A PROPOSED TAXONOMY AND CLASSIFICATION STRATEGY FOR WELL-DEFINED, SOFT-MATTER NANOSCALE BUILDING BLOCKS

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1.1 INTRODUCTION

The field of nanoscience has evolved explosively over the last two decades, generating a vast number of nanoscale structures and objects. These nanoconstructs may be derived from covalently bound molecules in the classical chemical sense or they may be supramolecular, self-assembled structures. That withstanding, in either case “well-defined nanostructures/objects” may be formed from the smaller discrete building blocks (i.e., atoms, small molecules, monomers, polymers, etc.) if certain “bottom-up” assembly processes are involved that ensure structure control of critical nanoscale design parameters (CNDPs) such as (a) size, (b) shape, (c) surface chemistry, (d) flexibility/rigidity, (e) architecture, and (f) composition. These resulting discrete, homogeneous nanostructures/objects constitute an important category of nanomaterials and are distinguished from other heterogeneous nano-assemblies by expressing well-defined interrelationship patterns and quantized stoichiometries with each other [1, 2]. The quantized stoichiometries and interparticle relationships exhibited by these well-defined nano-entities are a consequence of their structure-controlled precursor building blocks and their ability to transfer important critical atomic design parameters (CADPs) or critical molecular design parameters (CMDPs) to the nanoscale level.

This structural information is routinely transferred with high integrity to higher complexity in biological systems via certain evolutionary/genealogical aufbau strategies as described in Figure 1.8 and 1.1. Joyce [3, 4] has clearly demonstrated (a) the importance of these genealogical/evolutionary aufbau patterns involving well-defined nanoscale building blocks such as proteins, RNA, and DNA and (b) their ultimate role in the diversification of life.

In the case of abiotic systems, unique structure-controlled synthetic strategies and construction rules are usually involved in the formation of these well-defined nanostructures/objects. The importance of understanding these bottom-up construction rules and aufbau patterns cannot be overstated. They will be invaluable for developing classification and taxonomy schemes to define key nano-building blocks (i.e., nano-elements), as well as their hybridization pathways (i.e., nano-compounds/assemblies) and synthetic evolution to higher complexity in the nanoscale region. In many respects, our present insights are similar to previous historical growth phases in traditional chemistry during the nineteenth century that led to the Mendeleev Periodic Table in 1869. In essence, the patterns and categorization of atomic elements in Mendeleev’s periodic table constituted an elegant classification or taxonomy for all the known atomic elements [5, 6]. Mendeleev’s seminal atomic element taxonomy [7] has provided powerful insights and critical information useful for a priori predictions of elemental physicochemical behavior, as well as chemical reactivity, stoichiometries, assembly patterns, and so on, leading to the formation of traditional small molecular structures and assemblies as illustrated in Figure 1.2. The idea of classifying atomic elements or small molecules according to chosen criteria of similarity features or as a function of their interrelationships patterns/trends is not new. In fact, Swedish botanist Carl von Linnæus (1707–1778), the “Father of taxonomy,” initiated such a
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#### FIGURE 1.1. Timeline of events associated with the early history of life on Earth, with approximate dates in billions of years before the present [4]. Reprinted with permission of Macmillan Publishers Ltd., 2002.

<table>
<thead>
<tr>
<th>Event</th>
<th>Approximate Date (Billion Years Before Present)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formation of Earth</td>
<td>4.5</td>
</tr>
<tr>
<td>Stable hydrosphere</td>
<td>4.2</td>
</tr>
<tr>
<td>Prebiotic chemistry</td>
<td>4.2-4.0</td>
</tr>
<tr>
<td>Pre-RNA world</td>
<td>-4.0</td>
</tr>
<tr>
<td>RNA world</td>
<td>-3.8</td>
</tr>
<tr>
<td>First DNA/protein life</td>
<td>-3.6</td>
</tr>
<tr>
<td>Diversification of life</td>
<td>3.6-present</td>
</tr>
</tbody>
</table>

These scientific classifications have been described by May and Bock [8] as “the arrangement of well-defined entities” into a hierarchical series of nested classes. A class (i.e., taxon) is defined as “collection of similar entities.” Such a taxon consists of collections of entities that share certain similarity features consisting of attributes or traits in common. Similar or related classes at one hierarchical level are combined comprehensively into more exclusive classes at the next lower taxon level to more specifically narrow down the entity description. This process is demonstrated by a Linnaean classification downward from broader taxa to more specific taxa involving diverse entities such as humans, dogs, wolves, or bacteria as described in Figure 1.3. Variations of the Linnaean taxonomy system have been used to classify a wide range of biological diversity. Many of these classifications are less familiar to chemists and physical scientists; however, they are generally known by biologists and life scientists. Extensive classifications have been reported for complexity at the submicron scale level (e.g., viruses [9,10]) and progress to higher levels of complexity at the micron-scale/macro-scale level to include bacteria [11], yeasts [12], fungi [13], plants, and animals as illustrated in Figure 1.3. Presently these taxonomies and classifications are well established for entities.

