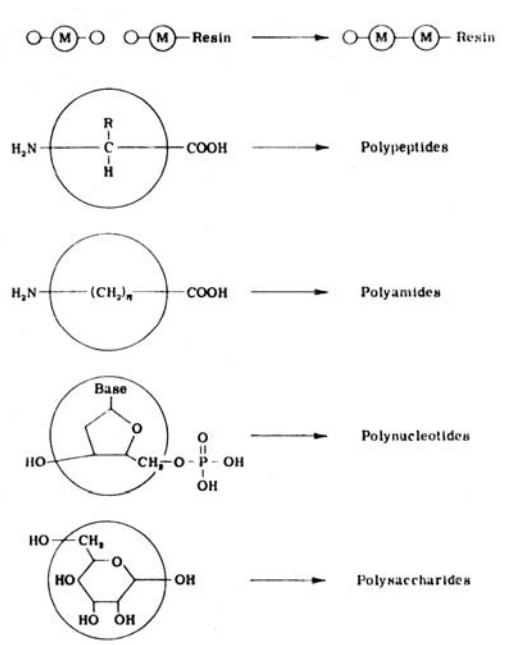


Figure 6.35. *1-D monomer units for solid phase synthesis of poly(peptides) and poly(nucleotides).*[12]

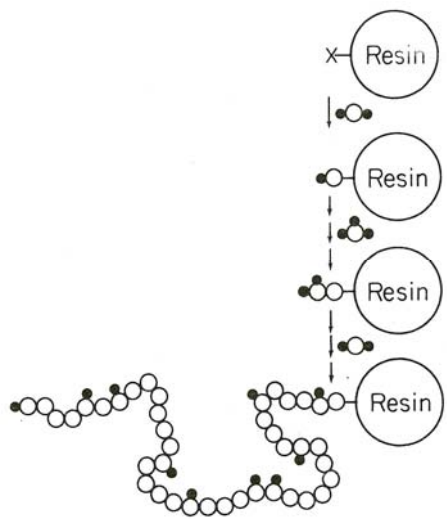


Figure 6.36. *General scheme for solid phase synthesis of poly(peptide) and poly(nucleotide) precursors to 0-D proteins and 1-D DNA/RNA nano-modules, respectively.*[12]

6.2.4.3 Zero-Dimensional (0-D) Protein Structures

Proteins constitute about half of the dry mass of the all living cells in organisms ranging from the humblest bacteria to humans. All 0-D protein structures found in nature involve a multi-step process for their construction. This process includes precise sequencing (polymerization) of the 20 essential alpha-amino acid monomers which have very definite chemical structures as shown in Figure 6.37.[64] Sequential polymerization of these monomers produces long, 1-D linear, polypeptide structures of very well-defined length and sequence to yield primary structures. Every protein consists of at least one polypeptide chain which is derived from the polymerization of these left-handed amino acid monomers. Secondary protein structures are produced by the self-assembly of these polypeptides based on sticky sites that are formed by the covalent connection of these monomers in definite patterns along this polypeptide backbone. These amino acid based "sticky sites" have an identical component (which forms the backbone of the amino acid polymer) and a distinctively different component (the pendant side chain, or "R group"). There is considerable variation in the physical properties of the side chains. Some are polar and others are non-polar. Some are charged and others are not. Some are small, others are large. Many novel amino acids have been created by varying this side chain functionality.

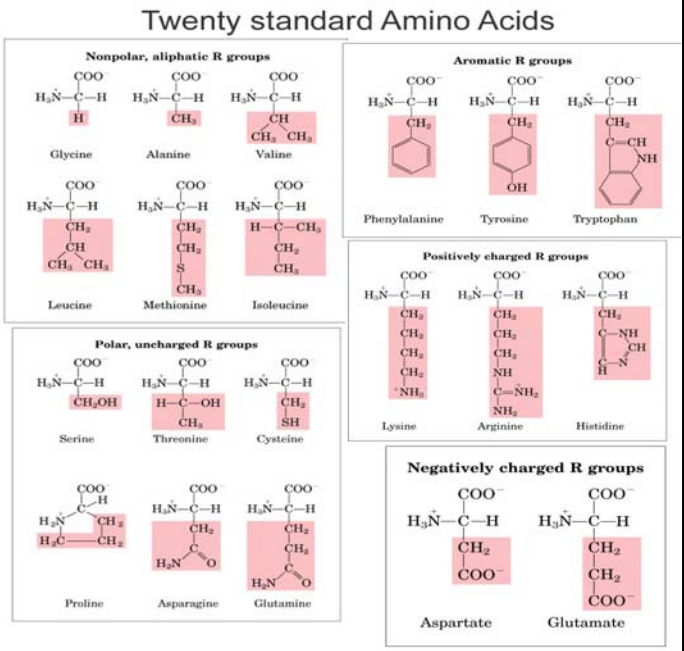


Figure 6.37. *The twenty standard l-amino acid monomers. They are divided into several structurally similar groups. Each amino acid may be considered as precise 1-D monomers. There are two enantiomers of each amino acid. All amino acids in proteins, from bacteria to humans, are "left-handed" amino acids. All polypeptides synthesized on ribosomes consist of left-handed amino acid residues. The handedness of amino acid subunits is crucial for the stereospecificity ligand binding sites and therefore the stereospecificity of reactions facilitated by protein catalysts, or enzymes. Novel amino acids can be designed by altering the structure of the side chain. Such amino acids will still combine with other amino acids by formation of a peptide bond in the polymer backbone.*[64]

The amino acid monomers can be strung together in an astronomical variety of sequences much like the limited set of letters of the more familiar Roman alphabet is used to form a tremendous variety of words. Different strings of amino acid monomers define different units of polymeric structure and a new hierarchical level of nanostructures. Some of these polymers will be more water soluble than others, some more charged than others, some more likely to form aggregates than others, some more likely to bind certain other kinds of molecule than others, some more likely to adopt a certain type of higher order structure than others. In any case, amino acids are what might be called distinctive types of nanoscale LEGO®, suitable for self-assembling these nanostructures in different ways.[195]

These monomeric sequences can yield at least five well known secondary folding motifs (Figure 6.38) which ultimately lead to more complex tertiary structures thus providing various shapes and domains that are found in completed 0-D protein structures (Figure 6.39). These infinite variations in nanoscale protein shapes, sizes and surface presentations of pendant alpha amino acid chemical functionality actually define their function in living organisms as: (a) structural, (b) functional or (c) catalytic (enzyme type) proteins.

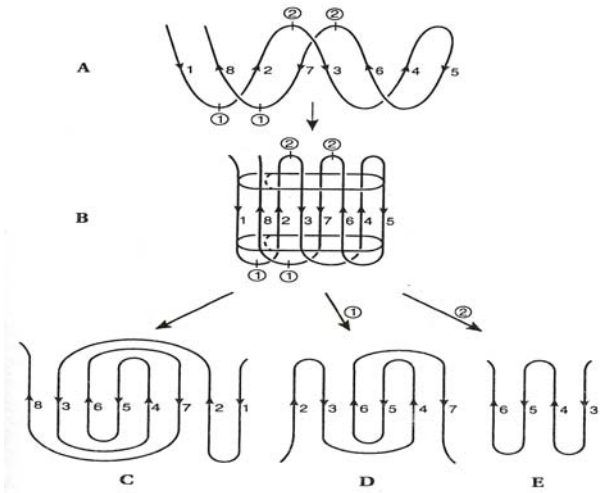


Figure 6.38. Topological *explanation of how the patterns of the folded polypeptides defining five of the main categories of domains could have arisen by a common mechanism.*[15]

The various amino acids, comprising the proteins in a cell, are either synthesized by the organism (non-essential amino acids) or obtained from its diet or from micro-organisms in the gastrointestinal tract (essential amino acids). In any case, natural amino acids are synthesized by enzymes. Moreover, the natural stringing together of amino acids into a polypeptide chain is catalyzed by enzymes. A single enzyme molecule will comprise at least one polypeptide chain. In most cases, the catalytic activity of an enzyme will be extremely specific. In some cases the rate of catalysis of an enzyme will be at or close to the diffusion limit, meaning that no change in the structure of the enzyme could enable it to operate at a higher rate. In general, the smaller the reactant molecule on which the enzyme acts: the faster the rate of catalysis under usual conditions. Most enzymes carry out their chemical reactions under relatively mild reaction conditions, very different from most industrial or inorganic catalytic processes.

Enzyme structure is hierarchical in nature. One or more chains of amino acids (primary structures) will adopt helical structure or pleated sheet structure (together called secondary structures) in what is for many enzymes a globular and rather definite “native state” (tertiary structure). Secondary structures are stabilized by hydrogen bonds and hydrophobic interactions (non-covalent interactions). Tertiary structures are stabilized by the same interactions as secondary structures; in some cases side chain-side chain electrostatic interactions contribute to the overall free energy. The folded enzyme is both highly ordered and highly compact. The diameter of a globular enzyme is on the order of 1-10 nm. The *core* of the globular structure resembles a periodic organic crystal and is generally hydrophobic in character. That is, the polypeptide chain of an enzyme is organized such that a large percentage of the side chains in the core will have a low solubility in water; whereas, the outer surface of the enzyme, its “shell,” will present a hydrophobic enzyme surface.[196]

More complicated poly(peptide)-based structures are known. For example, the protein hemoglobin consists of four subunits, two alpha chains and two beta chains (Figure 6.40). Hemoglobin is involved in oxygen transport in certain organisms, notably humans. The definite structure formed by the interaction of multiple subunits of a protein is called its quaternary structure. The definite character of the interactions between subunits in hemoglobin is crucial for protein functionality and therefore crucial to human life as we known it.

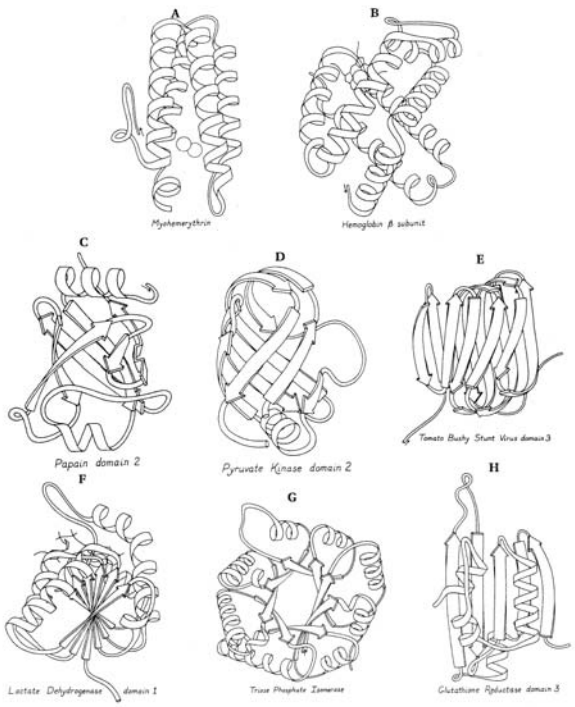
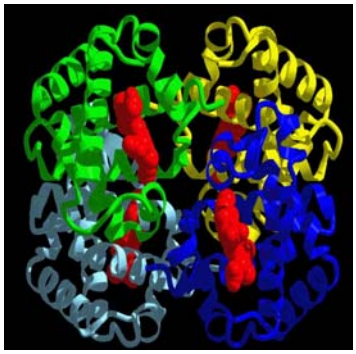


Figure 6.39. *Representative tertiary structure for eight major categories of a taxonomic system for shape classifying protein domains.*[15]

Figure 6.40. *Ribbon diagram of hemoglobin. Four polypeptide subunits interact in definite way. The character of this interaction plays a crucial role in determining the temperature-, ionic strength-, and pH-sensitivity of oxygen binding to heme. The non-covalently-bound heme groups are shown in red. Each heme group comprises a single iron atom. The oxidation state of this atom plays is another key determinant of oxygen binding affinity. There is a large overall proportion of helical structure in each of the protein subunits (image courtesy of D. Haynie).*



The nanoscale dimensions for proteins are very similar to those observed for dendrimers as shown below (Figure 6.41). In fact, dendrimers are widely referred to as *artificial proteins* based both on their similarity in dimensions, as well their ability to mimic protein function in some cases.[56]

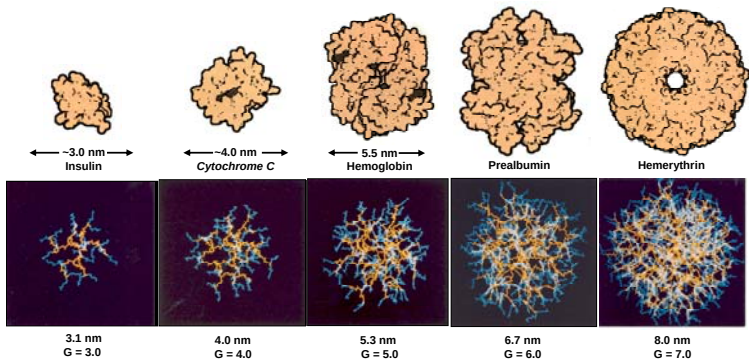


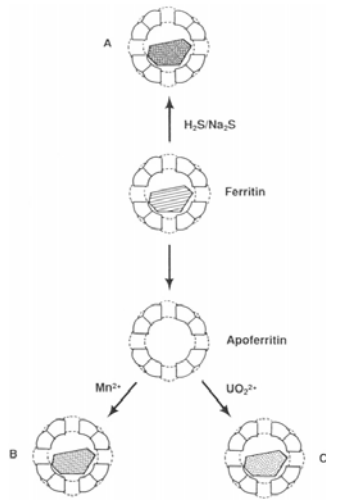
Figure 6.41. *Dimensional comparison of various generations of poly(amidoamine) (PAMAM) dendrimers with several well known functional and enzymatic proteins.*[21]

6.2.4.4 Core-Shell Proteins

In addition to the various protein functions described above, Nature has developed a variety of core-shell type proteins that function as nano-carriers or storage devices of metal ions or minerals. Most notable, are the ferritins which are found throughout the animal, plant and microbial kingdom.[27] They consist of a central hydrated iron (III) oxide core encapsulated within a multi-subunit protein shell. Ferritins are robust proteins that can tolerate higher temperatures (850 ^{o}C) and high pH (8.5-9) without appreciable disruption of their quaternary structure. Iron-free ferritin structures (apoferritin) are composed of 24 polypeptides subunits, which assemble into a hollow protein spheroid with a molecular weight ~ 500 KDa. The outer diameter is 12 nm, while the inner diameter is 8 nm.

Mann et al.,[69] reported pioneering work on the use of ferritins by modifying their interior core chemistry *via* replacement of iron from the internal domain with manganese or uranium as illustrated in Figure 6.42.

Figure 6.42. *Schematic representation of the use of ferritin in the synthesis of nanophase materials. (a) Iron sulfideformation by in situ reaction of native iron oxide cores. (b) Manganese oxide reconstitution by redox-driven reactions within apoferritin. (c) Uranyl oxy-hydroxide deposition by ion-binding and hydrolytic polymerization.*[27, 69]



Ueno, et al.[197] constructed a size selective hydrogenation bioreactor by utilizing apoferritin as a nano-container. A Pd nanocluster was formed in the interior of the apoferritin cavity by first encapsulating Pd (II) ions and then performing an *in situ* chemical reduction as illustrated in Figure 6.43.

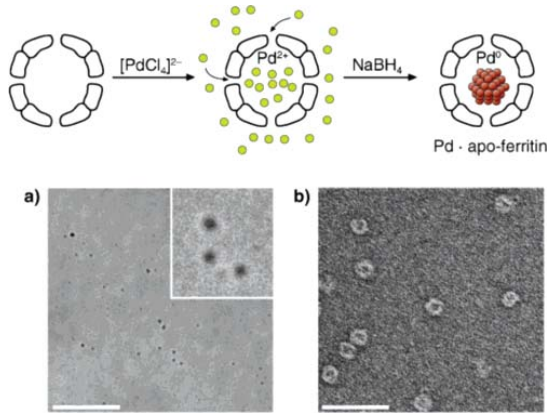


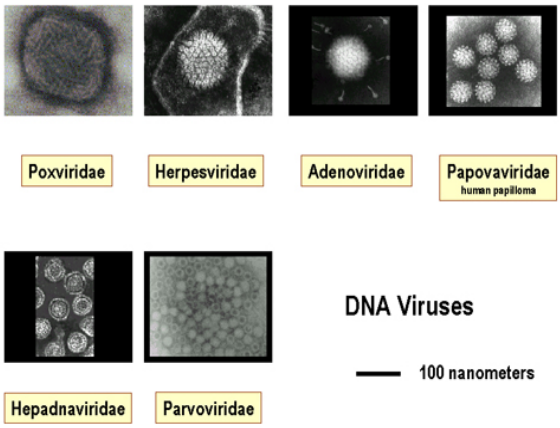
Figure 6.43. *Top: Scheme showing the preparation of Pdapoferritin. Bottom: TEM images of the Pd-apoferritin, (a) an ice-embedded unstained sample (inset magnification 4X), (b) a sample negatively stained with uranyl acetate. Scale bars represent 50 nm.* [27]

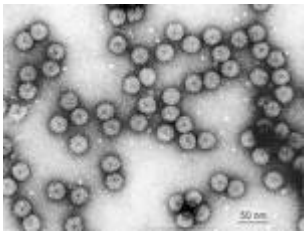
6.2.5 Viruses

6.2.5.1 Zero-Dimensional (0-D) Nanostructures

Most of these 0-D viral building blocks have evolved since the origin of life from biological sources. Due to their traditional perception as pathological entities they are categorically perceived as "bad nanoparticles". However, as described below there are many benign/non-pathological viruses that are available in gram quantities that may be viewed as "well defined" nano-building blocks suitable for nano-synthesis and modification. Although viruses may be viewed as extremely complex nano-structures, the power of synthesis/self-assembly should be pointed out. As early as 1991, the successful *in vitro* synthesis of a virulent polio virus with the empirical formula; $C_{332,682}H_{492,238}N_{98,245}O_{131,196}P_{7501}S_{2340}$ has been reported.[198]

The protein coat for virus particles may be constructed from well defined nanoscale protein building block components (i.e., 3-10 nm) and as such are substantially larger nanoscale objects (i.e., 20-100 nm). They typically consist of several hundred to thousands of protein molecules (i.e., viral capsids) that self-assemble to form a hollow scaffold, which holds the viral nucleic acid within the interior. The viral capsids (i.e., the self assembled protein cage) offer robust and monodisperse structures that exist in a large variety of sizes and shapes. Figure 6.44 illustrates a variety of such 0-D viruses.





Cucumber mosaic virus courtesy of NIH.

Figure 6.44. *Various 0-D Viruses.*
http://pathmicro.med.sc.edu/mhunt/intro-vir.htm

Moreover, these protein surfaces can be used as a synthetic platform for further chemical modification. Since certain types of viruses can be obtained in large quantities (i.e., Cowpea Mosaic Virus, CPMV) and manipulated at the genetic level, they afford a unique category of precise core-shell like nanoscale building blocks.

Pioneering work by Finn and Johnson,[199] has shown that CPMV is a well defined, robust 0-D nanostructure that has been characterized with atomic resolution. Furthermore they have shown that that this protein capsid can function as a convenient and programmable platform for a variety of chemical reactions. The CPMV capsid is formed from 60 copies of an asymmetric unit which contains two protein subunits; a small subunit, and a large subunit, the B+C domain as shown in Figure 6.45.

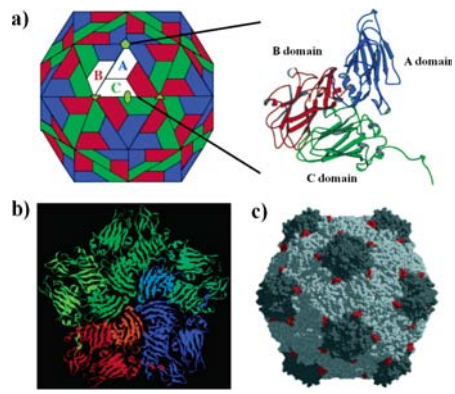


Figure 6.45. *Structure of cowpea mosaic virus and its crystals. (a) Left: Schematic representation of CPMV, showing the distribution of the subunits that comprise the asymmetric unit. Right: The folds of the two subunits, A and B+C. (b) Organization of five asymmetric units into a "pentamer" centered around a small hole at the 5-fold axis. (c) X-ray crystal structure of CPMV highlighting the EF-loop (in red) in the large subunit in which the cysteine-containing insert is made.*[27]

These 60 protein subunits self-assemble around a single-stranded RNA genome to form a virus particle that displays icosahedral symmetry, with a diameter of ca. 30 nm. The virus, therefore, is of potential use as a nanoscale building block. Both organic and inorganic structures can be attached to the CPMV capsid via amine and thiol functionalities on the protein surface.[200, 201] The exterior shell is readily decorated with appropriate functionality to attach fluorophores,[202] PEG functionality,[203] or hybridized with gold nanocrystals to form 3-D hybrid structure.[204]

Similarly, the bacteriophage MS2 is a virus with a structure similar to CPMV. The capsid shell of the MS2 virus comprises 180 sequence identical protein monomers that self assemble into an icosahedral 0-D nanostructure with an outer diameter of 27 nm. Furthermore, the capsid contains 32 channels (1.8 nm diameter) that allow access to the interior of the virus. Successful covalent modification of the viral outer shell by Francis and co-workers allowed the introduction of suitable targeting groups for drug delivery.[205]

6.2.5.2 One-Dimensional (1-D) Nanostructures

As such, both spherical (0-D, icosahedral) and cylindrical (1-D, rod shaped) viruses are precise nanoscale objects derived from the self-assembly of well defined protein-subunit building blocks. The 1-D, rod-shaped morphology of a tobacco mosaic virus (TVM) is readily observed by the electron micrograph shown in Figure 6.46. The primary objective of these viral protein self assemblies is to develop a protective coat around the fragile viral RNA or DNA components that are essential for replication. These protein coats generally possess cell adhesion ligands (i.e., hemagglutinin groups) that facilitate adhesion to healthy

Figure 6.46. *An electron micrograph of TMV obtained by transmission electron microscopy illustrating the 1-D shape of the virus.* (*http://www.apsnet.org/education/illustratedglossary/PhotosS-V/virus.htm)*

cells bearing sialic acid receptor moieties. It is this ligand-receptor complex that defines a cell adhesion event and constitutes the first step that a virus takes when it infects a biological cell.

For example, based on pioneering work by Nobel Laureate, A. Klug,[206] it is known that a tobacco mosaic virus contains 2,130 identical protein subunits (i.e., A-protein) that self-assemble in the presence of viral RNA and in its absence (Figure 6.47). When combined with the viral RNA, the protein subunits define the shape of the helical assembly while the RNA adopts a helical conformation and defines the length of the rod-like helical virus. Viral assembly is nucleated by insertion of a hairpin RNA into the central hole of the protein disc and in between the two layers of subunits. In the absence of the RNA component, the protein subunits self-assemble into discs that further organize into helical structures.

The amazing mimicry of these 1-D viral assemblies using shape designed dendrons reported by Percec, et al.[42] are described in Section 4.2.5.3. This indeed may be an example of a *shape directed nano-periodic pattern* that prevails for both synthetic dendrons and biologically derived protein sub-units.

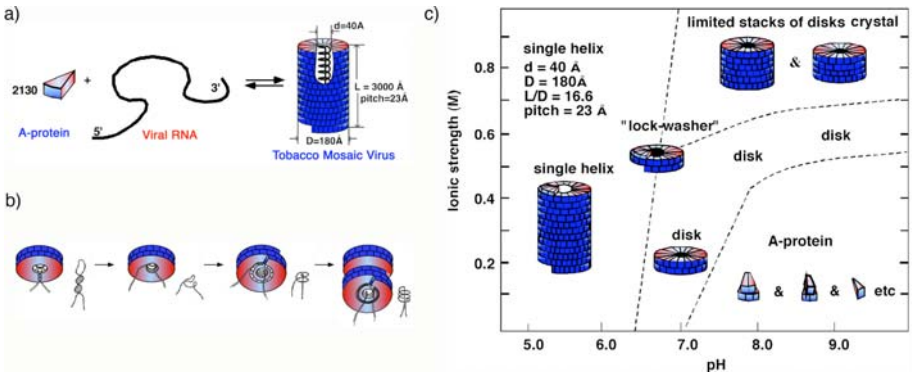


Figure 6.47. *(a) Self assembly of wedge shaped protein sub-units around the viral RNA for tobacco mosaic virus.(b) self-assembly as a function of pH and ion strength.*[42]

The tobacco mosaic virus (TMV) has been used extensively as a precise nanoscale template for synthesizing a variety of hybridized nanotube composites.[27 207] For example, the cylindrical TMV template was used for the *in situ* formation of anisotropic assemblies of 0-D Pt, Au or Ag nanocrystals as shown in Figure 6.48.

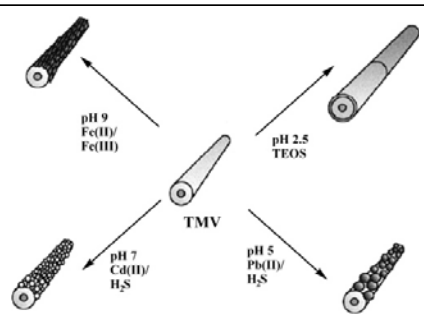


Figure 6.48. Clockwise from top right: sol-gel condensation (silica); coprecipitation (PbS and CdS nanocrystals); oxidative hydrolysis (iron oxide).[27]

Similar work by Belcher, et al.[208] using M-13 bacteriophage, rod shaped viruses has demonstrated that these (860 nm by 6.5 nm) rod-like scaffoldings may be genetically engineered to insert nucleation sites on their surfaces or specifically functionalized as illustrated in Figure 6.49 to yield a variety of hybridized (i.e., virus based nano-compounds).[209]

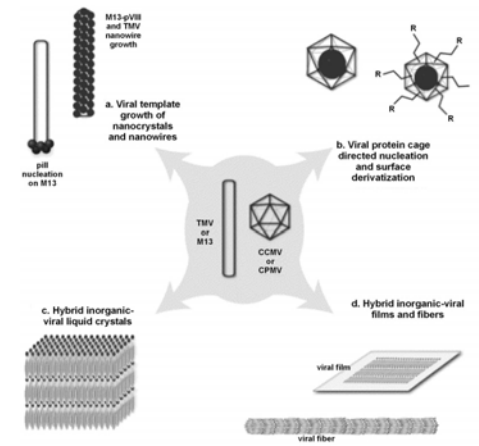


Figure 6.49. *Some of the routes followed to synthesize biohybrid materials using rod-shaped (TMV, M13) and cage-structured (CCMV, CPMV) viruses.*[27]

6.2.6 DNA/RNA: 1-Dimensional Structures

Synthetic strategies based on the pioneering solid phase synthesis methodologies of Merrifield and others[12] (Section 6.2.4.2; Figures 6.35 and 6.36), are generally used for DNA/RNA synthesis. Many extensive reviews [210] are available on this subject and will not be covered in this report.

It is notable, that DNA may be thought of as either a 0-D[211, 212] (N. Seeman type) nanomodule or a 1-D (C. Mirkin-type nanoscale connector.[54] It is well recognized, that designed DNA sequencing may be used for both *intra-molecular,* as well as *inter-molecular* assembly operations. In fact, aqueous self-assembly of designed DNA sequences may be used as a palette of robust nano-scaffolding ranging from octahedral to two dimensional lattices.[213-217] The objective of this portion of the report is to focus only on the 1-D features of DNA as a nano-connector or assembler. Actual TEM micrographs of single strand-DNA (ss-DNA) have been obtained as described in Figure 6.50. As a 1-D entity, DNA has been used extensively as a single strand, complementary 1-D functional building block that may be conjugated to either hard matter nano-elements (i.e., metal nanoclusters)[54, 65, 218] or soft matter nano-elements (i.e., dendrons/dendrimers).[60, 219] As such, the single strand DNA component has been shown to function as a selective self assembling connector for constructing designable nano-compounds[54] or 3-D crystalline nanolattices.[65, 218]

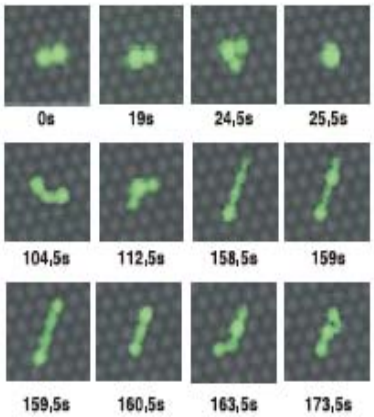


Figure 6.50. *A sampling at various times of configurations observed for a single strand 48.5-kbp DNA. The diffusing molecule has been recentered in each image.*[24]

When ssDNAs are used as nanoscale connectors, the forward and reverse sequences are independently attached (conjugated) to the targeted nano-modules which are to be connected. It is well known, that

(Crick-Watson type) complimentary, supramolecular bonding occurs to form a duplex assembly as shown in Figures 6.51 and 6.52 to complete the connection.

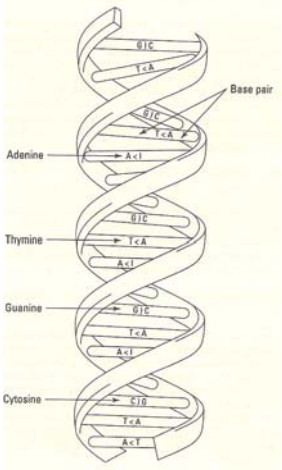


Figure 6.51. *DNA duplex.*

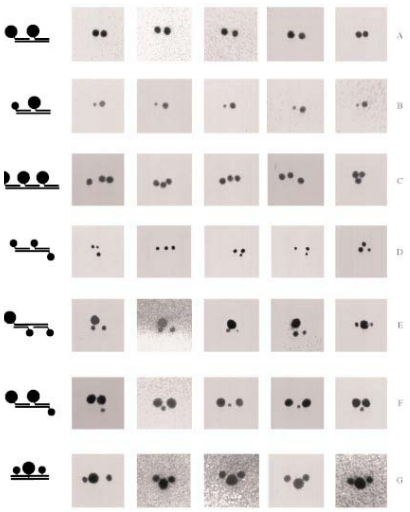


Figure 6.52. *Schematic illustrations and representative TEM images for specific nanocrystal molecules. See Scheme 1 for the synthesis strategies. A) 10-nm homodimer, synthesis strategy B; B) 10-/5-nm heterodimer, strategy B; C) 10-nm homotrimer, strategy B; D) 5-nm homo-trimer, strategy A; E) 10-/5-/5-nm heterotrimer, strategy A; F) 5-/10-/10-nm heterotrimer, strategy A; G) 5-/10-/5-nm heterotrimer, strategy C.*[54]

Both hard and soft material based nano-elements (i.e., gold nanoclusters and dendrons/dendrimers) have been assembled into well defined nano-compounds by the use of ssDNA as connectors. As early as 1996, Alivisatos, et al.[220] and Mirkin, et al.,[221] described the first self-assembly of hard nano-elements into nano-compounds (Figure 6.52). More recently, the self assembly of soft matter based dendrons has been demonstrated by Tomalia, et al.[60] as shown in Figure 6.53.

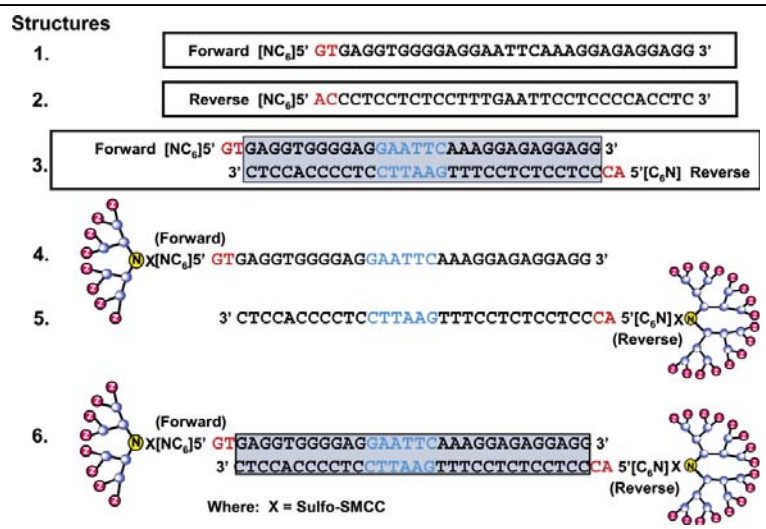


Figure 6.53. *Schematic of base pairing reaction. Two 5´amine-modified oligonucleotides, forward (1) and reverse (2), are complimentaryover 30 bases (blue) and contain a two base noncomplimentary spacer (red). These oligonucleotides were used in to make the dendrimeroligonucleotideconjugates G) 2-forward (4) and G) 3-reverse (5). Heating to 95 °C and slowly cooling to anneal allows a mix ofoliognucleotides (1, 2) to anneal to specifically make double stranded DNA (3) and a mix of the dendrimer-oligonucleotide conjugates (4and 5) to specifically make a base paired differentiated dendrimer (6).*[60]

Theoretically, the self-assembly of essentially any of the hard or soft nano-elements by Crick-Watson base pairing should be possible if the appropriate complimentary ssDNA units can be single site attached to the targeted nano-elements (i.e., proteins, dendrimers, quantum dots, viruses, etc.). A major consideration in such a strategy would be to understand the relative size scaling of all the components involved. Figure 6.54 illustrates the relative size scaling that exists between several proteins, dendrimers and DNA.

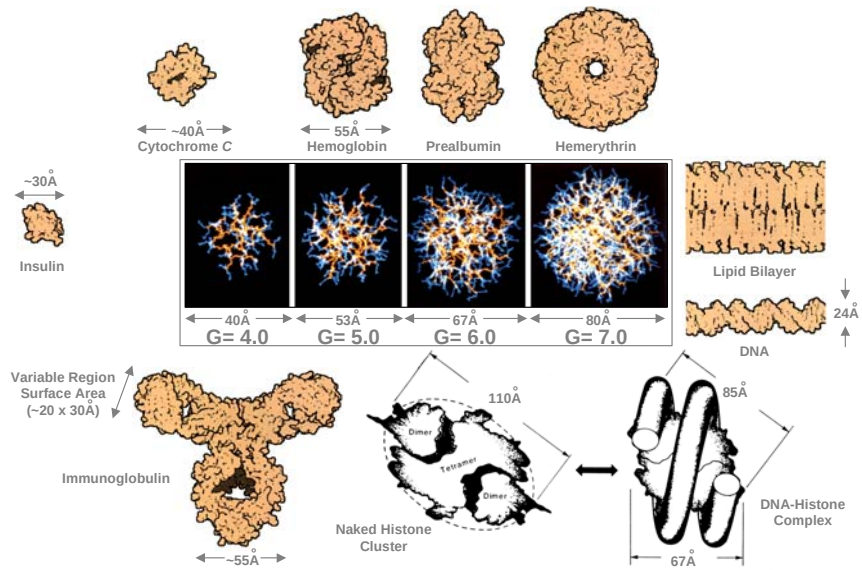


Figure 6.54. *A dimensionally scaled comparison of a series of poly(amidoamine) (PAMAM) dendrimers (NH_3 core; G = 4–7) with a variety of proteins, a typical lipid bilayer membrane and DNA.*[4]

7.0 Criteria for Defining Nano-Compounds

7.1 Historical

Although Dalton's representation of simple atoms (1808) appears to be planar as illustrated earlier in his periodic table (Figure 3.0 (b)), in reality Dalton's intuition about atoms occupying 3-D space was correct. In his lectures, he actually used wooden balls (spheroids) with various icons to represent and differentiate "simple atoms". In fact, Dalton was actually the first to work with molecular models in that he linked these "simple atoms" (i.e., wooden spheroids) with rods to represent what he called *compound atoms*. His second inclination was to combine the atoms to produce compound atoms that were as symmetrical as possible. It was not until (1874), that J. H. van't Hoff published his famous book entitled: *La Chimie dans l'espace* describing this bold opinion for tetra-valent carbon (Figure 7.0). In this work, he presented carbon valency in a symmetrical fashion from the four corners of a tetrahedron surrounding the core of the carbon atom.[5]

These fundamental concepts inspired us, as early as 1990, to hypothesize the desymmetrization of spherical dendrimers to mimic tetrahedral carbon atoms at the nanoscale level by differentiating a dendrimer surface into a tetravalent anisotropic structure consisting of quadrants (**A-D**) with orthogonally reactive groups –**w, x, y, z** as illustrated in Figure 7.1.[39] Subsequently, Fréchet, et al.[222] demonstrated such dendrimer surface differentiation was possible. Visualizing dendrimers as *artificial/super atoms,*[21, 59] the notion of forming artificial nano molecules (i.e., nano-compounds)[71] has been demonstrated by AFM analysis of a [core:1,2-diaminoethane];(Gen.=9);*dendri*-[PAMAM –$(NH_2)_{2048}$ dendrimer (i.e., dia. ~9 nm) on a mica surface.[81, 106] Considering these dendrimer molecules heuristically as carbon atoms, one can visualize the mimicry of many familiar organic hydrocarbon topologies (i.e., ethane, cyclopropane, pentane, etc.) at the nanoscale level (Figure 7.2).

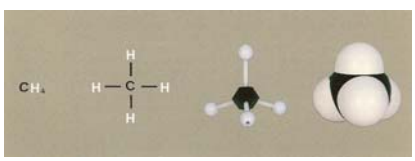


Figure 7.0. *Four representations of the tetravalency and directionality of carbon.*[5]

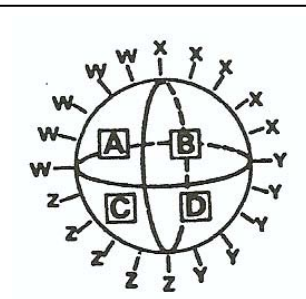


Figure 7.1. *Differentiated dendrimer core - (**A, B, C, D**). Differentiation of dendrimer quadrants with various dendron surface moieties (x,y,z,w).*

As early as 1993-94, [58, 59] we proposed the concept of using dendrimers as nanoscale atom mimics (i.e., building blocks) for the contraction of nanoscale molecules (i.e., compounds, monomers) and subsequent propagation to 1-D nanoscale macromolecules. These multiple dendrimer structures were referred to as *megamers.*[21, 106] They consist of a broad nanostructure category included nano-molecules, nano-oligomers and nano-polymers possessing dimensions and topologies much as illustrated by structures in Figure 7.2. It should be noted that, in addition to 0-D dendrimers, one can observe both 1-D and 2-D megamers in Figure 7.2.

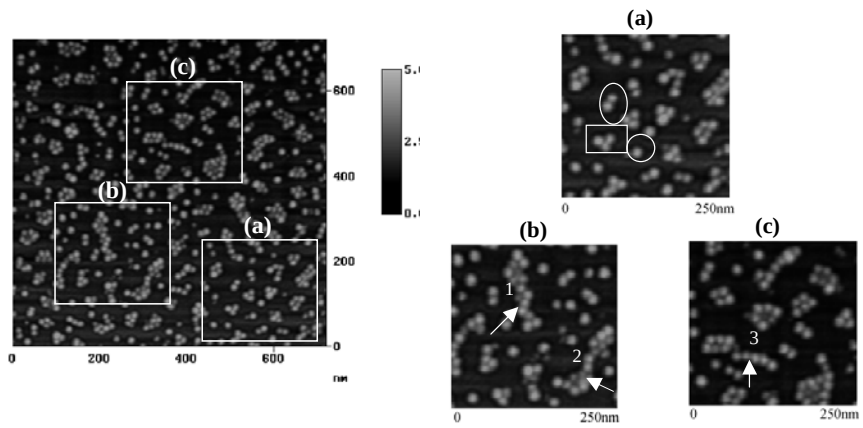


Figure 7.2. *Tapping mode AFM images of G=9; PAMAM dendrimer molecules on a mica surface.*[4]

More recently, Glotzer, et al.[223] extended this concept to hard nano-matter building blocks. Using molecular simulations, they showed that specific site tethered nanoscale shaped objects[52] (Figure 7.3) could be visualized as anisotropic building blocks leading to a wide variety of new nanoscale compounds and assemblies. Many recent new strategies to nanoparticle synthesis have led to a diverse spectrum of particle anisotropy types including: nanocubes,[224] Janus particles,[225] rods, arrows, and tetrapods[148] and polyvalent spheres,[70] etc. These particles possess many unique properties (i.e., electronic, optical, magnetic, etc.) due to their unusual shapes.[37] The diversity of these new building block anisotropies are dramatically different than the isotropic features of spherical particles that have been a primary focus of particle assembly to date. For atoms, it is well known that a combination of directional valency and a suite of highly symmetric near close-packed structures that balance the constraints of atomic size and charge neutralization tend to dominate. This motif also appears to hold very well at the nanoscale.[226] Nanoparticles, unlike atoms, have nearly continuous tunable sizes and charges. As such, ionic crystals/superlattices with no known atomic or molecular analogues have been discovered.[227]

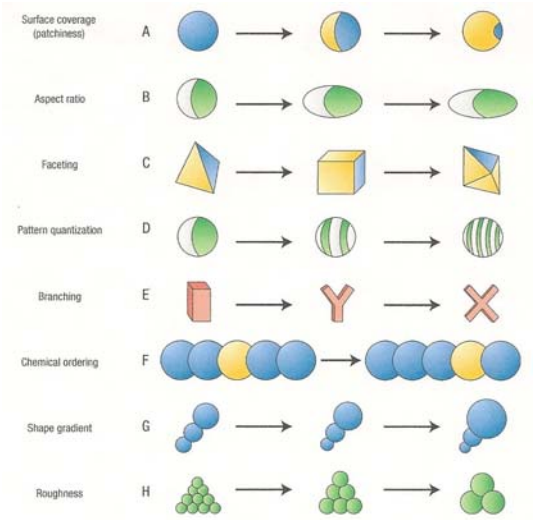


Figure 7.3. *Anisotropy dimesions used to describe key anisotropy attributres of particles. Homologous series of particles as the attribute corresponding to the anisotropy axis is varied from left to right. A: Interaction patchiness via surface coverage, B: aspect ratio, C: faceting, D: interaction patchiness via surface pattern quantization, E: branching, F: chemical ordering, G: shape gradient, H: roughness. Further dimensions, such as chirality are not shown.*[52]

7.2 Ideal Nano-Compound Profile

With this brief background, it is of interest to define criteria for chemically bonding combining so-called *nano-elements* to form *nano-compounds*. These criteria are described in the spirit and with the simplicity that J. Dalton invoked in 1808 for the 23 known atom elements to form *compound atoms*. Following many of the premises and criteria for compound atoms (i.e., molecule formation), several important criteria are as follows:

1. Nano-compounds will be robust, well defined nanostructures obtained by bonding two or more "nano-elements" as a result of surface chemical functionality or non-bonding assembly features. Bonding may occur by (a) self-assembly or (b) chemical bonding (i.e., involving any of the known traditional modes). The resulting "nano-compounds" must be sufficiently robust to be analyzed by traditional methodologies to yield reproducible values/parameters; i.e., (i) gravimetric analysis (i.e., as a function of precursor masses), (ii) elemental composition ratios, (iii) spectroscopically and/or by a variety of (iii) direct imaging methodologies (i.e., TEM, AFM, etc.). Reproducible sizes, shapes and reactivity should be observed. Crystallographic (i.e., single crystal-X-ray) may be applicable to hard matter nano-compounds, but may not be possible for many soft matter nano-compounds.