#### FIGURE 1.2. A comparison of taxonomies at the picoscale nanoscale and micron scale/macro-scale as a function of hierarchical complexity.
at the atomic/molecular level as well as higher complexity at the micron/macroscale. However, relatively little has been reported concerning classifications/taxonomies of structures and assemblies at the nanoscale level.

It is widely accepted that well-defined genealogy and evolutionary precursors played a critical role in the development of taxonomies at the micron-scale/macroscale levels [3, 4]. Similarly, it will be of high importance to define analogous taxa for well-defined module/entities at the picoscale, molecular, and nanoscale levels. It is proposed that the CHDPs for these well-defined precursors may very well provide appropriate criteria for evaluating bottom-up construction pathways, roles, and classification schemes for higher-complexity nano-building blocks as described in Figure 1.4. Historically, it is widely recognized that seminal atomic element classifications were critical in the ultimate evolution of an atomic periodic table/system by Mendeleev in 1869 [7]. Based on recent progress reported toward development of a similar nano-periodic system [2] and first examples of nano-periodic tables, a suitable taxonomy strategy appears to be both critical and timely.

In this chapter, we propose further steps toward the development of a universal nano-classification system. This account should be considered a “work in progress” and involves the use of “critical hierarchical design parameters” (CHDPs), namely, (a) sizes, (b) shapes, (c) surface chemistries, (d) flexibility/rigidity, (e) architectures, and (f) elemental compositions as described in Figure 1.4. It is proposed that these CHNPs should be considered as classification criteria (i.e., taxa) and used according to Linnaean principles for classifying various “aufbau precursors” to the 12 hard/soft nano-element categories described later in Section 1.7 (Figure 1.17). It is widely recognized that Linnaean taxonomy principles have been used successfully for classifying evolutionary/genealogical hybrids arising from fundamental entities in biological systems. In a similar manner, at the nanoscale it should be possible to use these CNDP-based taxa as classification criteria for defining future hybridizations of these nano-element categories into anticipated new libraries of nano-compounds and nano-assemblies. Finally, it is proposed that using these CNDPs according to Linnaean classification criteria should be considered as an approach for generating a specific taxonomy-based nomenclature.

1.2 ADAPTATION OF LINNAEAN TAXONOMY PRINCIPLES TO A NEW NANO-CLASSIFICATION SCHEME

Successful Linnaean-like taxonomies have been demonstrated for important soft nano-element categories and nano-compounds and their assemblies. Most noteworthy is the extensive classification of [S-4]-type proteins (Section 1.2.2). Secondly, the development of taxonomies for the combination (i.e., hybridization) of [S-4]-type protein subunits or [S-5]-type viral capsids with [S-6]-type RNA or DNA nano-elements to produce [S-6:S-4] or [S-6:S-5]-type viral nano-compounds, respectively, has been demonstrated as described in Section 1.2.3.
1.2.1 Taxonomy of Biological Structures and Organisms

The term taxonomy (Greek τάξις, arrangement or order, and νόμος, law or nemein, to distribute or govern) is defined as the science of biological classification. In a broader sense, this taxonomy concept involved the use of a protocol that provides three key features, namely: (a) identification, (b) classification, and (c) nomenclature. These three parameters have been used routinely for describing classifications and relationships between various biological organisms/residing in the higher-complexity dimensions of the micron–macroscale (i.e., 0.1 μm to meters) [14]. At least eight taxonomic parameters were deemed necessary for defining the higher complexity of micron-scaled biological systems. They are widely recognized and recalled with the mnemonic “Do kings play chess on fine-grained sand?” and include the following eight hierarchical parameters: (1) domain, (2) kingdom, (3) phylum, (4) class, (5) order, (6) family, (7) genus, (8) species [15].

A dominant feature that differentiates biological classification (taxonomy) from most other classification systems is evolution. The similarity between biological structures or organisms placed in a common taxon is not arbitrary. It is the result of shared descent from their nearest common ancestor. As such, these classifications require an evaluation of evolutionary stages and intrinsic genealogy that precedes each entity classification. In essence, these eight classification parameters not only capture similarities and differences, but also integrate critical biological entity features/properties such as (a) homogeneity, (b) size, (c) morphology/shape, (d) behavior/function, (e) flexibility/rigidity, (f) architecture, and (g) elemental composition as important evolutionary/genealogical selection criteria for these classifications [16]. Such Linnaean-inspired concepts have been studied extensively by essentially every generation of naturalist during the past 200 years, including Charles Darwin. Modified versions of these Linnaean taxonomic criteria and classifications presently serve as the “gold standard” for classifying all biological hierarchy/diversity residing in the micron-meter size range. Such taxonomy concepts have provided a universal and versatile system for classifying all micron- and macroscale biological entities (i.e., certain viruses, bacteria, fungi, plants, animals, etc.) and laid the foundation for the study of these complex systems.
foundation for modern biological taxonomy/classifications and nomenclature. This well-defined taxonomic scheme has served to organize, simplify, and unify wide ranges of diversity and complexity at the micron-scale and macroscale within biology. Most importantly, this well-defined taxonomic system has provided a critical, quantitated protocol for analyzing important patterns, trends, and relationships between classified biological entities. More contemporary modifications have involved the use of molecular level (i.e., DNA/RNA-based) data as a means for classification.