2. These well defined nano-compounds will be expected to exhibit reproducible mass combining ratios, stoichiometries and chemical/physical properties that are different than the nano-element precursors.

3. Desymmetrizing a highly functionalized nano-element surface may be expected to introduce well defined valency and bonding directionality in the nano-compound. Such bonding modes may be manifested as 1-D, 2-D or 3-D nano-molecular structures of reproducible sizes and shapes.

4. Nano-elements possessing highly functionalized/reactive surfaces may lead to nano-compound stoichiometries and limited bonding sites that are defined by so-called *nanoscale sterically induced stoichiometry (NSIS)* rules.[21, 39, 128]

5. Combinations of these nano-elements may be expected to produce isomeric nano-compound entities exhibiting properties analogous to traditional small molecule isomerism (i.e., asymmetric centers, geometric isomers, symmetry properties, etc.).

7.3 Combinations/Permutations Involving Chemically Bonding of Nano-Elements to Form Nano-Compounds

Based on traditional chemical compound categories, two broad areas of compositions and related features emerged; namely, *inorganic* and *organic* structures. The emergence of such similar categories in the nano-hierarchy has also been observed. We refer to these broad material classifications as (a) *hard matter-nanomaterials* and (b) *soft matter-nanomaterials*. A comparison of their elemental compositions reveals that they tend to parallel the broad areas of inorganic and organic structures, respectively. Just as 0-D atoms may combine to form 1-D, 2-D and 3-D type molecular structures, ample evidence at this time supports similar expectations for 0-D nanoscale elements.

We briefly examine an example of a proposed 1-D, hard matter, nano-element (i.e., SWNT; carbon nanotubes) (Section 6.1.5.2) and of a proposed 1-D, soft matter, nano-element (i.e., ss-DNA) (Section 6.2.6) because of the large amount of interest in the literature (Section 7.6.6; Figure 7.29). Presently, SWNTs do not completely fulfill the criteria for nano-elements largely because the challenge of controlling aspect ratios (i.e., nanotube lengths) has not been resolved.[183-186] In the case of 1-D, single strand DNA (i.e., ss-DNA), most examples of its use in nano-synthesis are as a *well defined nano-connector* rather than as a nanoparticle.

As such, we report present literature examples of nano-compound synthesis according to the following three nano-compound classifications: (1) *hard matter nano-compounds*, (2*) soft matter nano-compounds*, and (3) *hard matter-soft matter nano-compounds.* We use the shorthand notation for hard and soft nano-element categories as described earlier for the six proposed hard nano-matter types (i.e., **H1-6**) and six proposed soft nano-matter types (i.e., **S1-6**), to define the combinatorial formation of selected nano-compounds in this section. The intention was not to be exhaustive in our literature survey of all the combinatorial possibilities, but to demonstrate these classification motifs by highlighting certain prominent examples of highly studied categories.

7.4 Hard Matter Nano-Compounds

This section focuses on nano-compound categories formed by chemical bonding of two or more of the six proposed hard nano-element categories (i.e., **H-1** through **H-6**) that fulfill the proposed nano-compound criteria (Section 7.2). These elements, as shown below, present a combinatorial grid (Figure 7.4) that predicts at least 31 nano-compound possibilities. Space does not allow a comprehensive review, however, many examples of these of these categories have been reported in the literature and a few will be described below. Shorthand nomenclature (i.e., [H-n: H-n], *wherein*: **n=the 1-6 nano-element categories in the hard nano-element classifications**) will be used to broadly identify nano-compound categories and will not necessarily define stoichiometries.

Hard Matter-Nano Element Categories					
Metal (M°) (Nanoclusters)	Metal (Chalcogenide) (Nanocrystals)	Metal Oxide (Nanocrystals)	Silica (Nanoparticles)	Fullerenes	Carbon Nanotubes
H-1	H-2	H-3	H-4	H-5	H-6

Hard Matter Nano-Compounds						
Nano-Elements	Metal (M°) (Nanoclusters)	Metal (Chalcogenide) (Nanocrystals)	Metal Oxide (Nanocrystals)	Silica (Nanoparticles)	Fullerenes	Carbon Nanotubes
Metal (M°) (Nanoclusters)	H-1:H-1 1.	H-2:H-1	H-3:H-1 4.	H-4:H-1	H-5:H-1	H-6:H-1
Metal (Chalcogenide) (Nanocrystals)		H-2:H-2 4.	H-3:H-2	H-4:H-2	H-5:H-2	H-6:H-2
Metal Oxide (Nanocrystals)		H-2:H-3 3.	H-3:H-3 2.	H-4:H-3	H-5:H-3	H-6:H-3
Silica (Nanoparticles)		H-2:H-4	H-3:H-4	H-4:H-4	H-5:H-4	H-6:H-4
Fullerenes		H-2:H-5	H-3:H-5	H-4:H-5	H-5:H-5	H-6:H-5
Carbon Nanotubes		H-2:H-6	H-3:H-6	4-H:H-6	H-5:H-6	H-6:H-6

Figure 7.4. *A combinatorial grid of hard matter nano-compounds (i.e., **[H-n: H-n],** wherein**: n=1-6**) with references to reported examples.*

1. Metal Cluster-Metal Cluster: **[H-1:H-1]** Type Nano-Compounds[23, 70, 71, 228, 229]
2. Metal Oxide-Metal Oxide: **[H-3:H-3]** Type Nano-Compounds [9, 229]
3. Metal Chalcogenide-Metal Oxide: **[H-2:H-3]** Type Nano-Compounds[230]
4. Other: **[H-2:H-2], [H-1:H-3], [H-1:H-4]**[231] Type Nano-Compounds[37]

7.4.1 Metal Nanocrystal-Metal Nanocrystal: [H-1:H-1] Type Compounds

Recent work by Greiner, et al.,[22] has demonstrated an elegant strategy for surface functionalization of gold nanoparticles to produce mono-carboxylic acid functionalized nanocrystals (Figure 7.5). These monovalent nanocrystals were then allowed to react, thus exhibiting 2:1 stoichiometry with an alkylene diamine to produce an **[H-1:H-1]**; gold nanocrystal dimer as illustrated in Figure 7.6.

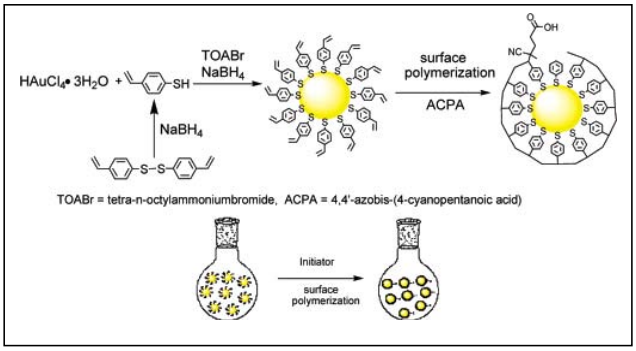


Figure 7.5. *Strategy for surface functionalization to produce monovalent gold nanoparticles.*[22]

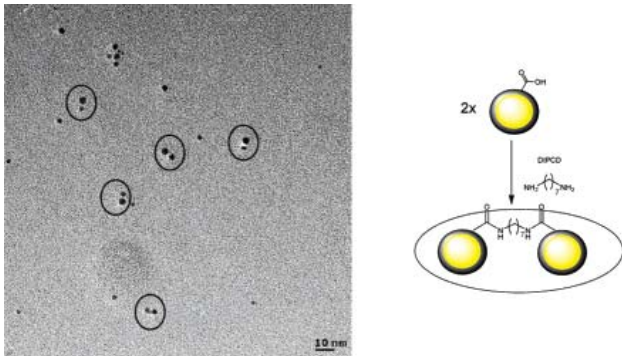


Figure 7.6. *Dimerization after coupling with 1,7-heptandiamine.*[22]

Similarly, recent work by Stellacci, et al.[70 232] describing the desymmetrization of gold nanocrystals to produce divalent gold nano-crystals laid ground work for the construction of extended, 1-dimensional nano-compound examples of this category. Synthesis of these 1-D extended arrays was reported in subsequent work by Perepichka, et al.[71] In an article appropriately entitled: *From "Artificial Atoms" to "Artificial Molecules"* they utilized intrinsic polar defects present on these nanoparticles (Figure 7.7 a) to selectively introduce dicarboxylic acid surface chemistry on these clusters. This then allowed them to

react the divalent gold nanocrystals with an alkylene diamine reagent to yield an extended **[H-1:H-1]**; linear array type nano-compounds (i.e., nano-polymers) as shown in Figure 7.7 (b) and Figure 7.8.

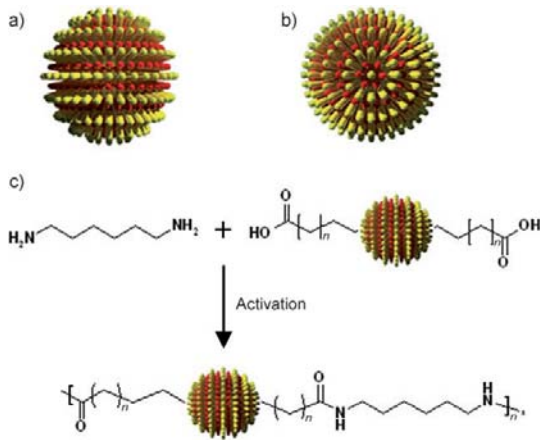
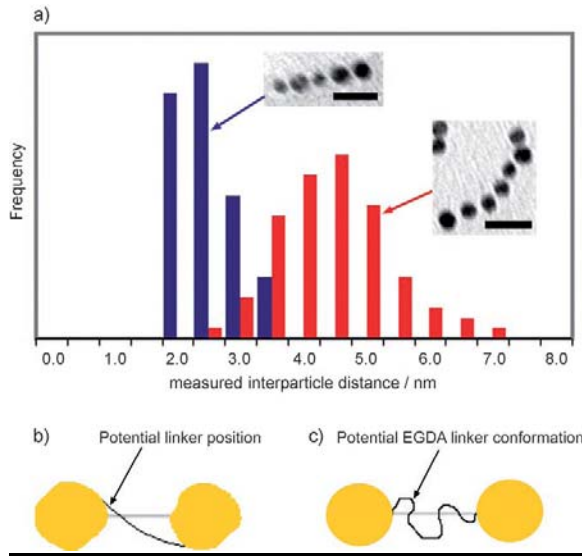


Figure 7.7. *a) Side view and b) top view of a rippled gold nanoparticle. Two polar defects allow the alternation of parallel rings of the two thiol ligands OT (yellow) and MPA (red). c) Polymerization of the carboxy-functionalized nanoparticles with 1,7 diaminohexane (DAH).*[70, 71]

Figure 7.8. *a) Distribution of interparticle distances in nanoparticle chains with DAH (blue) or EGDA (red) linkers. The interparticle distance is clearly correlated to the type of linker. Insets: TEM images of the corresponding nanoparticle chains (scale bars: 20 nm). b) A possible geometrical arrangement of linked nanoparticles that could result in the measured interparticle distance (gray line) being smaller than the linker length. c) The conformational freedom of EGDA that results in the broad distribution of interparticle distances observed for this type of linker.*[70, 71]



Many other examples of this **[H-1:H-1]** nano-compound category have also been reported.[23, 70, 71, 228, 229]

7.4.2 Metal Chalcogenide-Metal Chalcogenide: [H-2: H-2] Type Compounds [229]

One of the first reported examples of self-assembling the **[H-2:H-2]** category of nano-elements was reported by Springholz, et al.[79] This group demonstrated that semiconducting PbSe/Te nanocrystals (QDs) self assembled into 3-D superlattices with fcc-like stacking and tunable lattice constants.

A variety of other hetero-dimeric metal and metal/metal salt nano-compound categories have been reported and characterized by TEM as illustrated in Figure 7.9.

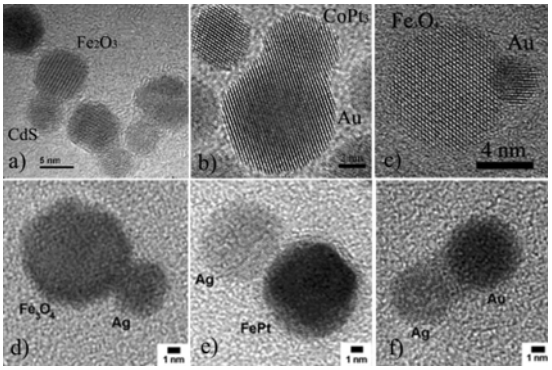


Figure 7.9. *High resolution TEM images of different types of heterodimers: (a) c-Fe2O3–CdS;*[44] *(b) CoPt3–Au; (c) Fe3O4–Au; (d) Fe3O4–Ag* [73] *(e) FePt–Ag; (f) Au–Ag.*[9, 73]

Many examples of these nano-compound categories were formed by assembly into 3-dimensional nano-metal alloy lattices have been reported as shown below in Figure 7.10. The size and shape can influence the assembly of the nanocrystal modules. In the assembly of 0-D (spheroids) nano-building blocks, the assembly arrangements generally obey the traditional predictions one might make from picoscale derived crystal models. The structures are quite predictable based on the ratio of nanocrystal sizes. This occurs much as the crystallographic alloy structure adopted by a mixture of two different metal elements depends on the physical dimensions and properties of its constituent atoms.[23] Thus it appears that certain geometric rules may be stated that appear to be adaptable at all dimensional hierarchical levels.[233]

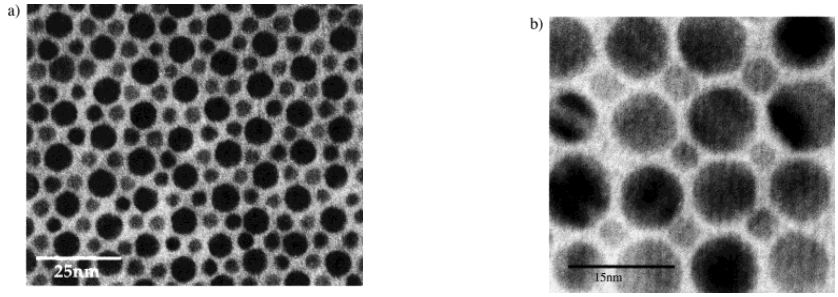


Figure7.10. *Rafts of bimodal nanoparticles forming a) ordered AB_2 and b) ordered AB superlattice arrays.*[23]

Extensive work by O'Brien, et al.[51, 227] has shown that **[H-2:H-3]** type nano-compounds can be obtained as 3-D, superlattices with very specific stoichiometries; namely, as **AB_2, AB_5, and AB_{13}** shown below (Figures 7.11, 7.12 and 7.13).

AB_2- Superlattice - Iron Oxide/Lead Sulfide

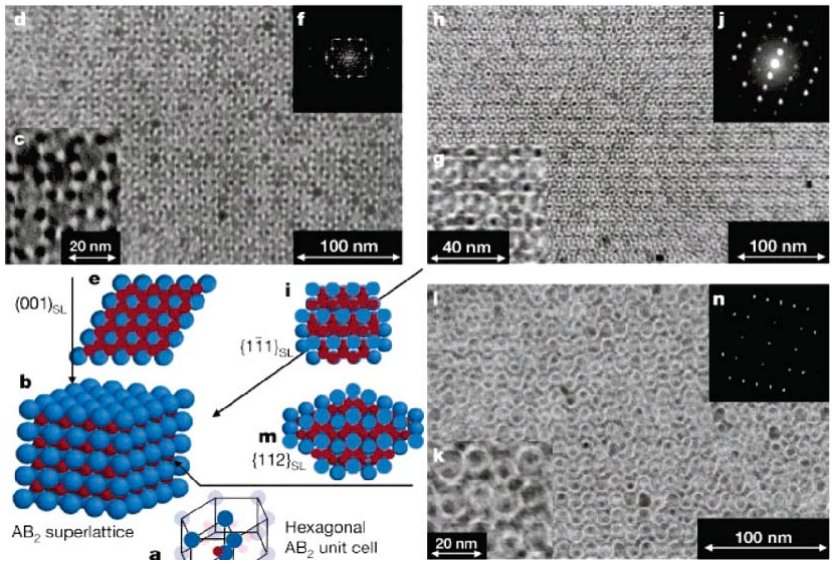


Figure 7.11 *TEM micrographs and sketches of AB_2 superlattices (isostructural with intermetallic phase AlB_2) of 11-nm γ-Fe_2O_3 and 6-nm PbSe NCs: (a) hexagonal unit cell of the AB_2 lattice; (b) AB_2 superlattice built up of alternating layers of large and small particles; (c) projection of the (001)SL plane; (d) same as (c) but at lower magnification; (e) depiction of the (001) plane; (f) FFT of (d); (g) projection of a $(111)_{SL}$ plane; (h) same as (g) but at lower magnification; (i) depiction of the projection of a $(11h1)_{SL}$ plane; (j) small-angle electron diffraction pattern from a 6-μm^2 $(112)_{SL}$ area; (k) projection of the $(112)_{SL}$ plane; (l) same as (k) but at lower magnification; (m) depiction of the projection of a $(112)_{SL}$ plane; (n) FFT of (l).*[37]

(AB_5 Superlattice) Iron Oxide/Lead Sulfide

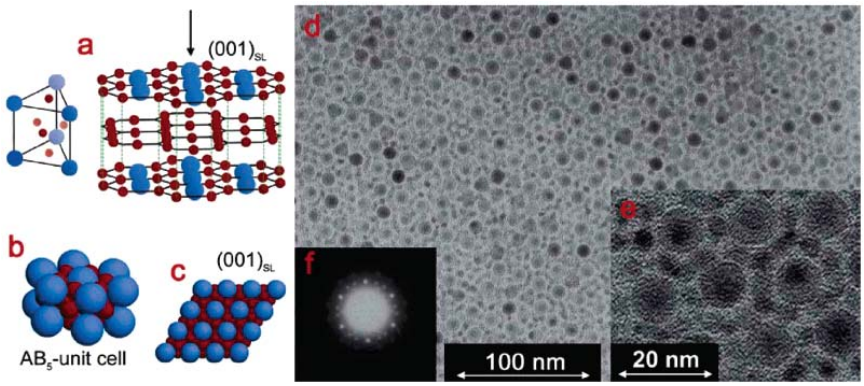


Figure 7.12 *TEM micrographs and sketches of AB_5 superlattices of 11-nm γ-Fe_2O_3 and 6.3-nm PbSe NCs: (a) depiction of the AB_5 structure as trigonal face-centered prism or layers; (b) hexagonal AB_5 unit cell; (c) depiction of the (001) plane; (d) projection of the $(001)_{SL}$ plane; (e) projection of the $(001)_{SL}$ plane at high magnification; (f) small-angle electron diffraction pattern from a 6 μm_2 (001) SL area.*[51]

(AB_{13} Superlattice) - Iron Oxide/Lead Sulfide

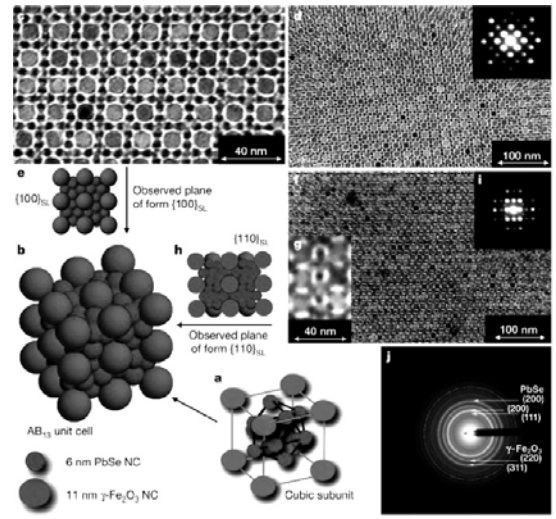


Figure 7.13. *TEM micrographs and sketches of AB_{13} superlattices of 11-nm -Fe_2O_3 and 6-nm PbSe NCs: (a) cubic subunit of the AB_{13} unit cell; (b) AB_{13} unit cell built up of eight cubic subunits; (c) projection of a $[100]_{SL}$ plane at high magnification; (d) same as (c) but at low magnification [(inset) small-angle electron diffraction pattern from a corresponding 6-μm^2 area]; (e) depiction of a [100] plane; (f) projection of a $[110]_{SL}$ plane; (g) same as (f) but at high magnification; (h) depiction of the projection of the [110] plane; (i) small-angle electron diffraction pattern from a 6-μm^2 $[110]_{SL}$ area; (j) wide-angle electron diffraction pattern of an AB_{13}-superlattice (SAED of a 6-μm^2 area) with indexing of the main diffraction rings for PbSe and -Fe_2O_3.*[51]

7.4.3 Metal-Silica Nanoparticle: [H-1:H-4] Type Nano-Compounds

Pioneering work by Halas, et al.[231, 234] beginning in the 1990s, described the synthesis of gold/silver nano-shells on monodisperse silica nanoparticles. These silica core-metal shell nano-compounds exhibited unique plasmon resonances that are tunable over a wide range of frequencies by merely changing the ratio of core-to-shell thickness (Figure 7.14) and absorbing light very strongly at different wavelengths throughout the visible and near-infrared region.[29]

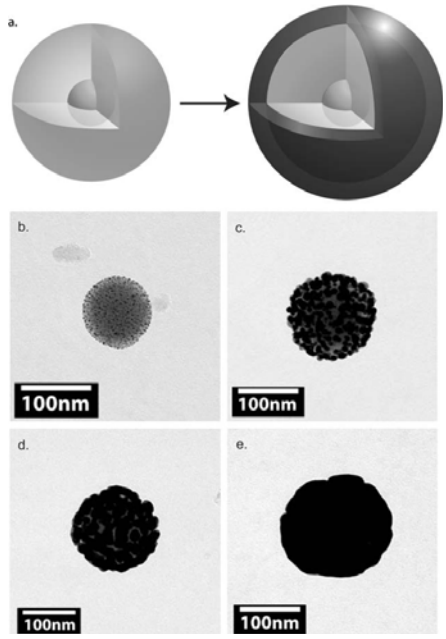


Figure 7.14. *(a) A schematic depiction of fluorescent core–shell silica nanoparticles encapsulated in a gold nanoshell, and (b–e) representative transmission electron micrographs (TEM) of fluorescent core–shell–gold nanoshell particles grown by step-wise synthesis as described in the text.*[29]

7.5 Soft Matter Nano-Compounds

This section focuses on nano-compound categories formed by chemical bonding of two or more of the six proposed soft nano-element categories (i.e., **S-1** through **S-6**) that fulfill the proposed nano-compound criteria (Section 7.2). These elements, as shown below, present a combinatorial grid (Figure 7.15) that predicts at least 31 compound possibilities. Space does not allow a comprehensive review, however, many examples of these of these categories have been reported in the literature and a few will be described below. Shorthand nomenclature (i.e., **[S-n: S-n],** *wherein*: **n= the categories 1-6 of the soft nano-element classification**) will be used to broadly identify nano-compound categories and will not necessarily define stoichiometries.

Soft Matter-Nano Element Categories					
Dendrimers Dendrons	Nano-latexes	Cross-linked Polymeric Micelles	Proteins	Viruses	RNA/DNA
S-1	S-2	S-3	S-4	S-5	S-6

Soft Matter Nano-Compounds						
Nano-Elements	Dendrimers Dendrons	Nano-latexes	Cross-linked Polymeric Micelles	Proteins	Viruses	DNA/RNA
Dendrimers Dendrons	S-1:S-1 1.	S-2:S-1 5.	S-3:S-1	S-4:S-1 2.	S-5:S-1 4.	S-6:S-1 3.
Nano-latexes		S-2:S-2	S-3:S-2	S-4:S-2	S-5:S-2	S-6:S-2
Cross-linked Polymeric Micelles		S-2:S-3	S-3:S-3 8.	S-4:S-3 7.	S-5:S-3	S-6:S-3
Proteins		S-2:S-4	S-3:S-4	S-4:S-4	S-5:S-4	S-6:S-4
Viruses		S-2:S-5	S-3:S-5	S-4:S-5	S-5:S-5	S-6:S-5
DNA/RNA		S-2:S-6	S-3:S-6	S-4:S-6	S-5:S-6 6.	S-6:S-6

Figure 7.15 *A combinatorial grid of soft matter nano-compounds (i.e.,[**S-n:S-n**], wherein: **n=1-6**) with references to reported examples.*

1. Dendrimer-Dendrimer: **[S-1:S-1]** Type Compounds [21, 32, 66, 80, 106, 235]
2. Dendrimer-Protein: **[S-1:S-4]** Type Compounds [67, 123, 236]
3. Dendrimer-DNA: **[S-1:S-6]** Type Compounds[60, 237, 238]
4. Dendrimer-Virus: **[S-1:S-5]** Type Compounds[239]
5. Dendrimer-Nano-latex: **[S-1:S-2]** Type Compounds[41]
6. Virus-DNA: **[S-5:S-6]** Type Compounds[240]
7. Protein-Protein: [**S-4:S-4**] Type Compounds[241]
8. Crosslinked Polymeric Micelle-Protein: [**S-3:S-4**] Type Compounds[242]

7.5.1 Dendrimer-Dendrimer: [S-1:S-1] Type Nano-Compounds

Saturated shell, nano-compounds (Figure 7.15) are prepared by a two-step approach which involved: (a) self-assembly of carboxylic acid terminated dendrimers (i.e., shell monomers) around a limited amount of amine terminated dendrimer (i.e., core) in the presence of LiCl and (b) covalent amide bond formation between the core and dendrimer shell monomers was accomplished by use of a carbodiimide reagent. These nano-compounds (i.e., saturated core-shell tecto (dendrimers), referred to as *megamers*, are prime examples of precise poly-dendrimer structures. These structures may be mathematically predicted by the Mansfield-Tomalia-Rakesh equation (Section 8.3.3; Figure 8.4)[21] and unequivocally verified by experimental mass spectrometry, gel electrophoresis and atomic force field microscopy (AFM).[21, 235]

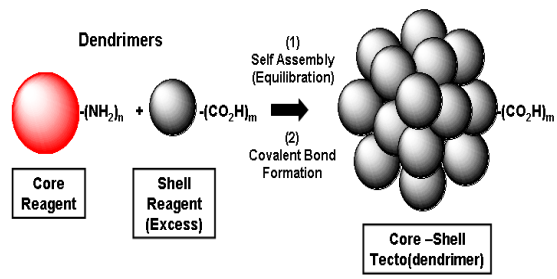


Figure 7.15. *The saturated-shell-architecture approach to megamer synthesis. All surface dendrimers are carboxylic acid terminated.*[38]

Unsaturated shell nano-compounds are prepared by a direct covalent-bond-formation method (Figure 7.16). This strategy involves the reaction of a limited amount of a nucleophilic dendrimer core reagent (i.e., amine terminated) with an excess of electrophilic (i.e., carbomethoxy ester terminated) dendrimer shell reagent (Step A).[32] This route involved the random parking of the reactive shell reagent on the core substrate surface. As a consequence, partially filled shell products are obtained (Figure 7.16) which possess relatively narrow, but not as precise molecular weight distributions as noted for saturated shell structures above. These distributions are determined by the core-shell parking efficiency prior to covalent bond formation. As shown (Figure 7.16), these unsaturated outer shell nanostructures will *auto-react* to form aggregates unless they are appropriately pacified as indicated in step B.

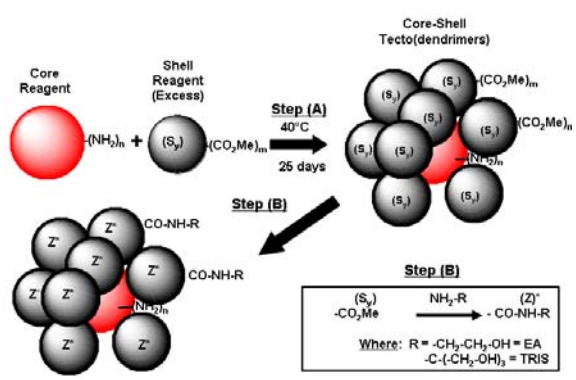


Figure 7.16. *Step A: the unsaturated-shell-architecture approach to megamer synthesis. Step B describes surface-capping reactions.*[32]

7.5.2 Dendron-Nanolatex: [S-1:S-2] Type Nano-Compound

Dendronized nano-latex structures were readily synthesized in aqueous solutions by allowing a nanolatex that had been surface functionalized with cyclam to react with dendrons possessing activated vinyl groups at their focal points (Figure 7.17).[41] The lower generation dendrons (i.e., Gen.=0) bonded to the latex surface with a mass ratio of 1 dendron:cyclam unit. The larger dendrons (i.e., Gen.=1 and 2) bonded to the nano-latex surface with mass ratios of 0.7 and 0.4: each cyclam, respectively. This may be evidence of *sterically induced nanoscale stoichiometry* (N-SIS) as we have described earlier.[21, 128]

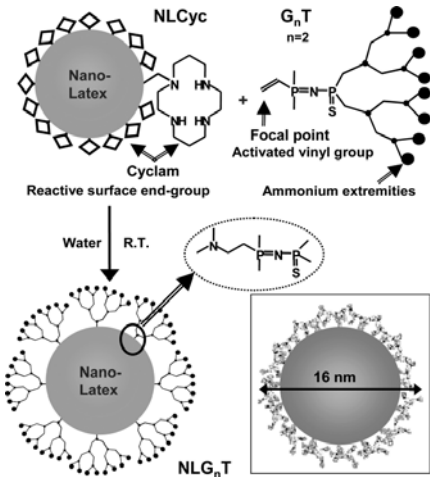


Figure 7.17. *Synthesis of dendronized nanolatexes; Generation n,* ***NLG_nT****. Insert: scaled cross-section of a dendronized nanoparticle* ***NLG_1T*** *showing the thin* ***G_1T*** *shell as CPK space filling molecular models.*[41]

7.5.3 Dendron-Protein: [S-1:S-4] Type Nano-Compounds

Kostiainen and Smith, et al.[67] recently reported the synthesis and thorough characterization of a 1:1 dendron-bovine serum albumin (BSA) compound as described in Figure 7.18. Synthesis of these precise **[1-S:4-S]** type nanostructures were achieved by allowing a dendron containing an N-maleimido group at its focal point to react *via* a 1,4-conjugate addition with a single free thiol group presented on the protein surface.

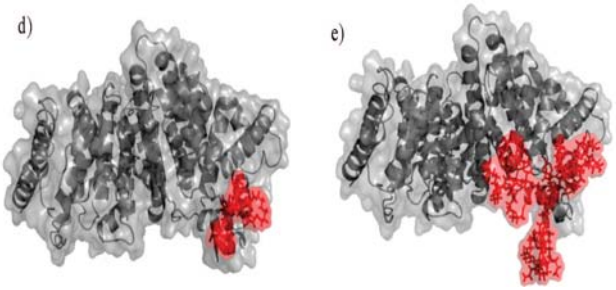


Figure 7.18. *Analytical data for protein–dendron conjugates. (a) Analytical HPLC chromatogram of the purified BSA, BSA-Gen.=1, and BSA-Gen.=2, showing decreasing retention volume with increasing dendritic generation; see Table 1 for values. (b) MALDI-TOF spectra of purified BSA, BSA-Gen.=1, and BSA-Gen.=2, showing increasing mass with increasing dendritic generation; see Table 1 for values. (c) CD spectra for all studied proteins and their dendron conjugates, confirming that the protein structure is not detectably changed by the attached dendron. Schematic computer generated models of (d) BSA-Gen.=1 and (e) BSA-Gen.=2. Cys-34 and the attached dendron are shown in red.*[67]

As early 1990, Tomalia/Roberts, et al.[236] were the first to report the conjugation of dendrimers to immuno-proteins (i.e., IgG antibodies) to form precise 1:1 nano-compounds, as illustrated in Figure 7.19. Since that time, substantial activity has focused on the synthesis and use of these precise conjugates as nano-devices for commercial cardiac marker diagnostics.[243 123]

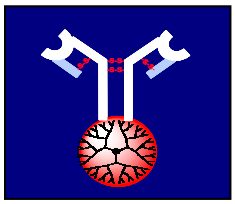


Figure 7.19. *Conjugation of amine terminated PAMAM dendrimers to the constant region of an IgG antibody.*

Similarly, Kannan, et al. [244] have reported the synthesis and characterization of a 1:1 dendrimer-protein (i.e., streptokinase, an enzyme) type nano-compound. Streptokinase is a 47kDa. single-chain protein that has been used clinically as an intravenous thrombolytic agent. Conjugation was accomplished using a standard activated ester procedure.

7.5.4 Dendron/Dendrimer- ssDNA: [S-1:S-6] Type Nano-Compounds

Marjoral, et al.[26] have recently reviewed this category of dendritic structure-DNA (i.e., soft-soft nanomaterial compounds). Samplings of the many reported DNA functionalized dendritic structural types (1-7) are as illustrated in Figure 7.20. We reported details on using dendritic structural type 3 (Figure 7.20) as a means for systematically controlling nanoscale shapes, as well as for designing differentiated terminal surface chemistry. Complementary single strand (i.e., ss-DNA) was conjugated to the focal points of various dendrons that were differentiated as a function of generation (i.e., size) and surface chemistry. These dendrons were then combined using Crick-Watson binding to produce the **[S-1:-S-6]** type nano-compounds as illustrated earlier in Section 6.2.5; Figure 6.47.

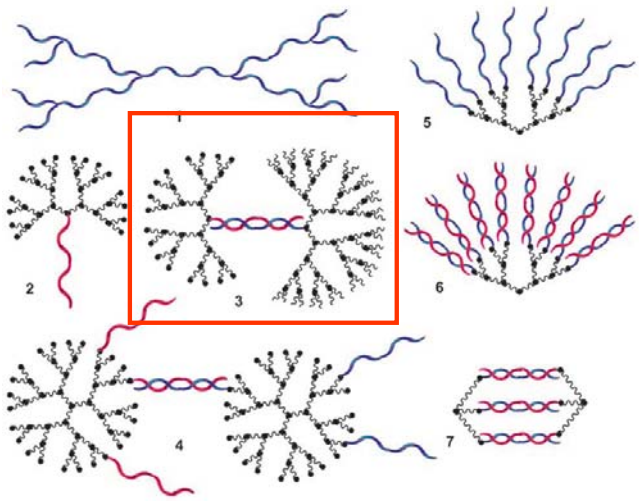


Figure 7.20. *Different types of dendritic structures incorporating oligonucleotides (nucleic acids) in their structure.*[26]

7.5.5 Virus- ssDNA-: [S-5:S-6] Type Nano-Compounds

Pioneering work by Finn, et al.[240] have shown that virions possessing complementary ss-DNA moieties may function as organizational scaffolding for DNA-directed assembly much like metal nanocrystals reported in Section 6.2.6; Figure 6.52.

7.6 Soft Matter-Hard Matter Nano-Compounds

This section focuses on nano-compound categories that fulfill the proposed nano-compound criteria (Section 7.2) by the chemical bonding of at least one or more of the six proposed soft nano-element categories (i.e., 1-S through 6-S) with one or more of the six proposed hard nano-element categories (i.e., H-1 through H-6). The soft and hard elements as shown below, present a combinatorial grid (Figure 7.21) that predicts at least 36 compound possibilities. Space does not allow a comprehensive review, however, many examples of these categories have been reported in the literature and a few will be described below. Shorthand nomenclature (i.e., **[S-n:H-n],** *wherein*: **n=the categories 1-6 of the soft (S) and hard (H) nano-element classifications**) will be used to broadly identify nano-compound categories, however, these notations will not necessarily define stoichiometries.

Soft/Hard Matter Nano-Compounds

Nano-Elements	Dendrimers Dendrons	Nano-latexes	Cross-linked Polymeric Micelles	Proteins	Viruses	DNA/RNA
Metal (M°) (Nanoclusters)	S-1:H-1 1.	S-2:H-1	S-3:H-1	S-4:H-1 9.	S-5:H-1	S-6:H-1 8.
Metal (Chalcogenide) (Nanocrystals)	S-1:H-2 2.	S-2:H-2	S-3:H-2	S-4:H-2 10.	S-5:H-2	S-6:H-2
Metal Oxide (Nanocrystals)	S-1:H-3 3.	S-2:H-3 6.	S-3:H-3	S-4:H-3 7.	S-5:H-3	S-6:H-3
Silica (Nanoparticles)	S-1:H-4 4.	S-2:H-4	S-3:H-4	S-4:H-4	S-5:H-4	S-6:H-4
Fullerenes	S-1:H-5 5.	S-2:H-5	S-3:H-5	S-4:H-5	S-5:H-5	S-6:H-5
Carbon Nanotubes	S-1:H-6	S-2:H-6	S-3:H-6	S-4:H-6	S-5:H-6	S-6:H-6

Figure 7.21. *A combinatorial grid of soft matter/hard matter nano-compounds (i.e.,[**S-n:H-n**], **where: n=1-6**) with references to reported examples.*

1. Dendrimer-Metal Nanocrystal: **[S-1:H-1]** Type Compounds [16, 245]
2. Dendrimer-Chalcogenide: **[S-1:H-2]** Type Compounds [245, 246]
3. Dendrimer-Metal Oxide: **[S-1:H-3]** Type Compounds [43]
4. Dendrimer-Silica: **[S-1:H-4]** Type Compounds [247]
5. Dendrimer-Fullerene: **[S-1:H-5]** Type Compounds [40, 248]
6. Nano-latex-Metal Oxide: **[S-2:H-3]** Type Compounds [20]
7. Protein-Metal Oxide: **[S-4: H-3]** Type Compounds [55]
8. DNA-Metal Nanoclusters: **[S-6:H-1]** Type Compounds [65, 218]
9. Protein-Metal Nanoclusters: **[S-4:H-1]** Type Compounds [249]
10. Protein-Metal Chalcogenide: **[S-4:H-2]** Type Compounds [250, 251]

7.6.1 Dendron-Metal Nanoclusters: [S-1:H-1] Type Nano-Compounds

Substantial work has been reported recently by Peng, et al.[252, 253] Fox, et al.[254] and Tomalia, et al.[245] that has focused on the dendronization of metal nanocrystals and cadmium chalcogenide (i.e., quantum dots). Initial dendronizations involved the self assembly of dendrons possessing thiol functionalized focal points by ligand exchange of the protective surfactants at the metal interface. Although these earlier thiol functionalized dendrons were found to reduce quantum dot fluorescence, it was subsequently found that replacing the thiol ligand with phosphine (Figure 7.22) improved fluorescence properties substantally.[11]

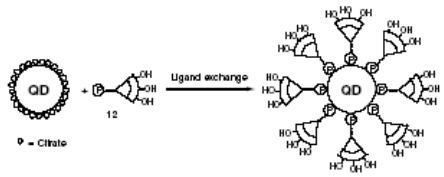


Figure 7.22. *Illustration of ligand exchange of phosphine functionalized dendrons with citrate protected quantum dots.*[11]

7.6.2 Dendrimer-Fullerene:[S-1:H-5] Type Nano-Compounds

Stoichiometric dendrimer core-fullerene shell nano-compounds were readily formed by allowing a generation=4; amine terminated (Z=64); poly(amidoamine) (PAMAM) dendrimer to react with an excess of buckminsterfullerene (C_{60}).[40] Approximately thirty (C_{60}) moieties bonded by Michael addition to the dendrimer surface to produce fullerene shelled structures with dendrimer cores as shown in Figure 7.23. These structures were exhaustively characterized by MALDI-TOF, TGA, UV-vis and FTIR. These nano-compounds exhibited fullerene type chemical features by readily generating singlet ($^1O_2$) in either aqueous or organic solvents.

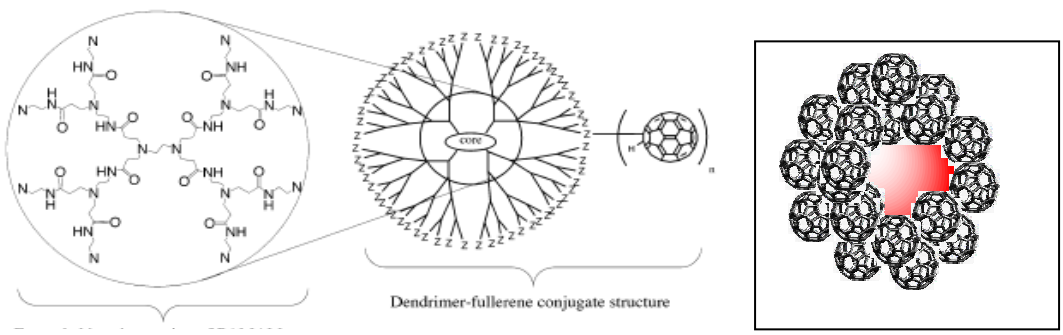


Figure 7.23. *Representative core-shell architecture of the PAMAM-fullerene conjugate (Z represents peripheral -NH_2 or-NH-, groups on the PAMAM dendrimer core component of the core-shell nano-compound).*[40]

7.6.3 Nanolatex-Metal Oxides: [S-2:H-3] Type Nano-Compounds

Core-shell type nano-latex: polyoxometalates (POM) compounds have been readily synthesized in aqueous solvents by the covalent attachment of thiol functionalized POMs to chlorobenzyl functionalized nano-latex surfaces.[20] Solutions of these nano-compounds did not exhibit significant aggregation even after several months. These nano-compounds were characterized by TEM, FTIR, EDX and TGA as

shown in Figure 7.24. The inorganic Dawson type POM shells were found to act as electron scattering domains and allowed their direct visualization by TEM that confirmed average nanoparticle diameters of 25 nm. Furthermore, photochromic properties normally associated with unbound POM compositions were observed for these POM shelled nano-compounds.