1.2.2 Protein Taxonomies

The nanoscale class of protein structures/assemblies has been proposed as a well-defined soft nano-element category designated as [5-4] based on its quantized CNDPs [2] (see Section 1.7.1). A structural classification of proteins (SCOP) was first pioneered as early as 1995 by Murzin et al. [17]. More recently, a very comprehensive protein taxonomy based on secondary structure was reported [18]. This taxonomy is generated automatically by computer and based solely on secondary protein structure. It takes the form of a cladogram/dendrogram-based “similarity tree” in which proteins with similar secondary structure occupy neighboring leaves. This taxonomy is largely in agreement with SCOP and is a multidimensional classification scheme based on homologous sequences and full three-dimensional structure, as well as information about the chemistry and evolution of the protein. A “similarity tree” based on this taxonomy is as illustrated in Figure 1.5. Much like dendrimer architecture, a similarity tree is heuristically composed of multiple dendron-like domains that are all connected to a central core.

**FIGURE 1.5.** A similarity tree derived from 183 diverse proteins are examined and classified into various cladograms or similarity domains designated by clusters of protein structures exhibiting similar features or functional properties. For example, domain (A) is associated with proteins that self-assemble into viral coats/capsids, domain (B) includes a cluster of proteins associated with enzymes and biological catalysts and domain (C) identifies specific protein types associated with oxygen transport properties [18]. Reprinted with permission of Macmillan Publishers Ltd., 1999.
of information. These dendron-like domains are referred to as cladograms or dendrograms. The core center contains conserved structural information that feeds into these various cladograms. Based on the hybridization of structural information that is connected to this conserved core, one observes branches of similar yet diverse protein features. As noted in the similarity tree (Figure 1.5), the various cladograms connected to the core serve to cluster similar features into specific domains (i.e., domains (A), (B), and (C)). These domains may be associated with specific properties/functions of interest. Thus, based on secondary protein structure, this taxonomy proved to be a versatile protein classification scheme for evolving differentiating cladograms that associated certain protein types with various biological structural or functional roles. For example, cladogram (A) identifies certain proteins that self-assemble to produce viral coats and capsids as opposed to cladogram (B), which defines clusters of proteins associated with a biological catalysis function (i.e., enzymes, etc.), or cladogram (C), which identifies specific protein types associated with oxygen transport properties (i.e., feritin, heme-type binding proteins). It is readily apparent that such a taxonomy based on secondary protein structure provides a simple scheme for classifying a large database of complex information. Successful use of such Linnaean taxonomic principles for microscale/macroscale plants/animals and now nanoscale protein molecules provides optimism for recognizing common features in each of these dimensionally differentiated hierarchical domains. These taxonomic differentiations should be suitable for defining ordered classes and ultimately evolving versatile and useful nomenclatures just as Mendeleev’s periodic table of atomic elements led to a classification scheme (i.e., taxonomy) and a universal nomenclature for the elements and their resulting compounds.

1.2.3 Virus Taxonomies

Based on their quantized, well-defined CNDPs, viral capsids have been proposed as an important soft nano-element category designated as [S-5] [2, 19]. As described in Section 1.3.3, they are derived from the stoichiometric self-assembly of category [S-4]-type protein subunits. Viruses, in turn, have been proposed as stoichiometric nano-compounds that are derived from the self-assembly of either [S-4]-type or [S-6]-type RNA or DNA cores (i.e., [S-4]-type or [S-6]-type nanoparticles) or the self-assembly of viral capsids around these RNA/DNA [S-6]-type cores. Meanwhile, an invaluable classification system has been introduced by Baltimore [9] that places viruses into one of seven groups based on an analysis of parameters such as (a) their core nucleic acid type (i.e., DNA or RNA), (b) strandedness (i.e., single strand versus double strand), (c) sense, and (d) method of replication [20] (see Section 1.9.3, Figure 1.31). Such DNA/RNA-driven taxonomy has produced invaluable assistance in the classification and determination of evolutionary termini (i.e., dead ends) confirming extinction or evolutionary gaps raising expectations for biological entities yet to be discovered [21, 22]. On the other hand, a more Linnaean-type taxonomy has been developed for viruses (i.e., the LHT System). This taxonomy is based on a comparison of physico chemical features such as (a) core nucleic acids (i.e., DNA/RNA), (b) symmetry (i.e., helical, icosahedral or complex), (c) presence of envelope components, (d) diameter of capsids, (e) number of capsids, and so on [23] (see Section 1.9.3; Figure 1.30).