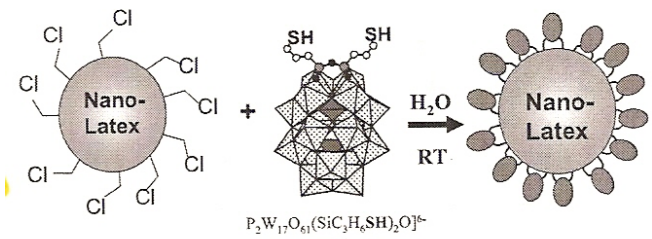
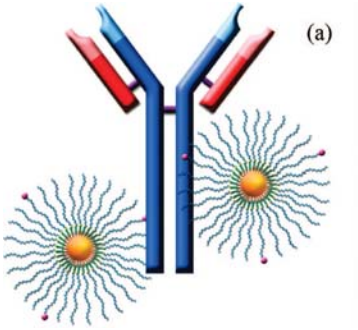


Figure 7.24. Synthesis of nano-latex: POM type nano-compounds at room temperature.[20]

7.6.4 Protein-Metal Oxide: [S-4:H-3] Type Nano-Compounds

Based on pioneering work by O'Brien, et al.[55] monodisperse, superparamagnetic γ-Fe_2O_3 nanoparticles with a core diameter of 5 nm have been coated with phospholipid reagents to give a covalently bonded coat contaiing maleimide functionality. These coated nanoparticles are monodispered with diameters of 10 nm (i.e., <10% deviation in diameter). They are then allowed to react with various IgG antibodies that have been modified using Traut's reagent to introduce thiol groups into their constant regions These thiol modified antibody proteins are allowed to react with the paramagnetic γ-Fe_2O_3 particles to produce stoichiometric nano-compounds with two metal oxide nanoparticles per protein as shown in Figure 7.25. These immuno-protein-metal oxide nano-compounds are able to target cells expressing specific target antigen receptor sites.

Figure 7.25. *(a) Schematic depicting the construction of the immuno targeted superparamagnetic iron oxide nanoparticle (ITSION). The iron oxide core (yellow, not to scale) is encapsulated in a brush-like shell of mPEG phospholipids. Maleimide functionalized mPEG phospholipids can bind to the antibody after modification to create R-SH groups, using Traut's reagent.*[55]



7.6.5 ss-DNA-Metal Nanocluster: [S-5:H-1] Type Nano-Compounds

7.6.5.1 One-Dimensional (1-D) Types

Earlier work by Mirkin, et al.[255] and Alivisatos/Schultz, et al.[54] reported a number of strategies involving the attachment of thiol functionalized ss-DNA to monodisperse nanocrystals of various sizes. These DNA functionalized nanocrystals were then allowed to undergo Crick-Watson base pairing to produce a wide variety of non-periodic homodimer, heterodimer, homotrimer and heterotrimer type nano-compounds as illustrated in Figure 7.26. *In all of these examples (i.e., 1-D and 3-D nano-compounds) ss-DNA functions primarily as a fundamental nanoscale* <u>*connector*</u> *module.* Many of these resulting binary nano-compounds are reminescent of those early examples of atom based compounds reported by J.Dalton in 1808 (Section 4.2.1: Figure 4.0).[5]

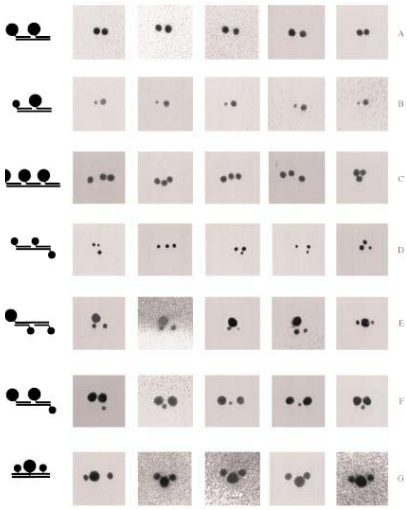


Figure 7.26. *Schematic illustrations and representative TEM images for specific nanocrystal molecules. See Scheme 1 for the synthesis strategies. A) 10-nm homodimer, synthesis strategy B; B) 10-/5-nm heterodimer, strategy B; C) 10-nm homotrimer, strategy B; D) 5-nm homo-trimer, strategy A; E) 10-/5-/5-nm heterotrimer, strategy A; F) 5-/10-/10-nm heterotrimer, strategy A; G) 5-/10-/5-nm heterotrimer, strategy C.*[54]

7.6.5.2 Three-Dimensional (3-D) Types

Earlier work by Mirkin, et al.[35] has shown that metal nanocrystals may be assymetrically functionalized with complementary ss-DNA and subsequently assembled into a variety of interesting architectures that includes: (a) cat paw, (b) satellite (i.e., core-shell tecto (dendrimer) like (Section 7.5.1; Figures 7.15-7.16) and (c) dendrimer-like architectures as shown in Figure 7.27.

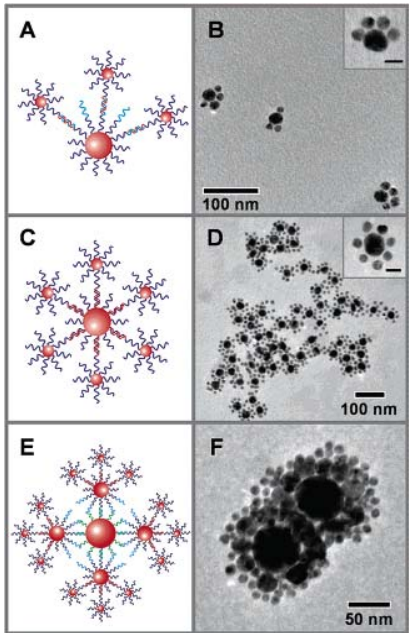


Figure 7.27. *Directional assembly of asymmetrically functionalized AuNPs into (A, B) cat paw, (C, D) satellite, and (E, F) dendrimer-like structures. Inset: scale bar) 20 nm.*[35]

Very recent work by Mirkin, et al.[65] and Nykypanchuk, et al.[218] has shown that complementary ss-DNA modules may be used as fundamental nanoscale connectors for guiding the assembly of well defined metal nanocrystals (i.e., **H-1 type nano-elements)** into crystalline 3-D super-lattices. These properties and features are truly reminescent of traditional picoscale atomic elements and their compounds. *It is very important as noted by Mirkin, et al.,*[65] *that the metal nanocrystals* <u>*have to be very monodisperse (i.e., >90%) as we have required in our criteria for nano-elements*</u> *(Section 5.2) in order to observe these 3-D crystalline properties.*

Gold nanocrystals (i.e.,10/15 nm), appropriately surface functionalized with tunable ss-DNA components as shown in (Figure 7.28), led to the assembly of a variety of crystalline superlattices. In a single-component system in which each particle can bind to every other particle with equal affinity, a close-packed face centered cubic (f.c.c.) structure is obtained; wherein, each particle has 12 nearest neighbors. On the other hand, in a binary system where a Au nanocrystal-x can bind only to Au-nanocrystal-y, the maximium number of hybridization events is achieved in a non-close packed body centered cubic (b.c.c.) structure; wherein, each particle has 8 nearest neighbors (i.e., such as a cesium chloride lattice).

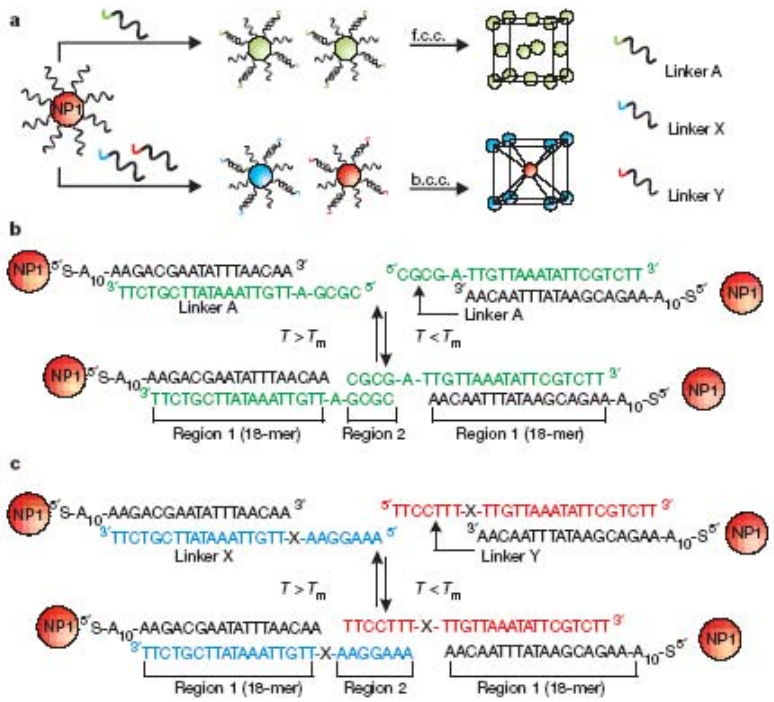


Figure 7.28. *Scheme of gold nanoparticle assembly method. (a) Gold nanoparticle–DNA conjugates can be programmed to assemble into different crystallographic arrangements by changing the sequence of the DNA linkers. (b) Single component assembly system (f.c.c.) where gold nanoparticles are assembled using one DNA sequence, linker-A. (c) Binary-component assembly system (b.c.c.) in which gold nanoparticles are assembled using two different DNA linkers -X and -Y. X in the DNA sequence denotes the flexor region: A, PEG6 or no base. NP1 indicates that the same gold nanoparticle- DNA conjugates were used in all experiments.*[65]

7.6.6 ss-DNA-(1-D Carbon Nanotubes): [S-5:H-6] Type Nano-Compounds

A very interesting strategy for coupling SWNTs, much as polymer chemists have traditionally coupled functionalized monomers to produce nylon, etc., has involved first: (a) chemically conjugating complementary ss-DNA to reactive SWNT termini by amidation, followed by (b) allowing the conjugated ss-DNA moieties to undergo Crick-Watson base pairing as shown in Figure 7.29. Although the stoichiometry of the base pairing is well understood, length control of the resulting extended SWNTs is questionable. We show this example to further emphasize the selective assembly function that ss-DNA can exhibit as a well defined nano-connector when conjugated to any of the earlier described hard or soft nano-element categories.

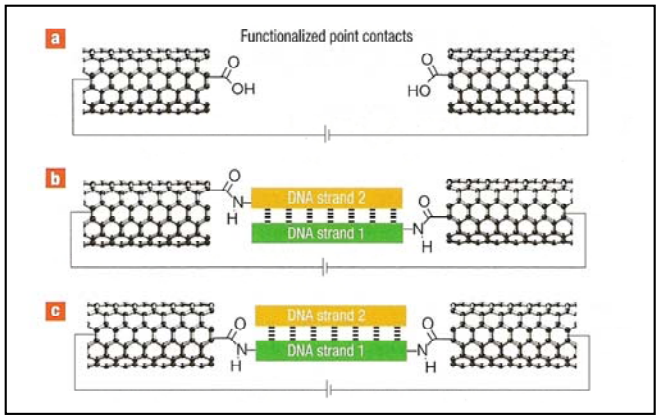


Figure 7.29. *A method to cut and functionalize individual SWNTs with ss-DNA strands. A, Functionalized point contacts made through the oxidative cutting of a SWNT wired into a device. B, Bridging by functionalization of both strands with amine functionality. C, Bridging by functionalization of one strand with amines on either end.*[48]

8.0 Observed Picoscale and Nanoscale Periodic Property Patterns

8.1 General Historical Comments

Historically, it took over 60 years from the time that J. Dalton first introduced his atom/molecular hypothesis (1808) until Mendeleev's Periodic Table was published and accepted in (1869) (Section 9.0, Figure 9.0). During that time, considerable activity was focused on the characterization and discovery of additional new elements, as well as the combinatorial synthesis and proliferation of new compounds derived from the chemical bonding of these elements. Also during that time, this activity led to the collection of an enormous array of **elemental periodic property patterns.** Most importantly, it was the critical archiving and analysis of these important periodic property patterns by Mendeleev, Lothar Meyer and others that made it possible to visualize the "grand order" that is compatible with modern theory that we now enjoy in our contemporary Periodic Table of the Elements.

It should be remembered that all of this activity occurred well before there was a deep and thorough understanding of chemical bonding theory, elemental bonding directionality, as well as the barest rudiments of electronic/quantum mechanical theory, etc. In spite of this scientific immaturity and naivety, the rational interpretations and logic applied to the empirical understanding of these observed periodic patterns served the science of chemistry and physics very well. From its inception to the present, the periodic table has been routinely replied upon as a dependable platform from which to predict important properties such as: (a) chemical reactivity,(b) physical properties,(c) toxicology, (d) materials function, (e) the prediction of new elements and (f) the design of new compound structures/materials to mention a few.

8.2 Overview of Observed Periodic Property Patterns

8.2.1 Picoscale Elements: 0-Dimensional Picoscale, Core-Shell Module (Atom) Periodicity

These periodic relationships and patterns are based primarily on *quantized, non-Newtonian type energy relationships (i.e., electron charge neutralization) involving core (proton/neutron nuclei) interactions with electrons occupying electron shells surrounding the nuclei, especially involving the outer electron shells*. These quantized, charge neutralization relationships define discrete energy levels that manifest unique systematic picoscale: (a) sizes (i.e., size/atom mass enhancement with atomic number, neutral vs. ionic atom sizes), (b) shapes (i.e., atomic orbital shapes, bonding directionalities, valencies), (c) atom surface reactivities (i.e., chemistry based on saturation level of outer electron shell) and (d) flexibility (i.e., polarizabilty of atom structure). These four critical atomic design parameters (CADPs) control and manifest (i) **physical properties** (i.e., metallic vs. non-metallic, physical state - gas, liquid, solid), as well as the observed (ii) **chemical properties** for all the elements of the universe. These parameters define the systematic, periodic patterns of behavior that become very predictable when organized and analyzed according the ***Mendeelev-Periodic Table of Elements*** (1869).

8.2.2 Nanoscale Elements: 0-Dimensional Nanoscale, Core-Shell Module Periodicity

Ideal periodic relationships/patterns for core-shell type structures in this dimensional hierarchy would be expected to be based on *quantized, Newtonian driven functional relationships between the core and concentric type surrounding shell domains of the nano-constructs (i.e., nano-elements). These relationships would especially involve composition, chemical connectivity, spacial arrangements/dynamics, band gap features and non-bonding interaction relationships that exist between the core and surface shell components (i.e., atoms, monomers, functional groups, etc.). Other such periodic property relations may also emerge from external interactions between unique nanoscale sizes,*

shapes, surface chemistries or flexibilities/polarizabilities that result from perturbations by temperature, electromagnetic radiation or interaction with other matter in various physical states. (i.e., gas, liquid, solid, etc.).

8.3 Reported Nano-Periodic Property Patterns

Although many reported examples of nano-periodic property patterns can be found in the literature, to our knowledge, no attempt has been made to organize these property patterns as a function of nanomaterial categories or in the context of an overall "nanomaterials big picture". In this section, we will focus on a few selected examples of property pattern categories that have been associated with traditional features of atom based elements in the past, namely: (a) physical, (b) photonic, (c) chemical reactivity and (d) toxicological. It was such archiving and classification of these atom based elemental periodic properties during the early 19th century that provided the first steps toward the evolution of the Mendeleev Periodic Table.

8.3.1 Periodic Physical Property Patterns

As a nano-cluster becomes smaller, the percentage of surface atoms becomes greater (Figure 8.0). Therefore, as the coordination number of the surface atoms becomes smaller than 9, these atoms are more easily rearranged than those in the center. Thus the melting process begins earlier. This accounts for periodic and systematic decrease in melting points as a function of nanoscale size as shown in Figure 8.1. Such a periodic property does not exist in bulk materials of the same elemental composition. The "magic numbers" associated with the shell saturation levels (Figure 8.0) have been well documented by mass spectrometry[112] and represent a very important nano-periodic property pattern.

TABLE 2.1 The relation between the total number of atoms in full shell clusters and the percentage of surface atoms

Full-shell Clusters		Total Number of Atoms	Surface Atoms (%)
1 Shell		13	92
2 Shells		55	76
3 Shells		147	63
4 Shells		309	52
5 Shells		561	45
7 Shells		1415	35

Figure 8.0. *The relationship between the total number of atoms in full shell clusters and the percentage of surface atoms.*[1]

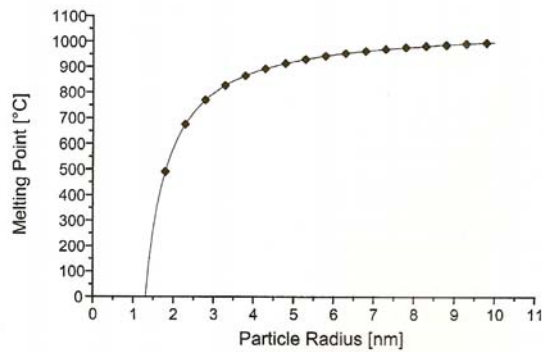


Figure 8.1. *The relationship between gold nanocrystal size and their melting points.*[1]

8.3.2 Periodic Photonic Property Patterns

When carriers and excitations are confined in all three dimensions in a 0-D nano-entity smaller than a De Broglie wavelength they manifest quantum confinement behavior and such systems are referred to as

quantum dots.[99] Accordingly, it is well known that hard nanoparticles (i.e., metal nanocrystals and semi-conducting cadmium chalcogenides) exhibit such periodic, size dependent photonic behavior and produce various emission colors in the visible region (Figure 8.2).

8.3.2.1 Hard Nano-Element Photonic Behavior

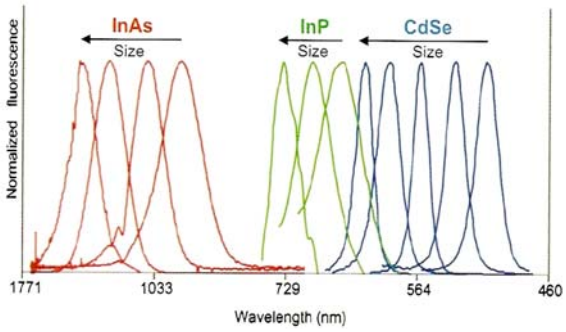
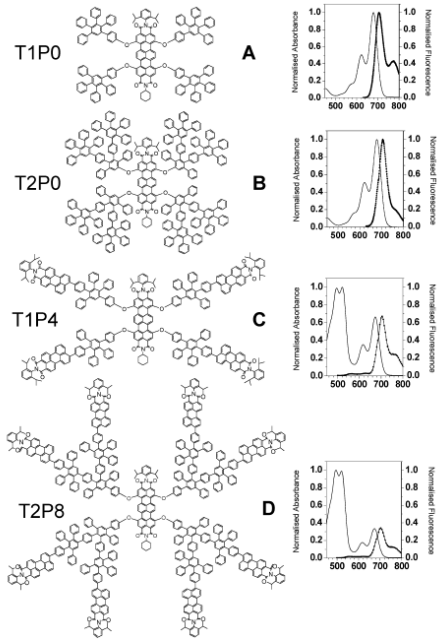


Figure 8.2. *A fluorescence image showing the bright colors achievable with quantum, and size and composition dependence of the optical emission spectra of capped InAs, InP and CdSe nanoclusters.*[36]

Recent work by De Schryver, et al.[63] has shown that similar photonic behavior occurs in dendrimer based soft nano-elements in which chromophores are presented from a dendritic scaffolding separated by rigid polyphenylene arms. Such a *single molecule* nano-property is referred to as an *intramolecular directional Forester resonance energy transfer effect*. This photonic property appears to be size (i.e., generation) dependent and related to the rigidity of the dendritic structure (Figure 8.3).

8.3.2.2 Soft Nano-Element Photonic Behavior

Figure 8.3. *Structures of the investigated dendritic compounds together with the corresponding ensemble steady-state absorption and emission spectra in toluene for the (A) first-generation model compound T1P0, (B) second-generation model compound (T2P0), (C) first-generation perylenemonoimide-terrylenediimide dendrimer (T1P4), and (D) second-generation perylenemonoimide-terrylenediimide dendrimer (T2P8).*[63]



8.3.3 Periodic Chemical Reactivity/Physical Size Property Patterns

Recent work on soft matter nano-elements (i.e., dendrimers),[21] has demonstrated that mathematically defined, periodic size properties of spheroidal dendrimers determine chemical reactivity patterns that are involved in the assembly of precise dendrimer clusters (i.e., core-shell (tecto) dendrimers). Mathematical

relationships (i.e., the Mansfield-Tomalia-Rakesh Equation) predict dendrimer cluster saturation levels (i.e., magic numbers for dendrimer shells) as a function of the size of the core dendrimer relative to the size of the shell dendrimers that are being used to construct the dendrimer cluster. These periodic property patterns and magic shell relationships (Figure 8.4) are very reminiscent of those observed for metal nanocrystals (Figure 8.0).