1.3 HOW DOES NATURE TRANSFER STRUCTURAL INFORMATION FROM A LOWER HIERARCHICAL LEVEL TO HIGHER COMPLEXITY?

The clustering of similar secondary protein structure as observed in the similarity tree (Figure 1.5) suggests that critical features are conserved and transferred up the hierarchy ladder to produce the higher complexity observed at the nanoscale in cladograms (A), (B), and (C) above. As such, one must ask: Are there conserved critical hierarchical design parameters that maintain informational integrity and robustness when transferred to higher complexity? Anecdotal evidence supports the notion that certain critical design parameters at the atomic, molecular, nanoscale, and microscale level can effectively transfer important structural information to higher hierarchical complexity. Many well-known examples of molecular self-assembly, genetic expression, and evolution clearly demonstrate these principles. The critical role of atoms and molecular level monomers (i.e., alpha-amino acids) is clearly illustrated in Figure 1.6a. As demonstrated in the protein taxonomy (Figure 1.5) it appears that secondary/tertiary structure is far better conserved than specific protein sequence. It is well known that secondary/tertiary protein structures are directly dependent on CNDPs such as (a) size, (b) shape, (c) surface chemistry, and (d) flexibility/rigidity. A clear example is readily illustrated by the conservation of nanoscale protein (i.e., collagen) secondary/tertiary structure throughout its respective hierarchical micron-scale self-assembly steps to produce biological tendons as shown in Figure 1.6b.

In 1917, Dr. Arcy Thompson (1860–1948) published a seminal biological treatise entitled On Growth and Form [16]. This work provided deep insights and answers to the question above. It clearly articulated the importance of preferred and controlled “critical micron-scale/macroscopic design parameters” (CMicDPs) such as (a) size, (b) shape, (c) surface function, (d) flexibility/rigidity, (e) architecture, and (f) atomic composition features in the successful evolution of all biological structures and organisms. As early as 1990–1993, it was stated that analogous “critical atomic, molecular and
nanoscale design parameters” were conserved and inextrica-
ably associated with the transfer of information in all well-
deﬁned structures throughout the atomic to microscale hier-
archical continuum [24, 25].

1.4 THE USE OF CLADOGRAMS FOR
CLASSIFICATIONS OF WELL-DEFINED
BIOLOGICAL (MICRON SCALE/MACROSCE),
ATOMIC (PICOSCAE), AND NANOSCAE
BUILDING BLOCKS

1.4.1 Taxonomy of Biological Entities
Cladograms (i.e., dendrograms) as illustrated in Figure 1.5
for nanoscale proteins and in Figure 1.7 for macroscopic ani-
mals (i.e., vertebrae) have been used traditionally for deﬁn-
ing evolutionary (i.e., precursor-type) relationships and path-
ways leading to clusters of similar entities based on several
pervasive criteria. In Figure 1.7, the vertebrate classifica-
tions (i.e., cladograms) are based on similar evolutionary and
genealogical features such as sizes, shapes/morphologies,
and functions resulting from hybridization to produce cer-
tain well-deﬁned families of organisms. Prior to the advent
of DNA sequencing, nearly all cladogram-based biological
systematics involved the use of morphology or shape data
classiﬁcations for deﬁning genealogy and evolutionary path-
ways. Presently, both molecular and morphological system-
atics are used extensively for this purpose [11]. Many of
these issues have been examined in detail by Zuckerkandl
and Pauling [26].

1.4.2 Taxonomy of Atomic Elements
Nearly concurrently, Lavoisier [1743–1794; Traite Elemen-
taire de Chemie (1789)], Prout [1754–1844; Law of Deﬁnite
Proportions (1797)], Dalton [(1766–1844; Law of Multiple
Proportions/New System of Chemical Philosophy (1808)],
and others began the classiﬁcation of less complex hierar-
chical entities such as the atomic elements. This activity led
to Mendeleev’s (1834–1907) seminal periodic element pro-
posal wherein he classiﬁed and organized known elements
according to their periodic properties and chemical behavior.
This led to a taxonomic framework (i.e., Mendeleev Peri-
dodic Table) that could be adapted to and interpreted accord-
ing to the earlier Linnaean template for biological structures
and organisms. For example, the elements were organized
into domains of reactive versus inert types (i.e., unsaturated
versus saturated valence shells), vertical elemental groups
(i.e., metals, metalloids, and nonmetals; Groups I–VIII),
inorganic type elementals versus organic, horizontal peri-
ods (i.e., atomic weights), mono-isotope versus poly-isotopic
elements, and so on. Rich [27] refers to such a periodic tax-
onomy as a view of the relationship patterns that exist among
the elements. Similarly, one can visualize a crude taxonomy
for the atomic elements based on the well-known mnemonic
and classical Linnaean taxonomy template used for clas-
siﬁying biological structures/organisms as described in
Figures 1.8 and 1.9.

The elements are different aggregates of the atoms of pri-
medial hydrogen.

—Prout’s Hypothesis (1815)
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Based on genealogical and evolutionary principles described for the formation of heavier atomic elements from lighter elements [28], one may view Niels Bohr’s seminal perspective of the Mendeleev Periodic Table as an evolutionary cladogram for tracing the transformation and evolution of light to heavier atomic elements as shown in Figure 1.8. Based on a Linnaean template, the classification of elements into families based on genealogy or electron shells (i.e., periods) in the context of sizes, shapes, function (i.e., surface chemistry), and complexity is readily apparent.

In general, the Mendeleev Periodic Table has evolved and been viewed as a very articulate taxonomic account of all the known atomic elemental building blocks. Most notable during this periodic table development was the emergence of certain patterns/trends (i.e., vertical elemental groups and horizontal periods) that contained a number of empty positions. These unoccupied elemental positions within these taxonomic patterns suggested the existence of yet undiscovered elements with properties that could be extrapolated from the property patterns/trends of the surrounding elements. Without the benefit of knowing or understanding anything about atomic structure, electronic theory, or quantum mechanics, Mendeleev provided a powerful predictive taxonomic concept that still remains rational and consistent with accepted contemporary understanding of atomic structure and their physicochemical properties.

Furthermore, it is now recognized that the Mendeleev Periodic Table provides a very rich taxonomy for classifying and predicting important CADPs [25] such as (a) size, (b) shape, (c) reactive/inert surface chemistry, (d) flexibility/polarizability and (e) architecture. These periodic trends and property patterns are as described in Figure 1.8 and 1.9. It is obvious, that hybridization of these various co-reactive atomic elements would produce their own unique and differentiated cladograms of small molecule structures and assemblies.

Such an approach might prove to be an interesting template for organizing and classifying various aufbau-type precursors leading to well-defined nano-building blocks (i.e., nano-element categories) as well as their subsequent hybridization into nano-compounds and assemblies. These issues will be discussed later in Section 1.7.1.

1.4.3 In Quest of a Taxonomy for Nonbiological Nanoscale Structures and Assemblies

Hierarchical taxonomies are widely recognized and used routinely for building blocks as small as picoscale atomic elements and well-defined biological structures as well as for
THE USE OF CLADOGRAMS FOR CLASSIFICATIONS OF WELL-DEFINED BIOLOGICAL ATOMIC AND NANOSCALE BUILDING BLOCKS

FIGURE 1.8. Linnaean taxonomy categories wherein the “order classification” of the elements is presented in a Bohr-type periodic-type cladogram associated with atomic elemental families that are defined as a function of CADPs that include; vertical periods of electronic shells (i.e., sizes, orbital shapes, flexibility/sturdiness, surface chemistry (reactivity)) and horizontal classes of electronic shells (i.e., sizes, reactivities, increasing masses, etc.).

FIGURE 1.9. Structure-controlled critical atomic design parameters (CADPs) for atomic elements classified in a Mendeleev periodic table as a function of (a) size, (b) shape, (c) reactive surface chemistry, (d) flexibility/polarizability, (e) architecture, and (f) elemental composition.
organisms as large as micron/meter scale. With the exception of biological-type taxonomies offered recently for proteins [29] and for viruses [20] based on messenger DNA/RNA precursors and genealogy, relatively little attention has been focused on nonbiological structures, assemblies, or entities in the 1 to 100-nm dimensional region. As shown in Figure 1.10, this nanoscale region is bracketed by well-demonstrated taxonomies for the atomic elements (i.e., the Mendeleev Periodic Table), as well as by Linnaean-type taxonomies for the micron-scale–macroscale region. As such, it seems plausible to expect a continuum of conserved CHDPs to connect these two hierarchical levels.

It is noteworthy that in spite of enormous activity in the nanotechnology field during the past several decades, only highly specific/limited strategies have been proposed [30]; however, no such universal Linnaean-type taxonomic scheme has been suggested for classifying and unifying well-defined nanostructures, assemblies, or clusters until recently.