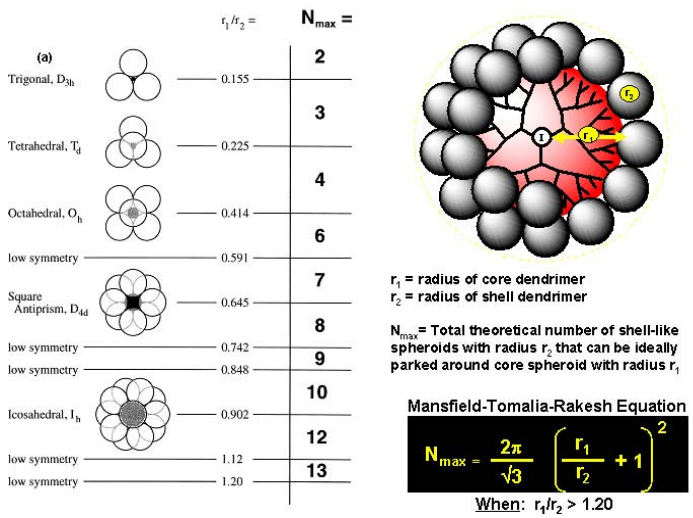


Figure 8.4. *(a) Symmetry properties of core–shell structures, where $r_1/r_2 > 1.20$. (b) Sterically induced stoichiometry (SIS) based on the respective radii of core and shell dendrimers. (c) Mansfield–Tomalia–Rakesh equation for calculating the maximum shell filling when $r_1/r_2 > 1.20$.*[21]

8.3.4 Periodic Toxicological Property Patterns

Important structure dependent nanotoxological properties for 1-D carbon nanotubes have been reported recently by several international groups.[256-258] This work clearly demonstrated a periodic property pattern that appears to show that related asbestos-type toxicity may be associated with carbon nanotube structure/architecture as a function of their 1-D aspect ratios (Figure 8.5).

These studies showed that high aspect ratio (i.e. >20 μm) multi-walled nanotubes (MWNTs) interact in *vivo* with the mesothelium domain in normal mice causing inflammation and granulomas. The authors also show that, in contrast, short MWNTs (i.e. <10 μm) do not interact with the mesothelium.[258] These results appear to parallel similar results noted in the past concerning the carcinogenicity of asbestos.[259] Apparently, short, highly functionalized multi-walled nanotubes (f-MWNTs) are excreted in the urine without any apparent physiological abnormalities in normal mice.[257] This is an important observation in that unique physical, chemical and electronic properties of carbon nanotubes (CNTs) have initiated considerable activity for their use in a variety of nanomedical applications.

Similarly, periodic nanotoxological patterns have been noted by Colvin, et al.[46] for 0-D fullerenes that are based on the type and amount of nanoparticle surface functionality. Generally, higher levels of water solubilizing functionality on a fullerene surface tended to reduce toxicity (Figure 8.6). An extensive review covering periodic cytotoxicity property patterns for a large variety of hard (i.e., 0-D and 1-D) has recently been published by Lewinski, et al. [260]

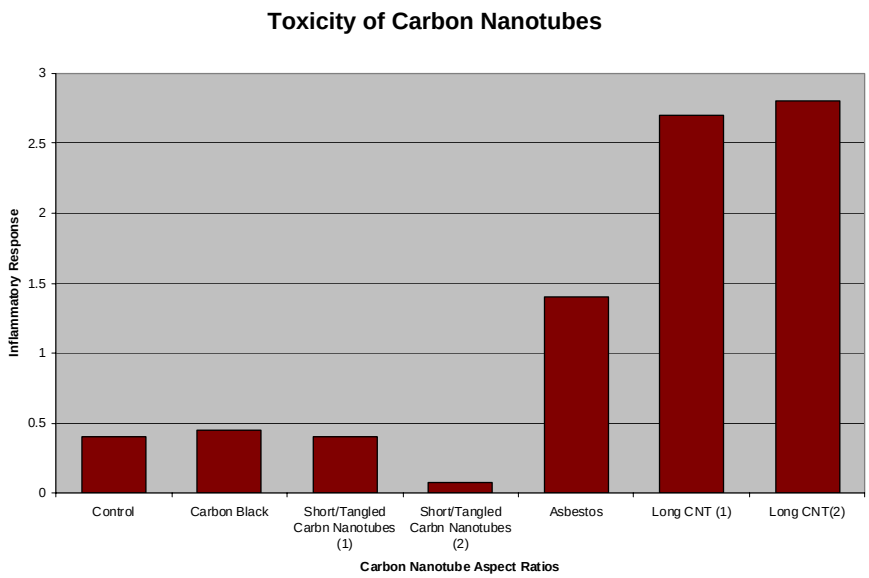


Figure 8.5. *A comparison of inflammatory response for MWCNT's as a function of aspect ratio compared to asbestos and controls.*

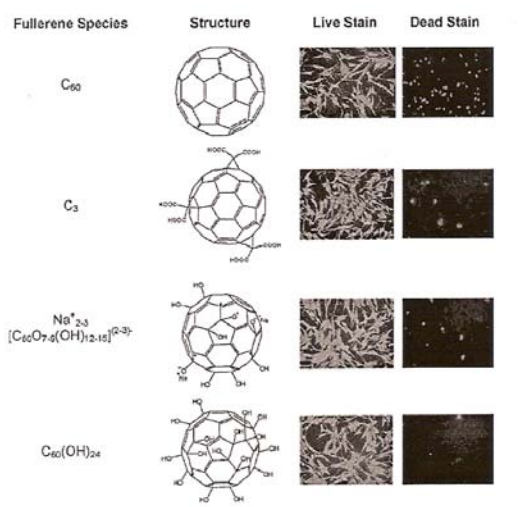


Figure 8.6. *Structures and human dermal fibroblast live/dead cell viability assay results for C_{60} and derivatives.*[46]

8.4 Periodic Magnetic Property Patterns

Rotello, et al.[43, 261] prepared a series of PAMAM dendrimer-magnetic Fe_2O_3, type 3-D lattices by charge neutralization of cationic surface modified magnetic metal oxide nanocrystals with increasingly larger generations of anionic surface modified PAMAM dendrimers (Figure 8.7). As a function of dendrimer generation, they were able to control interparticle spacing of the magnetic nanoparticles over a 2.4 nm

range (Figure 8.8). This allowed them to demonstrate very effective modulation of collective magnetic behavior by systematically lowering the dipolar coupling between particles to provide a systematic, periodic change in magnetic properties as shown in Figure 8.9.

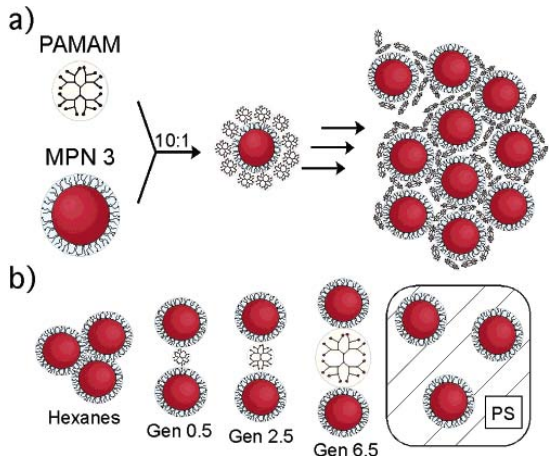


Figure 8.7. *(a) SAXS plots shown after background subtraction and normalization. (b) The systematic increase in interparticle spacing as the PAMAM generation increased. (Average spacing: d (Å)) 2ð/q).*[43]

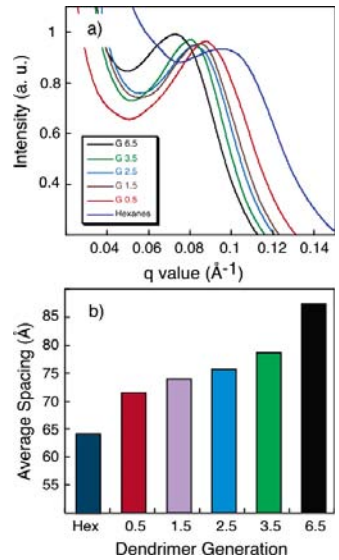


Figure 8.8. *(a) Schematic depiction of dendrimer-mediated nanoparticle assembly. (b) Increase in average interparticle spacing upon assembly with PAMAM dendrimers, as well as hexane and polystyrene controls.*[43]

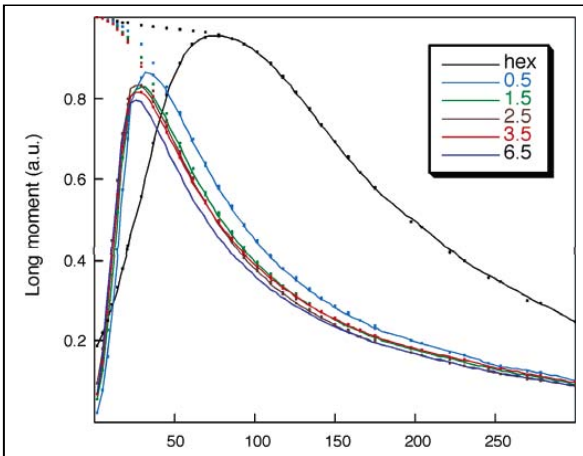


Figure 8.9. *Field cooled (FC) and zero field cooled (ZFC) magnetization plots for each sample, showing the steady decrease in T_B (magnetism) as the particles are spaced farther apart from one another.*[43]

9.0 Conclusions

Atom mimicry with wooden spheroids, according to Dalton (1808), provided the first working premise and rationale for understanding the relationships and behavior of our *well defined* picoscale building blocks (i.e., atomic-elements) as we recognize them in our traditional chemistry paradigm.

It now appears that Dalton's concepts and rationale may be used for describing similar atom mimicry at the nanoscale. As such, certain structure controlled ***critical nanoscale design parameters (CNDPs)*** exhibited by both hard and soft matter nano models have encouraged us to define, so-called ***nano-elements***. This atom mimicry with structure control is well demonstrated in the two major nanomaterial categories; namely, ***hard nano-matter (i.e., metal nanocrystals) and soft nano-matter (i.e., dendrimers).*** Furthermore, there is substantial experimental evidence in the literature for accepting the concept of chemically linking these proposed nano-elements to produce ***nano-compounds.***

Intrinsic ***nano-periodic property patterns*** have been noted for a variety of nano-modules (Section 8.0) that appear to fulfill the profile (criteria) proposed for nano-elements, as well as their use for the synthesis of corresponding nano-compounds. Nano-elements should be expected to manifest totally different periodic patterns and emerging properties than those observed for atoms according to Nobel Laureate P.W. Anderson.[82] Preliminary evidence indicates, that these nano-periodic patterns appear to be following that prediction

Where Are We in the Evolution of a Philosophy for Nano-Elements and a Nano-Periodic Table?

From a historical perspective, one can observe the patterns of progress and regression toward our contemporary philosophy for picoscale elements and subsequent evolution to Mendeleev's Periodic Table (Figure 9.0). From A. Lavoisier's first introduction of atomism to J. Dalton's introduction of a chemical philosophy for understanding combining weights/ratios, etc. to account for molecular compound formation, etc. it took 19 years (i.e., 1789-1808). Undoubtedly, the French Revolution and opponents such as Berthollet slowed down more rapid development of Lavoisier's atomist concept. It should be noted, that from Dalton's introduction of his first primitive periodic table and *Philosophy for a Chemical System* (1808) to the acceptance of Mendeleev's Periodic Table (1869), it took over 61 years for this evolution. This evolutionary progress required the accumulation of innumerable picoscale periodic property patterns that were pioneered by the legendary list of scientists that made contributions between Dalton and Mendeleev (Figure 9.0).

Thus far, nanomaterial periodic property patterns observed for both soft and hard nano-matter categories appear to offer a very promising premise. With further development, it should be possible to evolve a deeper understanding of these patterns. Future documentation of such nano periodic property patterns should inspire the initiation of appropriate new concepts, theories and rules that, with experimental confirmation, should allow the *a priori* prediction of properties/behavior patterns for a wide range of nanomaterials, both known and yet to be discovered. More specifically, understanding such nano periodic property patterns arising from chemical/physical/energy perturbations and their interactions with biological/environmental systems should be expected to provide invaluable information for designing more effective nano-device function as well as for defining reasonable nanomaterial risk/benefit parameters.

In conclusion, it is proposed that with well grounded step logic, supported by historical precedence, as well as by specific peer reviewed literature examples, we have taken the first steps toward defining a ***systematic, central dogma for synthetic nano-chemistry.*** Furthermore, based on peer reviewed literature

examples of ***nano-periodic property patterns*** documented in this report, there is considerable optimism that appropriate first steps have been taken toward defining a ***future Nano-Periodic Table(s).***

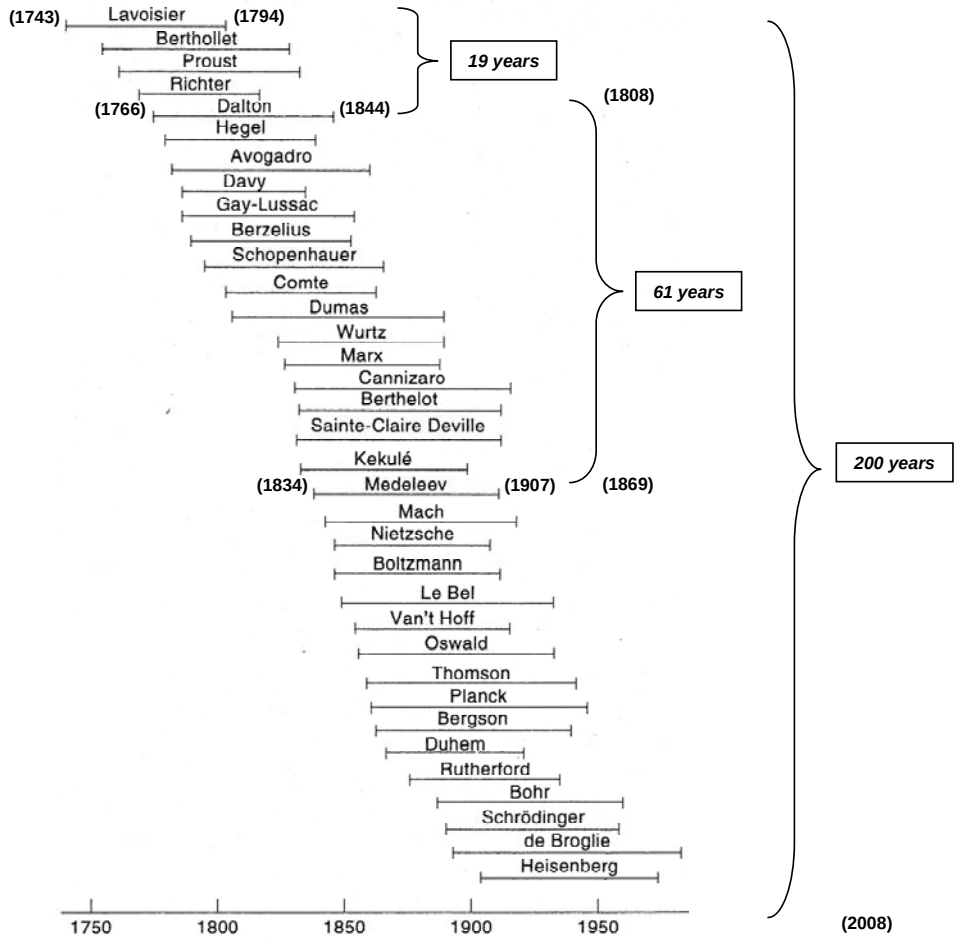


Figure 9.0. *Chronological list of proponents and opponents of (atomistic) picoscale elemental concepts/periodic table and contemporary traditional chemistry dogma.*[8]

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Appendix: A - Abstracts/Biographies

National Science Foundation Workshop

Periodic Patterns, Relationships and Categories of Well-Defined Nanoscale Building Blocks

(September 24-25, 2007)

Central Michigan University
Mt. Pleasant, Michigan 48859

NNI Context and Workshop Goals

M.C. Roco
National Science Foundation and National Nanotechnology Initiative

Nanoscience and nanotechnology have opened an era of integration of fundamental research and engineering from the atomic and molecular levels, increased technological innovation, and an enabling base for improving human health and cognitive abilities in long term. The rudimentary capabilities of nanotechnology today are envisioned to evolve in four overlapping generations of new nanotechnology products: passive nanostructures, active nanostructures, systems of nanosystems, and molecular nanosystems.

This introductory presentation will provide the context of international nanotechnology development and an overview of the National Science Foundation and National Nanotechnology Initiative support to nanoscale research and education. The particularities and challenges in characterizing the nanoscale building blocks (nanoscale modules, nanoparticles) will be discussed. The need for a new approach of classification based on the internal and surface structure will be underlined. On this basis, the goals of the workshop will be outlined.

Biography

Dr. M.C. Roco is the Senior Advisor for Nanotechnology at the National Science Foundation (NSF) and a key architect of the National Nanotechnology Initiative. Dr. Roco is credited with thirteen patents and contributed over two hundred articles and fifteen books, including recently "Nanotechnology: Societal Implications - Maximizing Benefits to Humanity" (Springer, 2006) and “Managing Nano-Bio-Info-Cogno Innovations” (Springer, 2007). Under his stewardship the nanotechnology federal investment has increased from about $3 million to $1.3 billion in 2006. Dr. Roco is a corresponding member of the Swiss Academy of Engineering Sciences and a member of the International Risk Governance Council. He is a Fellow of ASME, AIChE and Institute of Physics, and was elected as Engineer of the Year by the U.S. Society of Professional Engineers and NSF in 1999 and again in 2004. Forbes magazine recognized him in 2003 as the first among “Nanotechnology’s Power Brokers” and Scientific American named him one of 2004’s top 50 Technology Leaders. Dr. Roco coordinated the preparation of the U.S. National Science and Technology Council (NSTC) reports on "Nanotechnology Research Directions" (NSTC, 1999) and "National Nanotechnology Initiative" (NSTC, 2000).

The Big Picture: From Synthetic Small Molecule Chemistry (1808) to Synthetic Nano Chemistry (2008)

Donald A. Tomalia
Dendritic Nanotechnologies, Inc./Central Michigan University, Mt. Pleasant, MI

Elemental classifications characterized by well defined elementary compositions provided the basis for A. Lavoisier to publish his *Traite Elementaire de Chimie (1789).* This document described the first 23 known elements at that time. These early categories of "well defined, atom building blocks" with J.L. Proust's *Law of Definite Proportions* (1797) allowed J. Dalton to present his seminal proposal entitled: *New System of Chemical Philosophy* (1808). This proposal, presented nearly 200 years ago, embraced the principles of module chemical bond formation with well defined valency. Based on his naivety of atomic structure, Dalton utilized wooden spheres labeled with special icons as *atom mimics* to identify unique elemental internal structures and as yet undefined surface interactive properties. This new vision inspired countless numbers of disciples during the 19-20th century to use these well-defined modules as a palette for the combinatorial preparation of literally millions of more complex compounds/assemblies/ materials possessing a vast array of novel architectures, reactivities and physico-chemical features. Most profound was the fact that these new molecular compounds exhibited unique, new properties that were dramatically different than the intrinsic properties of the building blocks. For example, many of these new complexities exhibited toxicology and corrosion properties that were dramatically different than the intrinsic features of their building blocks (e.g., NaCl). Most importantly, many of these molecular complexities have manifested enormous benefits and applications that have dramatically enhanced the human condition. We now recognize the science of constructing these molecular level complexities as the basis and core of our *sub-nanoscale,* "traditional synthetic chemistry" paradigm.

In this bicentennial moment of history, the time is appropriate to examine and apply the proven principles of Lavoisier and Dalton for defining the next hierarchical level of complexity. In the context of atom mimicry, it will be important to understand quantized nano-properties, periodic size/shape patterns, stoichiometries and surface chemistry features of our present well-defined nano-modules.[1-3] An expected consequence of using our present well-defined nano-modules in the rational synthesis of higher level nano complexity (i.e., nano compounds) will be a deeper articulation of these important combining parameters and the evolution of many new nanoscale rules.[3-4] The emergence of this science should be expected to offer a systematic basis for defining benefit driven nano-constructs (devices) that will provide attractive nano engineering solutions for the enhancement of society. I will review several examples of atom mimicry, quantized nano-properties,[5] a successful commercial nanodevice (i.e., Stratus® diagnostics,[6] Siemens AG) and a surprising new fluorescence property observed with nano-modular dendrimers.

1. D.A. Tomalia, *Advanced Materials*, 6, 7/8, 529 (1994).
2. S. Uppuluri, D.R. Swanson, L.T. Piehler, J. Li, G.L. Hagnauer, D.A. Tomalia, *Adv. Mater.*, 12(11), 796-800 (2000).
3. D.A. Tomalia, H.M. Brothers II, L.T. Piehler, H. Dupont Durst, D.R. Swanson, *Proc. Nat. Acad. of Sciences*, 99(8), 5081-5087 (2002).
4. M.L. Mansfield, L. Rakesh, D.A. Tomalia, *J. Chem. Phys.*, 105(8), 3245-3249 (1996).
5. D.A. Tomalia, *Prog. Polym. Sci.*, 30, 294-324 (2005).
6. "*Dendrimers and Other Dendritic Polymers*," D.A. Tomalia and J.M.J. Fréchet, J. Wiley, (2001).

Biography

Dr. Tomalia received his B.A. in chemistry from the University of Michigan and while at The Dow Chemical Company (1962-1990) completed his Ph.D. in physical-organic chemistry from Michigan State University (1968) under the mentorship of Professor Harold Hart. His discovery of the cationic polymerization of 2-oxazolines led to two international industrial research awards (R&D-100) for creative research in 1978 and 1986. His discovery of dendrimers (dendritic architecture) in 1979 led to a third R&D-100 Award in 1991 and the Leonardo da Vinci Award (Paris, France) in 1996. He recently received the Society of Polymer Science Japan (SPSJ) Award for Outstanding Achievement in Polymer Science (2003) for discovery of the fourth major macromolecular architectural class, *dendritic polymers*.

In 1990, he joined the Michigan Molecular Institute (MMI) as Professor and Director of Nanoscale Chemistry & Architecture (1990-99). Dendritech, Inc., the first commercial producer of dendrimers, was co-founded by Dr. Tomalia in 1992 after which he was named founding President and Chief Scientist (1992-2000). He became V.P. of Technology for MMI (1998-2000) while simultaneously serving as Scientific Director for the Biologic Nanotechnology Center, University Michigan Medical School (1998-2000).