1.4.3.1 Taxonomy of Nanostructure/Assemblies

(a) Dendrimers/Dendrons as a Window to a Nanoscale Taxonomy. Recently, we described the use of dendrons/dendrimers as a window to a new nano-periodic system for defining quantized, discrete categories of nano-building blocks (i.e., nano-elements) [31]. They may be thought of as heuristic, core-shell-type atom mimics that share many atom-like combining properties with atoms to yield stoichiometric nano-compounds. Based on more than 12,000 published references in the literature, it has been clearly demonstrated that dendrons/dendrimers are structure controlled nanoscale constructs that exhibit quantized critical nanoscale design parameters (CNDPs) such as (a) size, (b) shape, (d) flexibility/rigidity, and (e) architecture. A variety of dendrimer surface reactions or guest–host assemblies have been shown in the literature to produce stoichiometric nano-compounds including (a) dendrimer–dendrimer, (b) dendrimer–protein, (c) dendrimer–fullerene, and (d) dendrimer–metal nanocluster structures, to mention a few [2]. Meanwhile, as part of this comparison, dendrimers have been shown to exhibit heuristic cladogram properties similar to the atomic elements as illustrated in Figure 1.11, where they are displayed according the Niels Bohr format. Further comparisons can be made by projecting the first three generations of a dendrimer in a Mendeleev-type periodic format [1] as shown in Figure 1.12.

1.5 HEURISTIC MAGIC NUMBER MIMICRY AT THE SUBATOMIC, ATOMIC, AND NANOSCALE LEVELS

Many legendary scientists have made profound historical statements concerning the importance of number theory to the periodicity of matter. The following are just a small sampling:

- Prout’s Hypothesis published anonymously in (1815): “The elements are different aggregates of the atoms of primordial hydrogen.”
**Heuristic Magic Number Mimicry at the Subatomic, Atomic, and Nanoscale Levels**

Many of these issues are examined extensively by Boeyens and Levendis [32] and provide a scientifically valid examination of the critical role that "magic numbers" play relative to the periodicity of matter.

A seminal publication by Jena and Castleman [33] describes the routine observation of so-called "magic numbers" associated with clusters that include unique associations and stabilities of atomic particles [34] and, more recently, nanoscale particles such as metal nano-clusters [33, 35–37] and dendrimers [2, 24, 25]. Furthermore, it appears that such magic numbers may also be associated with micron-scale/macroscale objects that are referred to as Fibonacci numbers [38]. As stated by these authors, "it was surprising to observe such similarities between magic numbers in nuclei and atom clusters in spite of the fact that the binding forces in nuclei are very different from those that bind atoms in clusters." That notwithstanding, it has been found that well-defined numbers of atoms in a cluster of a given size or shape and/or given arrangement/disposition exhibit magic numbers corresponding to various symmetrical, close-packed polygons in two dimensions (2-D) or polyhedrons in three dimensions (3-D) [39]. In this context, magic numbers count the number of spheres in sphere packings of platonic solids and related polyhedral [40]. In essence, magic numbers may be viewed as the result of "atom counting" wherein atoms behave as spheres in well-defined clusters that are structurally controlled as a function of size, shape, surface function, flexibility/rigidity [41], and architecture. These relationships are readily observed in "bravais lattices" wherein cluster geometry depends on crystal structures [39] and precisely defines interrelationship and stoichiometries between participating spheroids (atoms). These "geometrical/mathematical-based magic number" relationships undoubtedly account for their pervasive occurrence at the atomic level, as well as at the nanoscale level when comparing atoms to dendrimers (Figure 1.13) and as well as when comparing atoms to soft clusters (i.e., dendrimers) and hard clusters (i.e., gold nano-clusters) as shown in Figure 1.15.

**1.5.1 Heuristic Atom Mimicry of Dendrimers: Nano-Level Core–Shell Analogues of Atoms**

A heuristic comparison of the core–shell architectures that are present in dendrimer-based nanoscale modules and...
picoscale atoms was made as early as 1990 [24,42,43]. Furthermore, it appears that a very interesting size continuum exists in the transition from picoscale (atomic) structures to nanoscale dendrimer structures as illustrated in Figure 1.13. This comparison was used to point out the unique similarities that exist between aufbau components in atoms (i.e., cores and branch cell monomers). Remarkable analogies were also noted between recognized, but dimensionally, different parameters shared by both systems such as (a) electron shells versus monomer shells (generations), (b) electron shell versus monomer shell aufbau filling patterns (i.e., mathematically defined), (c) electron shell versus monomer shell saturation levels, (d) atomic weights versus dendrimer molecular weights as a function of shell level and saturation level, and (e) atomic (elemental) reactivity versus dendrimer reactivity as a function of shell saturation level (Figure 1.12). We have referred to these remarkable similarities between picoscale (atomic elements) and nanoscale dendrimers as atom mimicry, keeping in mind that picoscale structures are best described by non-Newtonian physics, whereas the dendrimer structures are expected to adhere to and be described by Newtonian physics. As noted in Figure 1.14, the specific bottom-up building block aufbau leading to dendrimers and higher complexity can be described both mathematically and in the context of CHDPs. This aufbau pathway leading to dendrimers involves a hierarchical transfer sequence of structural information which may be precisely defined mathematically. As such, it appears rational to assume that the CHDPs at each dimensional level are conserved from the picoscale (CADP) to molecular level (CMDP) to nanoscale (CNDP) to micron-scale (CMicDP) levels as illustrated in Figure 1.14.

In summary, one observes the involvement of quantized “magic numbers” of electrons to reach electron shell saturation levels at the picoscale level. Similarly, the
ELEMENT CATEGORIES AND THEIR HYBRIDIZATION INTO NANO-COMPOUNDS AND NANO-ASSEMBLIES

1.6 ELEMENT CATEGORIES AND THEIR HYBRIDIZATION INTO NANO-COMPOUNDS AND NANO-ASSEMBLIES

1.6.1 A Brief Overview of Nano-classifications (Taxonomies)

One of the first efforts to develop a nanoscale classification (i.e., taxonomy) system evolved from a quest to unify and define nanoscience based on the same “first principles” that underpinned the “central paradigm” for traditional small molecule chemistry [2]. Briefly stated, it was based on a nanomaterials roadmap that focused on well-defined, monodisperse (i.e., >90% monodisperse/homogeneous) nanostructures, nano-assemblies, and exhibited some degree of atom mimicry. As illustrated in Figure 1.16, these entities were referred to as nano-element categories. The initial list consisted of 12 nano-element types that were divided into six hard (i.e., inorganic) and six soft (i.e., organic) nanoparticle categories. It was then proposed that based on their atom mimicry features, these nano-element categories could be combined and hybridized into combinatorial libraries of nano-compounds/assemblies. Just as is observed with traditional atom/small molecule chemistry, many literature examples have demonstrated analogous periodic behavior at the nanoscale level. These entities exhibited unique nano-periodic property patterns that were dependent on one or more CNDPs. In the case of the [S-1]-type nano-element category (i.e., dendrimers), these CNDP-driven nano-periodic property patterns accounted for essentially all dendritic effects reported in the literature [2, 45]. Within the past several years, seminal work by Percec, and co-workers [46] has fulfilled and confirmed these hypotheses by publishing first examples of Mendeleev-like nano-periodic tables. These Percec nano-periodic tables demonstrated that by using CNDPs for [S-1]-type amphiphilic dendrons, it was possible to make a priori predictions for their mode of self-assembly with 85–93% accuracy.

The remaining sections of this account will review these issues in more detail and will conclude by connecting these accomplishments to present and future efforts to
1.7 A NANO-PERIODIC SYSTEM FOR DEFINING AND UNIFYING NANOSCIENCE

Initial criteria for a nanoscale classification (i.e., taxonomy) system were recently reported by us [2, 31]. Briefly stated, the taxonomy was based on well-defined, monodisperse (i.e., >90% monodisperse/homogeneous) nanostructures, nano-assemblies with dimensions of 1–100 nm, possessing collections of $10^3$ to $10^9$ atoms and masses of $10^4$ to $10^{10}$ daltons. These well-defined nano-entities were generally obtained by structure-controlled, bottom-up synthetic strategies, as opposed to top-down engineering approaches. Prime examples of such bottom-up aufbau approaches include biological protein or DNA/RNA synthesis, divergent/convergent dendrimer synthesis, and linear polymer synthesis based on Grubbs-type catalysts [47], to mention a few.

Furthermore, it was proposed that these well-defined nano-collections of atoms should possess certain quantized features/properties that manifested some degree of heuristic atom mimicry. Atom mimicry was defined as well-defined, nanostructures/assemblies or collections of atoms that exhibited heuristic structural features or quantifiable combining ratios/stoichiometries reminiscent of atoms. These selected candidates were referred to as nano-element categories and divided into types based on (a) conducting, (b) semiconducting, and (c) nonconducting properties. This classification led to two major classes: namely, those reminiscent of traditional inorganic elements (i.e., hard nano-elements) and organic elements (i.e., soft nano-elements). These initial criteria provided broad classifications for dividing well-defined nano-entities into broad taxa or classifications. Using Linnaean-type taxonomy criteria, we now propose further-down selections into more specific taxa (i.e., categories) based on the use of six universal CNDPs. More specifically, these taxa or criteria are related to (a) sizes, (b) shapes, (c) surface chemistries, (d) flexibility/rigidity, (e) architectures, and (f) elemental compositions. These six CHDPs, when structurally controlled, are tangible features that may be quantified and associated with each of the increasingly complex.
A NANO-PERIODIC SYSTEM FOR DEFINING AND UNIFYING NANOSCIENCE

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FIGURE 1.15. Comparison of “magic numbers” for atomic picoscale particles, hard nanoparticles, and soft nanoparticle evidence for atom mimicry at the nanoscale level [2]. Center image hard matter reproduced with permission from Elsevier [44].