Dr. Tomalia founded Dendritic Nanotechnologies, Inc. (DNT), Mt. Pleasant, Michigan, in a joint venture with Starpharma Pooled Development (Melbourne, Australia) (2002). He serves as Chief Scientific Officer of this dendrimer-based nanotechnology company with production and laboratory facilities located at Central Michigan University, Mt. Pleasant, Michigan. Dr. Tomalia was recently appointed scientific director of the National Dendrimer & Nanotechnology Center located on the Central Michigan Campus (2004). Presently, Dr. Tomalia is the DNT Principal Investigator in the Massachusetts Institute for Technology/Institute for Soldier Nanotechnologies (MIT/ISN) (2003). Other positions currently held by Dr. Tomalia include *Distinguished Visiting Professor* (Columbia University), *Distinguished Research Scientist/ Professor* (Central Michigan University), Chairman - External Peer Review Panel for Environmental Protection Agency (EPA) "Nanotechnology White Paper" (2006), Washington, D.C. and a member of the Board of Directors of the American Academy of Nanomedicine (AANM) (2006).

He is listed as the inventor of over 110 U.S. patents and is author/coauthor of more than 200 peer reviewed publications. Over 170 papers are focused in the dendrimer/dendritic polymer field, including a monograph entitled "*Dendrimers and Other Dendritic Polymers"* (J. Wiley) co-edited with J.M.J. Fréchet (2001). Dr. Tomalia serves as Associate Editor for Nanomedicine (Elsevier) (2006-), editorial advisory board of *Bioconjugate Chemistry* (1999-) and is a founding member of the editorial advisory board for *NanoLetters* (2000-2004).

Theory and Simulation Applied to Nanoscale Building Blocks

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The critical challenge in meeting the promise of nanotechnology is controlling and restructuring matter at the scale of 0.1 to 100 nm. Enormous progress has been achieved with the synthesis and characterization of amazing nanostructures, some of which are now being organized to form active nanosystems with applications ranging from superdense memory to drug delivery systems. The challenge in the next few years is to develop the additional active nanocomponents required for a variety of applications and then to build these active elements into nanosystems.

Theory and simulation to predict accurately the structures, properties, and dynamics of nanoscale systems are essential to making the progress needed to guide these developments. It is essential to predict these properties in advance of synthesis and characterization and to analyze the observed performance to improve the nanosystems.

We will describe some of the new methods being developed to enable such applications with examples on their recent applications. This includes

- ReaxFF reactive force fields for predicting the chemical processes of large-scale nanosystems (millions of atom)
- The eFF method for describing the plasma processing of such processes with an emphasis on damage free low energy electron etching (LE4)
- The CMDF (computational materials design facility) for multiparadigm multiscale simulations on systems with millions of atoms,

Then we will discuss some of the challenges in developing the theory and simulation toward the applications of the next decade.

We will illustrate the progress with examples on dendritic macromolecules, which are emerging as a most versatile class of nanoscale building blocks. These “soft” nanoparticles, with sizes in the range of 1 to 10 nm, provide useful hosts for cations, anions, and organic solutes. Dendritic macromolecules are also useful as scaffolds and templates for the preparation of metal-bearing nanoparticles with tunable electronic, optical, and catalytic properties. They have already been successful as delivery vehicles or scaffolds for bioactive compounds. Dendritic macromolecules can be functionalized with a variety of surface groups to make them soluble in appropriate media or bind onto appropriate surfaces. They can also be covalently linked to each other or attached to other macromolecules to form supramolecular assemblies. These unique properties of dendritic macromolecules provide new opportunities for developing novel functional materials for a range of applications including chemical separations and catalysis, chemical sensing, medical imaging, DNA/drug delivery, energy conversion/storage and water purification. We will illustrate the opportunities and progress with an overview of recent advances in the simulation of the structures and host-guest properties of PAMAM and PPI dendrimers in aqueous solutions.

Biography

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Current Positions at the California Institute of Technology:
Charles and Mary Ferkel Professor of Chemistry, Materials Science, and Applied Physics
Director of Materials and Process Simulation Center (MSC)

Previous Professional Positions (all at Caltech):

2001-present	Charles and Mary Ferkel Professor of Chemistry, Materials Science, Appl. Phys.
1990-present	Director of Materials and Process Simulation Center (MSC)
1984-2001	Charles and Mary Ferkel Professor of Chemistry and Applied Physics
1992-1997	Director of NSF Grand Challenge Applications Group at Caltech
1965-1978	Assistant, Associate, and Full Professor of Theoretical Chemistry
1984-1990	Director of NSF Materials Research Group at Caltech
1978-1984	Professor of Chemistry and Applied Physics

Education:
Ph.D. Engineering Science (minor physics), California Institute of Technology, 1965;
B. S. Engineering (Highest Honors), University of California, Los Angeles, 1960.

Awards and Honors:
Awarded National Science Foundation Predoctoral Fellowship (1960-1964)
Awarded Alfred P. Sloan Research Faculty Fellowship (1967-1969)
Awarded Buck-Whitney Medal of NY Section of American Chemical Society (1978)
Elected Member of National Academy of Science (1984)
Elected Member of International Academy of Quantum Molecular Science (1988)
Elected Fellow of American Physical Society (1988)
Winner American Chemical Society Award for Computers in Chemistry (1988)
Elected Fellow of American Association for the Advancement of Science (1990)
Awarded Richard M. Badger Teaching Prize in Chemistry, Caltech (1995)
Awarded Feynman Prize for Nanotechnology Theory (1999)
Awarded NASA Space Sciences Award (2000)
Awarded Richard Chase Tolman Prize from the Southern California Section of the ACS (2000)
Named by ISI as a most Highly Cited Chemist for 1981 to 1999 (http://isihighlycited.com)
Winner 2002 Prize in Computational Nanotechnology Design from the Institute for Molecular Manufacturing
Awarded Honoris Causa Philosophia Doctorem, Chemistry, Uppsala U., Sweden, January 2004
Winner American Chemical Society Award for Theoretical Chemistry (2007)

Other Professional Activities:

Consultant (at various times): General Electric, General Motors, Shell Development, Imperial Chemical Industry, BP, Exxon, Chevron, SOHIO, Dow Chemical, AT&T Bell Labs, Union Carbide, Celanese, Allied Signal, UOP, 3M, Proctor and Gamble, Dow Corning, Nissan, MSI (Accelrys), Schrödinger, Eidogen, Systine, Allozyne

Member, Board of Trustees Gordon Research Conferences 1988-1994

Cofounder of Molecular Simulations Inc. (now named Accelrys) (1984), San Diego CA. Member Board of Directors (84-95), Chairman Board (84-91)

Cofounder of Schrödinger Inc. (1990), New York City. Member Board of Directors 1990-2000

Cofounder Eidogen Inc (now Eidogen-Sertanty San Diego CA) (2000), Chairman Board of Directors (2000-2005)

Cofounder Systine Inc. Pasadena CA (2001), Chairman Board of Directors 2003-present

Cofounder-Allozyne Inc. (2004), now in Seattle Washington, Member Scientific Advisory Board

Cofounder Qateomix Inc., Covina CA (2005), Chairman Board of Directors.

Current Research Interests:

- New methodology for quantum chemistry, force fields, molecular dynamics, mesoscale dynamics, statistical mechanics
- Applications of atomistic simulations to chemical, biological, and materials systems, including catalysis (homogenous and heterogeneous), polymers, semiconductors, ceramics, and metal alloys
- protein structure prediction (GPCRs), drug design, incorporation of non-natural amino acids
- Applications of theory to industrial problems in catalysis, polymers, fuel cells, energetic materials, and drug design.
- Computational Nanotechnology with applications to nanoelectronics.

Current Research Funding: National Science Foundation, National Institutes of Health, Department of Energy, Defense Advanced Research Projects Agency, Army Research Office, Office of Naval Research, Environmental Protection Agency, Chevron, Sanofi-Aventis, Berlex Biopharma, Nissan Corp, Intel Corp., Dow-Corning, Pfizer, Boehringer-Ingelheim.

Research publications: Over 710, see http://www.wag.caltech.edu/publications/papers/
Web site: http://www.wag.caltech.edu/

Autobiography of the early period in Goddard's career: "Critical Points and Random Events that Shaped the Early Career of William A. Goddard III" in J. Phys. Chem. A 104, 2147 (2000) (the Goddard Festschrift containing articles celebrating Goddard's 60th birthday http://pubs3.acs.org/acs/journals/toc.page?incoden=jpcafh&indecade=0&involume=104&inissu=11)

Scientific genealogy

- William A. Goddard III obtained his Ph.D. in Engineering Science with a minor in Physics in October 1964 from Prof. Pol Duwez, Professor of Materials Science at Caltech, Pasadena CA

- Pol Duwez received his D.Sc. in 1933 from Prof. Emile Henriot, Professor of Physics at U. Brussels in Belgium
- Emile Henriot received his D.Sc. in Physics in 1912 from Prof. Marie Curie at the Sorbonne, Paris France
- Marie Curie received her D.Sc. in 1903 from Prof. Henri Becquerel at the Ecole Phys. Chim. Ind, Paris France
- (Antoine) Henri Becquerel obtained the Engineer's Degree in 1877 from the École des Ponts et Chaussées (Bridges and Highways School; 1874-77) and was Administrator Ponts et Chaussées (1877-1906). He received his PhD from at the Ecole Phys. Chim. Ind, (ESPCI) Paris in 1890 working with Charles Friedel in the laboratory of mineralogy
- Charles Friedel obtained a BS in Strasbourg (1850) and a PhD in chemistry and mineralogy 1869) from the Sorbonne with Adolphe Wurtz. He was Prof. Mineralogy (1876-1884) and Chemistry (1884-1899)at the Sorbonne He developed Friedel-Crafts chemistry in 1877.
- (Charles) Adolphe Wurtz (1817-1884) MD Strasbourg 1843. Assistant to Jean Baptiste Dumas Ecole Medicine, Paris. (1845-1852). Prof. Organic Chemistry at the Ecole Medicine. He was Founder of the School of Chemistry, Sorbonne.
- Jean Baptiste (Andre) Dumas (1800-1884). Prof. Chemistry Ecole Polytechnique (1835)

From Complex Self-Assembling Dendrons and Dendrimers to Supramolecular Nanostructures, Functions and Systems

Virgil Percec
Roy & Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104-6323, USA

Our laboratory is involved in the use of biological systems as models for the elaboration of new concepts at the interface between macromolecular, supramolecular and biological sciences by using self-assembling dendrons and dendrimers as building blocks. These concepts are subsequently used in the design of nanostructures, functions and systems by following the biological principles, structure determines functions.[1-9] This lecture will first discuss the principles used in the design and synthesis of libraries of self-assembling dendrons and dendrimers via retrostructural analysis. Subsequently the use of these dendrons for the elaboration of helical porous supramolecular structures as mimics of helical porous transmembrane proteins such as Aquaporin and their use in the reconstruction of the cell membrane and of its fundamental transport will be outlined. Additional biological systems will be used as models to assemble complex matter that acts as molecular machines and provides high charge carrier mobility. The design of complex soft matter that displays the most primitive sign of intelligence such as memory effect, and of molecular machines will also be discussed.

1) S. D. Hudson, H.-T. Jung, V. Percec, W.-D. Cho, G. Johansson, G. Ungar and V. S. K. Balagurusamy. *Science* **1997**, *278*, 449-452.
2) V. Percec, C.-H. Ahn, G. Ungar, D. J. P. Yeardley, M. Moeller and S. S. Sheiko. *Nature* **1998**, *391*, 161-164.
3) V. Percec, M. Glodde, T. K. Bera, Y. Miura, I. Shiyanovskaya, K. D. Singer, V. S. K. Balagurusamy, P. A. Heiney, I. Schnell, A. Rapp, H.-W. Spiess, S. D. Hudson, and H. Duan. *Nature* **2002**, *419*, 384-387.
4) G. Ungar, Y. Liu, X. Zeng, V. Percec and W.-D. Cho. *Science* **2003**, *299*, 1208-1211.
5) X. Zeng, G. Ungar, Y. Liu, V. Percec, A. Dulcey and J. K. Hobbs. *Nature* **2004**, *428*, 157-160.
6) V. Percec, A. Dulcey, V. S. K. Balagurusamy, Y. Miura, J. Smidrkal, M. Peterca, S. Nummelin, U. Edlund, S. D. Hudson, P. A. Heiney, H. Duan, S. N. Magonov and S. A. Vinogradov. *Nature* **2004**, *430*, 764-768.
7) V. Percec, A. E. Dulcey, M. Peterca, M. Ilies, S. Nummelin, M. J. Sienkowska and P. A. Heiney. *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 2518-2523.
8) V. Percec, B. C. Won, M. Peterca, P. A. Heiney. *J. Am. Chem. Soc.* **2007**, *129*,11265-11278.
9) M. S. Kaucher, M. Peterca, A. E. Dulcey, A. J. Kim, S. A. Vinogradov, D. A. Hammer, P. A. Heiney, V. Percec. *J. Am. Chem. Soc.* **2007**, *129*, 11698-11699.

Biography

Professor Virgil Percec was born and educated in Romania (PhD in 1976 with C.I. Simionescu at the Institute of Macromolecular Chemistry in Iasi). In 1981 he defected from his native country and after short postdoctoral stays at the University of Freiburg in Germany (with H.-J. Cantow) and the University of Akron (with J.P. Kennedy), he joined the Department of Macromolecular Science at Case Western Reserve University in 1982 as an Assistant Professor. He was promoted to Associate Professor in 1984 and to Professor in 1986. In 1993 he was awarded the Leonard Case Jr. Chair at Case Western Reserve University and then in 1999 he moved to the University of Pennsylvania as P. Roy Vagelos Professor of Chemistry.

He has been repeatedly a visiting professor at the Universities of Freiburg, Ulm and at the Max Planck Institute for Polymer Research in Mainz (all in Germany) and at the Royal Institute of Technology in Stockholm.

Percec's list of awards includes Honorary Foreign Member to the Romanian Academy (1993), Humboldt Award (1997), NSF Research Award for Creativity in Research (1990, 1995, 2000), PTN Polymer Award from the Netherlands (2002), the ACS Award in Polymer Chemistry (2004), the Staudinger-Durrer Medal from ETH (2005), Dr. honoris causa (University of Iasi, 2007). He is a Fellow of IUPAC (2001), PMSE Division of ACS (2003) and of AAAS (2004).

Percec chaired and organized numerous symposia including the US-Japan Seminar on Polymer Synthesis (1993), the first European (1997) and the US (1998) Gordon Research Conferences on Polymers and the 35th International IUPAC Symposium on Macromolecules (1994).

Percec's research interest is at the interface between organic, supramolecular and macromolecular chemistry. He has contributed over 575 refereed publications, 36 patents and over 950 endowed, invited and plenary lectures including the Aggarwal Lecture at Cornell (1997), the Woodward Lecture "Frontiers in Chemical Sciences" at Harvard University (2004), the 7th Rohm and Haas Lecture at UC Berkeley (2005), the Staudinger-Durrer Lecture at ETH (2005). He is the editor of the Journal of Polymer Science Part A: Polymer Chemistry (since 1996) and serves on the Editorial Boards of 20 international journals.

Nanocrystal Superlattices

Stephen O'Brien
Dept. Applied Physics and Materials Research Science and Engineering Center, Columbia University, New York, NY 10027, USA

Nanocrystals prepared by modern materials chemistry methods can be used as building blocks to form simple ordered arrays, called superlattices, which resemble the close-packed structures of atoms in crystals or hard spheres. The procedure can be described as a co-crystallization of nanocrystal dispersions following appropriate choice of solvents, substrates and conditions for self-assembly. The driving forces for the assembly of nanoparticles are understood in terms of a combination of entropy and favorable interparticle interactions, such as dipolar or van der Waals forces. The superlattices that result exhibit remarkable structural and compositional diversity, representing a variety of close packed structures reminiscent of binary alloy phases, and spanning a combination of magnetic and dielectric oxides, semiconductors and metals. Superlattices with AB, AB_2, AB_3, AB_4, AB_5, AB_6 and AB_{13} stoichiometry with cubic, hexagonal, tetragonal and orthorhombic symmetries have been identified. The methodology can be thought of as a toolkit to assemble a wide range of structures intended for generating smart materials: thin films with enhanced functionality as a consequence of nanoscale manipulation.

Biography

Stephen O'Brien completed his doctoral work in the Inorganic Chemistry Labs at Oxford University with Professor Dermot O'Hare. His first post-doc was with Galen Stucky (UCSB) in mesoporous materials chemistry. His second with Louis Brus (Columbia) and Chris Murray (IBM) in nanoparticle science. His was appointed to assistant professor at Columbia University in 2000 and Associate Professor in 2005, and manages a research group on synthesis and characterization.

Surface Nanopatterns with Tunable Periodicity via Molecular Engineering Approach

Dmitrii F. Perepichka
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Self-assembly of functional organic molecules on solid surface via supramolecular interactions can be used to create a variety of nano-scale patterns. The symmetry and periodicity of such nanopatterns is sensitive to the structure of a molecular "building block" used, although it is still difficult to predict the specific pattern formed during the self-assembly. We have recently shown that in a multicomponent system, the type and symmetry of the periodic structure can be fixed by keeping the structure of one component constant, while the exact periodicity can be rationally modulated by changing the second component (eg. long-chain alcohol).[1] Using Scanning Tunneling Miscroscopy we demonstrate a great variety of surface nanopatterns which can be created with this approach. I will show and *discuss the examples of "nanoperiodicity"*, where changing the size of molecular building blocks results in qualitatively different types of patterns created on the surface.

Such nanopatterns can be used as templates to guide deposition of other functional materials, such as organic semiconductors. I will also describe our most recent achievements in using surface self-assembly and surface-confined polymerization approaches to pattern conjugated polymers (aka molecular wires).

[1] K.G.Nath et al. *J. Am. Chem. Soc.* **2006**, *128*, 4212.
[2] J.M.McLeod et al. *Nanotechnology* **2007**, in press
[3] K.G.Nath, et al. *J. Phys. Chem. C* **2007**, in press.

Biography

Assistant Professor (2005- , Department of Chemistry, McGill University)
Assistant Professor (2003-2005, Institut National de la Recherche Scientifique, CANADA)
Post-doctoral researcher (2001-2002, UCLA, Prof. Wudl)
Research Associate (1999-2001, Durham University, UK, Prof. Bryce)
PhD, organic chemistry (1999, Institute of Physical Organic Chemistry, UKRAINE, Prof. Popov)
BSc, chemistry (1994, Donetsk State University, UKRAINE)\
Quebec Strategic Research Professor (2003-2006)
DuPont Young Professor (2005-2008)

Dr. Perepichka's research is the area of synthetic materials chemistry and molecular self-assembly. His group of 6 graduate students and 5 post-doctoral fellows is working on molecular electronic devices, based on low-gap donor-acceptor diad molecules and asymmetrically functionalized carbon nanotubes; novel molecular and polymer semiconductors for organic electronics; self-assembly of molecular building blocks on atomically flat surfaces; and on the concept of two-dimensional conjugated polymers. His research results were disseminated in over 40 papers in high-rank journals.

Nanoparticle-Based Ionic Materials (NIMS)

Emmanuel P. Giannelis
Materials Science and Engineering
Cornell University

Nanoparticle-based ionic materials (NIMS) recently discovered at Cornell offer exciting opportunities for research at the forefront of science and engineering. NIMS are hybrid particles comprised of a charged oligomeric corona attached to hard, inorganic nanoparticle cores (Fig. 1). NIMS are distinguished from conventional micro-scale and nano-scale colloidal fluids in at least three ways: *(i) The hybrid nature of NIMS facilitate straightforward design and synthesis of new, stable materials systems with tunable properties. (ii) The tethered corona and associated counterions are the suspending medium for the cores. (iii) The covalently attached corona and unscreened electrostatic charge stabilizes the particles.* These features are advantageous for a broad range of applications, including zero-vapor pressure solvents, heat-transfer liquids and lubricants, thin-film optoelectronic devices, high refractive index liquids for immersion lithography, where colloidal suspensions either cannot be used or require specialized design conditions to reduce solvent loss.

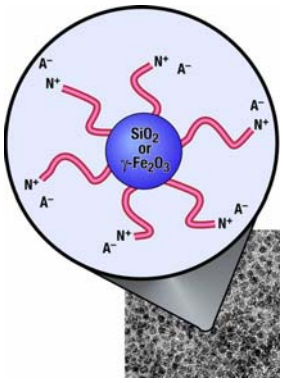

Fig. 1. Schematic and TEM image of model NIMS

Biography

Education: B.S, 1980 (Chemistry) University of Athens, Greece
PhD, 1985 (Chemistry) Michigan State University

Giannelis is the *Walter R. Read Professor of Engineering* and *Director* of Materials Science and Engineering at Cornell University. In addition to his primary appointment, he is a member of the Fields of Chemistry and Chemical Biology and Chemical and Biomolecular Engineering at Cornell. His research interests include polymer nanocomposites, nanobiohybrids, nanoparticle fluids and flexible electronics. His group is internationally recognized as one of the leading groups in polymer nanocomposites.

Giannelis is a member of several organizations and serves or has served on the editorial boards of *Small*, *Chemistry of Materials* and *Macromolecules*. He has co-organized half a dozen conferences or symposia on Nanocomposites and has delivered more than 350 Invited Talks and Seminars. He is the author or co-author of ~150 papers and 10 patents. He is a member of several professional organizations and a corresponding member of the European Academy of Sciences. He is a highly cited author in Materials Science (http://www.ISI HighlyCited.com) and he is listed as one of the top 25 cited authors on *Nanotechnology* by ISI (http://www.esi-topics.com/nano/index.html).

Nanoparticle Gene Regulation Agents

Dwight S. Seferos
International Institute for Nanotechnology, Northwestern University, USA

We have recently reported that oligonucleotide-functionalized gold nanoparticles act as agents for both cellular transfection and for control of protein expression in cells. These "antisense particles' exhibit a range of unique properties that make them very well-suited for intracellular applications. Antisense particles resist nuclease digestion, have high and tailorable binding constants for target mRNA, and exhibit efficient entry into numerous cell types. Further, we can tailor the chemistry on the nanoparticle surface, and thus control the particles' binding strength for a complementary target sequence, ultimately demonstrating that changing the binding strength or surface chemistry offers a means to control the percentage of protein expression. We have also developed nanoparticle agents for visualizing and quantifying RNA in living cells. These developments represent significant advances in antisense and siRNA technology.

Biography

Dwight S. Seferos earned his B.S. degree at Western Washington University (2001) and his Ph.D. degree from the University of California, Santa Barbara (2006), where he studied the design, synthesis, and electronic application of pi-conjugated molecules under the guidance of Professor Guillermo C. Bazan. In 2006 he began postdoctoral studies as a member of Professor Chad A. Mirkin's group at Northwestern University and is an American Cancer Society Fellow. His current research focuses on the cellular uptake and application of DNA-modified gold nanoparticles.

Organic Superatoms in the Green Manufacture of Nanostructured Materials

Donald T. Haynie
Artificial Cell Technologies, Inc./Central Michigan University

This talk will argue that specific combinations of atoms, called "superatoms," will enable increasing control over the structure of matter at the nanometer scale and will therefore form the next generation of building blocks of materials. Organic superatoms are particularly interesting for the creation of environmentally benign materials from a renewable source. This talk will focus on the superatoms known as amino acids and on short specific sequences of amino acid residues. An astronomical number of different amino acid sequences are not only possible but indeed realizable by genetic engineering methods and by chemical approaches. Important for technology development and commercialization, large-scale production of such polymers is increasingly routine. Layer-by-layer self-assembly (LBL) is a simple, "green," and versatile "bottom up" method of fabricating nanostructured ultrathin films. Such films have tremendous potential for the rational design of multifunctional materials. This talk will show how manipulating matter at the nanometer scale by controlling peptide structure and the film fabrication process leads to control over mesoscale properties of the resulting materials, even when those properties cannot be predicted a priori. The closing section of the talk will highlight several practical applications of peptide- and protein-based materials.

Biography

Don Haynie has degrees in physics and biophysics. On completing the doctorate at Johns Hopkins University, he was awarded an NSF post-doctoral fellowship for study of the physical biochemistry of proteins at University of Oxford. His first faculty position was in the Department of Biomolecular Sciences at University of Manchester Institute of Science and Technology. He was subsequently Associate Professor of Biomedical Engineering and Physics at Louisiana Tech University, where he was also principal investigator of a multi-university research consortium, a faculty affiliate of the Institute for Micromanufacturing, and founder and director of the Bionanosystems Engineering Laboratory. In 2005 Don's company, Artificial Cell Technologies, Inc., was incorporated in Delaware; since February 2006 the Company has been headquartered in Science Park at Yale, New Haven. He became full-time with the Company as Vice-President of Research and Development in June 2006 but remains affiliated to academia as Research Professor of Biochemistry and Biophysics at Central Michigan University and a clinical professor in the University of Connecticut School of Medicine. Don is inventor or co-inventor on 14 pending patents. Over 60 peer-reviewed scientific journal articles and meeting abstracts have been published from his laboratory since February 2004. His first book, *Biological Thermodynamics*, is published by Cambridge University Press. This title has reached a sales rank of #1 in thermodynamics, #3 in biophysics, and #14 in biochemistry on Amazon.com. The second edition will appear in February 2008. Don is a member of the Board of Directors of the American Academy of Nanomedicine and a member of Editorial Board the Academy's journal, *Nanomedicine*. He is also on the editorial advisory board of recent patents in nanotechnology.

Interfacing Bio-inspired and Composite Materials - Emergence of Nanotechnology-Based Diagnostic and Therapeutic Solutions for Cancer

Piotr Grodzinski
Program Director, NCI Nanotechnology Alliance
National Cancer Institute

National Cancer Institute is engaged in efforts to harness the power of nanotechnology to radically change the way we diagnose and treat cancer. The intersection of materials science with biology and working at the interfaces of soft and composite materials offer unique opportunity for the development of novel, multi-functional nanodevices. These devices will be capable of detecting cancer at its earliest stages, pinpointing its location within the body, delivering anticancer drugs specifically to malignant cells, and determining if these drugs are effective. Functionalized nanoparticles would deliver multiple therapeutic agents to tumor sites in order to simultaneously attack multiple points in the pathways involved in cancer. Such nano-therapeutics are expected to increase the efficacy of drugs while dramatically reducing potential side effects. *In vivo* biosensors would have the capability of detecting tumors and metastatic lesions that are far smaller than those detectable using current, conventional technologies. Finally, predictive models for interaction of multi-functional nanoparticles with physiological fluids, individual organs, and biological cells can aid the design of appropriate particle systems.

In order to further these research goals, NCI Alliance for Nanotechnology in Cancer has been formed in 2004. The Alliance is investing $144.3 million over the next 5 years to pursue applied nanotechnologies for cancer detection, therapy, and prevention with an aim to achieve clinical translational stage of these technologies towards culmination of the program. The Alliance funds Centers of Cancer Nanotechnology Excellence, the development of nanotechnology platforms, and intramural Nanotechnology Characterization Laboratory (NCL). NCL provides a spectrum of data on the physical parameters and pharmacological and toxicological characteristics of clinically promising.

This presentation will describe the details behind the organization and science and technology of the Alliance.

Biography

Dr. Piotr Grodzinski is a Director of Nanotechnology for Cancer programs at Nanotechnology Alliance of National Cancer Institute in Bethesda, Maryland. He coordinates program and research activities of the Alliance which dedicated $144M over next 5 years to form interdisciplinary centers as well as fund individual research and training programs targeting nanotechnology solutions for improved prevention, detection, and therapy of cancer.

Dr. Grodzinski is materials scientist by training, but like many others found bio- and nanotechnology fascinating. In mid-nineties, he left the world of semiconductor research and built a large microfluidics program at Motorola Corporate R&D in Arizona. The group made important contributions to the development of integrated microfluidics for genetic sample preparation with its work being featured in Highlights of Chemical Engineering News and Nature reviews. After his tenure at Motorola, Dr. Grodzinski joined Bioscience Division of Los Alamos National Laboratory where he served as a Group Leader and an interim Chief Scientist for DOE Center for Integrated Nanotechnologies (CINT).

Dr. Grodzinski received Ph.D. in Materials Science from the University of Southern California, Los Angeles in 1992. He is an inventor on 15 patents and authored over 100 technical publications and conference presentations. Dr. Grodzinski has been an invited speaker and served on the committees of numerous bio- and nano-MEMS conferences in the past years.

Scalable Enhanced Nonlinear Optical and Emission Properties in Organic and Metal Assemblies

Theodore Goodson III
Department of Chemistry, University of Michigan, Ann Arbor MI

Organic conjugated macromolecules have received great attention due to their use in optical and electronic applications. Certain molecular assemblies have shown enhanced nonlinear optical properties by virtue of excitonic coupling in the multi-chromophore system. Organic dendrimers and other branched multi-chromophore systems (were the chromophores are covalently attached) have also shown characteristic properties of strong intra-molecular interactions which have been utilized in light harvesting processes, light emitting diodes, as well as for enhanced nonlinear optical effects. The mechanism of the strong intramolecular interactions in branched chromophores depends on the nature of the branching center, the geometrical orientation of covalently attached chromophores, and the extent of delocalization in the dendrons. Through steady-state and time-resolved spectroscopy, we have characterized the mechanism of energy transport and the relative strength of intra-molecular interactions. In this presentation, organic dendrimers and other branched chromophores are described by their time-resolved fluorescence and absorption properties. A similar methodology has been carried out for small metallic assemblies as well. For particular assemblies the processes of efficient energy transfer, fast energy re-distribution, enhanced two-photon absorption crosssections, and a delocalized excitation for organic systems will be discussed.

Representative Publications

Varnavski, O. P.; Ranasinghe, M.; Yan, X.; Bauer, C. A.; Chung, S.-J.; Perry, J. W.; Marder, S.R.; Goodson, T., III *Ultrafast Energy Migration in Chromophore Shell-Metal Nanoparticle Assemblies J. Am. Chem. Soc.;* **2006**; *128*(34); 10988-10989.

Bhaskar, A.; Ramakrishna, G.; Lu, Z.; Twieg, R.; Hales, J. M.; Hagan, D. J.; Van Stryland, E.; Goodson, T., III *Investigation of Two-Photon Absorption Properties in Branched Alkene and Akyne Chromophores J. Am. Chem. Soc.;* **2006**; *128*(36); 11840-11849.

Bhaskar, A.; Guda, R.; Haley, M. M.; Goodson, T. G., III *Building Symmetric Two-Dimensional Two-Photon Materials J. Am. Chem. Soc.;* **2006**; *128*(43); 13972-13973.

Goodson, T "Optical Excitations in Organic Dendrimers Investigated by Time-Resolved and Nonlinear Optical Spectroscopy" Accts. Chem. Res. **2005**; *38*(2); 99-107.

Varnavski, O and Goodson, T "Exciton Dynamics in a Branched Molecule Probed with Three Pulse Photon Echo Peak Shift and Transient Grating Spectroscopy", *J. Phys. Chem*., **2004**, *108*(29); 10484-10492.

Wang, Y; Ranasinghe, M.; Goodson, T.; "Mechanistic Studies of Energy Transport in a Phosphorous Cored Branching Structure," *J. Amer. Chem. Soc.* **2003**, 125, 9562-9563.

Ranasinghe, M.I.; Varnavski, O.P.; Pawlas, J.; Hauck, S.I.; Louie, J.; Hartwig, J.F.; Goodson, T., "Femtosecond Energy Transport in Triarylamine Dendrimers," *J. Am. Chem. Soc.* **2002**,*124*, 6520-6521.

Biography

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Professional Preparation:

Undergraduate Institution:	Wabash College, Indiana, B. Sc. 1991
Graduate Institution:	University of Nebraska, Lincoln Nebraska, Ph.D. 1996.
Post-Doctoral Institutions:	University of Chicago, Chemistry, 1996.
	University of Oxford, Physics, 1997.

Appointments:

2004 – Present:	Professor, University of Michigan
2002 – 2004:	Associate Professor, Wayne State University
1998 – 2002:	Assistant Professor, Wayne State University

Research Publications:

1. Ramakrishna, Guda; Dai, Qiu; Zou, Jianhua; Huo, Qun; Goodson III, Theodore. "Interparticle Electromagnetic Coupling in Assembled Gold-Necklace Nanoparticles". *Journal of the American Chemical Society* **2007**, 129(7), 1848-1849
2. Ramakrishna, Guda; Goodson III, Theodore. "Excited-State Deactivation of Branched Two-Photon Absorbing Chromophores: A Femtosecond Transient Absorption Investigation**".** *Journal of Physical Chemistry A* **2007**, 111(6), 993-1000
3. Bhaskar, Ajit; Ramakrishna, Guda; Hagedorn, Kevin; Varnavski, Oleg; Mena-Osteritz, Elena; Baeuerle, Peter; Goodson, Theodore, III. "Enhancement of Two-Photon Absorption Cross-Section in Macrocyclic Thiophenes with Cavities in the Nanometer Regime"**.** *Journal of Physical Chemistry B* **2007**, 111(5), 946-954.
4. Varnavski, Oleg; Yan, Xingzhong; Mongin, Olivier; Blanchard-Desce, Mireille; Goodson, Theodore, III."Strongly Interacting Organic Conjugated Dendrimers with Enhanced Two-Photon Absorption**".** *Journal of Physical Chemistry C* **2007**, 111(1), 149-162
5. Wang, Ying; Goodson, Theodore, III. "Early Aggregation in Prion Peptide Nanostructures Investigated by Nonlinear and Ultrafast Time-Resolved Fluorescence Spectroscopy"**.** *Journal of Physical Chemistry B* **2007**, 111(2), 327-330

Other Significant Publications:

1. Guo, Meng ; Yan, Xingzhong; Kuon, Young; Hayakawa, Teruoki; Kakimoto, Maso-aki; Goodson, Theodore, III. "High Frequency dielectric response in a branched phthalocyanine" *J. Am. Chem. Soc*. (Communication) **2006,** 128(46); 14820-1482
2. Dong-Ik Lee and Theodore Goodson III. "Entangled Photon Absorption in an Organic Porphyrin Dendrimer". *Journal of Physical Chemistry B* **2006**, 110(51), 25582-25585
3. Varnavski, Oleg P.; Ranasinghe, Mahinda; Yan, Xingzhong; Bauer, Christina A.; Chung, Sung-Jae; Perry, Joseph W.; Marder, Seth R.; Goodson, Theodore, III. "Ultrafast Energy Migration in Chromophore Shell-Metal Nanoparticle Assemblies**".** *J. Am. Chem. Soc*. **2006,** 128(34), 10988-10989
4. Anand Smriti; Varnavski Oleg; Marsden Jeremiah A; Haley Michael M; Schlegel H Bernhard; Goodson Theodore III " Optical excitations in carbon architectures based on dodecadehydrotribenzo[18]annulene". *J. Phys. Chem. A* **2006**, 110(4), 1305-18.
5. Yan, X. Z.; Goodson, Theodore, III. " High Dielectric Hyperbranched Polyaniline Materials." *J. Phys. Chem. B* **2006**, 110(30), 14667-14672.

Synergistic Activities:

American Chemical Society Project SEED Preceptor 1999-present

National Organization for Black Chemist and Chemical Engineers 2001-present

Senior Editor for the ACS Journal of Physical Chemistry

Low-Temperature Routes to Carbon Nanofibrous Growth and Metal Oxide Nanoclusters

Bradley D. Fahlman
Department of Chemistry, Dow Science 357, Mt. Pleasant, MI 48859

A variety of metallic nanoparticles have been used to catalyze the growth of carbonaceous nanostructures (*e.g*., nanotubes, nanofibers, etc.). The most heavily used compositions include Fe, Fe_xO_y, Co, Ni, Ni/Y, and Co/Ni species. Carbon nanotubes are thought to grow from these catalysts via a vapor-liquid-solid (VLS) mechanism, which was first postulated *ca*. 30 years ago for the growth of semiconductor wires. We recently discovered methods to generate carbonaceous nanostructures via surface-nucleation mechanisms, whereby growth occurs at temperatures as low as room temperature – far below the melting point of the catalyst seed. In addition to this work, the room-temperature growth of dendrimer-stabilized metal oxide nanoclusters will also be discussed. Though most dendritic-entrained/stabilized nanoclusters have featured metallic compositions, this work extends the efficacy of the dendritic structure to oxides – of importance for catalysis, sensor, and nanomagnetic applications.

Biography

Dr. Fahlman received his B.Sc. (High Hons.) from the University of Regina (Regina, Saskatchewan, Canada) in 1996, and his Ph.D. in Inorganic Chemistry (with Andrew R. Barron) from Rice University in 2000. After serving two years as Director of Advanced Laboratories and Lecturer in Chemistry at the University of California, Irvine, Dr. Fahlman joined the faculty at Central Michigan Unversity, receiving early tenure and promotion to Associate Professor of Chemistry in 2005. His current research interests include low-temperature routes to nanostructural growth and chemical vapor deposition (CVD) and atomic layer deposition (ALD) of high-k dielectric thin films, including novel precursor design. In addition to co-authoring over 30 peer-reviewed publications, Dr. Fahlman is the sole author of an undergraduate textbook entitled “Materials Chemistry” (Springer, released Aug. 2007), which focuses on the structure vs. property relationship and characterization techniques for various classes of materials.

Silica Based Hybrids: From Nanoscale Modules to Materials

Uli Wiesner
Materials Science & Engineering, Cornell University, Ithaca, NY 14853-1501 USA

In this contribution it is shown how silica sol-gel chemistry provides a toolbox to produce materials from well-defined nanoscale modules. In the first part fluorescent core-shell silica nanoparticles are introduced (C dots) that lead to brightness values approaching those of same-sized quantum dots (q dots) and enhanced photostability compared to free dye in aqueous solutions. From this work the idea of a “lab-on-a-particle” is emerging in which different functionalities are provided in distinct shells of a single nanoparticle. In the second part blocked macromolecules are used as structure directing agents for silica nanoparticle modules to provide hybrid materials for various applications. Similar to biology information about structure and function of the final assembly is determined through the primary monomer sequence of the macromolecules. It is further demonstrated that in this “systems from nanosystems” approach besides the enthalpic contributions entropic effects need to be considered in order to understand the mixing behavior between the structure directing polymers and the nanoscopic modules. It will be shown that there is a size dependent transition from mixing to demixing which can be generalized beyond the use of silica as nanomodules. Examples where these considerations may provide novel design criteria for next generation nanostructured materials will be discussed with emphasis on energy production and storage.

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http://www.ccmr.cornell.edu/~uli/

Biography

Uli Wiesner studied Chemistry at the Universities of Mainz and California, Irvine. He received his Chemistry Diploma in 1988 from the University of Mainz, Germany, and gained his Ph.D. in 1991 with work on optical information storage in liquid crystalline polymers in the group of Prof. H. W. Spiess at the Max-Planck-Institute for Polymer Research, Mainz. After his Ph.D. he was a postdoctoral fellow at the Ecole Superieure de Physique et de Chimie Industrielle de la ville de Paris (E.S.P.C.I.), France, with Prof. L. Monnerie studying the morphology and dynamics of aromatic terpolyesters. In 1993 he returned to the group of Prof. H. W. Spiess were he finished his Habilitation in 1998 with work on structure, order, and dynamics in self-assembled block copolymer systems with additional interactions. He joined the Cornell MS&E faculty in 1999 as an Associate Professor and became a Full Professor in 2005. Since his arrival at Cornell he works at the interface between polymer science and solid-state chemistry. The goal of his research is to combine knowledge about the self-assembly of soft materials with the functionality of solid-state materials to generate novel hierarchical and multifunctional hybrid materials. Uli Wiesner is the author of about 100 articles in peer-review journals and books and is currently an editorial and advisory board member of multiple scientific journals. Based on work at Cornell in 2003 he co-founded Hybrid Silica Technologies, Inc., Ithaca, NY, with the goal to provide “green” multifunctional hybrid for life science applications and beyond. He is the recipient of multiple awards, including a Ph.D. Award of the Hoechst AG, the Carl Duisberg Memorial Award of the German Chemical Society, an IBM Faculty Partnership Award and Mr. & Mrs. Richard F. Tucker’50 Excellence in Teaching Award of Cornell University. Since 2007 he is a member of the Nanotechnology Technical Advisory Group (nTAG) of the President’s Council of Advisors on Science and Technology (PCAST).

NCL Data: Trends in Bio Compatibility and Toxicity

Scott E. McNeil
Nanotechnology Characterization Laboratory
National Cancer Institute at Frederick, MD 21702

The Nanotechnology Characterization Laboratory (NCL) conducts preclinical efficacy and toxicity testing of nanoparticles intended for cancer therapeutics and diagnostics. The NCL is a collaborating partnership between NCI, the U.S. Food and Drug Administration and the National Institute of Standards and Technology. As part of its assay cascade, NCL characterizes nanoparticles' physical attributes, their in vitro biological properties, and their in vivo compatibility using animal models. The Laboratory accelerates the transition of basic nanoscale particles and devices into clinical applications by providing critical infrastructure and characterization services to nanomaterial providers. It is a national resource available to investigators from academia, industry and government. The presentation will provide an overview of the NCL; discuss parameters that are critical to nanoparticle biocompatibility, and present assays used for preclinical characterization of nanoparticles.

Biography

Dr. McNeil serves as Director of the Nanotechnology Characterization Laboratory (NCL) for the National Cancer Institute at Frederick (NCI-Frederick), where he coordinates pre-clinical characterization of intended for cancer therapeutics and diagnostics. The NCL performs and standardizes preclinical characterization of intended for cancer therapeutics and diagnostics. The NCL provides infrastructure support to NCI's Alliance in Nanotechnology, and is a national resource available to investigators in academia, government, and industry, to aid in the translation of nanotech cancer therapeutics into clinical applications.

Prior to joining NCI-Frederick (i.e., SAIC-Frederick), Dr. McNeil served for three years as Senior Scientist in the Nanotech Initiatives Division at SAIC where he transitioned basic nanotechnology research to government and commercial markets. He is a member of several governmental and industrial working groups related to nanotechnology development, policy, standardization and commercialization. Dr. McNeil's professional career includes tenure as an Army Officer, with tours as Chief of Biochemistry at Tripler Army Medical Center, as a Combat Arms officer in the Gulf War. He is an invited speaker to numerous nanotechnology-related conferences and has six patents pending related to nanotechnology and biotechnology. He received his bachelor's degree in chemistry from Portland State University and his doctorate in cell biology from Oregon Health Sciences University.