1.7.1 Bottom-Up Synthetic Strategies to Soft Nano-element Categories

Presently, the broad grouping of soft nano-element categories can be divided into two general types: namely, synthetic (i.e., [S-1], [S-2], [S-3]) and biopolymers (i.e., [S-4], [S-5], hierarchical levels as described in Figure 1.2. Furthermore, significant data are accumulating which clearly show that these six taxa (CHDPs) dramatically influence many documented nano-periodic patterns/trends. Quantitation of these six taxa (CNDPs) in the dendrimer field have recently been shown to strongly influence and direct so-called dendritic effects [45]. Furthermore, seminal work by Percec and co-workers [46] has shown that these six taxa (i.e., CNDPs) clearly influence the validity of his first examples of Mendeleev-like nano-periodic tables described later in Section 1.8.4 (Figure 1.27).

Using “first principles and step logic” underpinning traditional chemistry, a template and strategy for the evolution of a new “nano-periodic system” and “central dogma” for nanoscience have been advanced [2]. Briefly stated, this concept proposed the following:

1. Creation of a nanomaterials roadmap focused solely on well-defined (i.e., >90% monodisperse) (0-D) and (1-D) nanoscale materials.
2. These well-defined materials were divided into hard and soft nanoparticles, broadly following compositional/architectural criteria for traditional inorganic and organic materials.
3. A preliminary table of hard and soft nano-element categories consisting of six hard-matter and six soft-matter particles was proposed, (Figures 1.16 and 1.17). Nano-elemental category selections were based on “atom mimicry” features and the ability to chemically combine or self-assemble like atoms.
4. These hard and soft nano-element categories were shown to produce a wide range of stoichiometric nanostructures by chemical bonding or nonbonding assembly. An abundance of literature examples provides the basis for a combinatorial library of hard-hard, hard-soft, and soft-soft nano-compounds, many of which have already been characterized and reported. However, many such predicted constructs remain to be synthesized and characterized [2, 31, 45].
5. Based on the presumed conservation of critical module design parameters (i.e., CADP → CMDP → CNDP) (Figure 1.4), many new emerging nano-periodic property patterns have been reported in the literature for both the hard and soft nano-element categories and their compounds [2].
A PROPOSED TAXONOMY AND CLASSIFICATION STRATEGY FOR WELL-DEFINED, SOFT-MATTER NANOSCALE BUILDING BLOCKS

FIGURE 1.16. The first examples of Mendeleev-like nano-periodic tables have recently fulfilled these expected nano property pattern/trend predictions [2, 31]. Percec/Rosen [46] have reported the first three nano-periodic tables for predicting the self-assembly patterns for [S-1] type amphiphilic dendrons with predictive accuracies of 85% to >90% based on knowledge of the primary dendron CNDPs: namely, (a) size, (b) shape, (c) surface/apex chemistry, and (d) flexibility/rigidity [45]. See color insert.

[S-6]) based on the specific aufbau strategies that are used to produce them (Figure 1.18). Several well-known synthesis strategies are shown that have been reported to produce highly structure-controlled aufbau pathways to each category with associated conservation of all CNDPs. It should be noted that specific procedures are generally available to produce these soft element categories in a variety of architectures as noted in Figure 1.18. In this account, we focus mainly on dendrons and dendrimers as well as proteins, viral capsids, and DNA/RNA—all of which have been proposed as important soft-matter, nano-element categories for defining a new nano-periodic system [2]. Since the discovery of dendrimers several decades ago [1, 24, 25, 48–50], significant evidence clearly shows that these nanomaterials react and self-assemble as discrete, quantized nano-units. These well-defined collections of covalently bonded atoms exhibit many features normally associated with traditional elemental atoms (i.e., atom mimicry). As such, dendrimers behave much as soft particle nano-elements to produce well characterized core-shell (tecto)dendrimers (i.e., dendrimer-dendrimer-type nano-compounds). Similarly, combining [S-6]-type RNA/DNA cores with [S-5]-type protein subunits to form nano-compounds such as tobacco mosaic virus as shown in Figure 1.19 and will be described in Section 1.8.3. These results optimistically portend the extension of this concept to a wide variety of other well-defined soft-particle nano-elements, as well as hard-particle nano-elements (i.e., metal oxide nanocrystals, metal chalcogenide nanocrystals, etc.) which have been reported elsewhere [2].

1.8 CHEMICAL BOND FORMATION/VALENCE AND STOICHIOMETRIC BINDING RATIOS WITH DENDRIMERS TO FORM NANO-COMPOUNDS

Using first principles and step logic invoked by Dalton (i.e., Philosophy for a Chemical System, 1808 [51] and others, it was possible to experimentally demonstrate that certain quantized nano-modules (i.e., dendrimers, fullerenes, metal nano-clusters, or metal oxide nanocrystals) could be chemically combined or assembled to produce stoichiometric nano-compounds/assemblies possessing well-defined mass combining ratios. Furthermore, these 12 soft and hard nano-elements, designated [S-n] and [H-n], respectively, have been reported to form a wide range of soft-particle and
FIGURE 1.17. Concept overview: Using first principles and step logic that led to the “central dogma” for traditional chemistry, the criteria of nanoscale atom mimicry was applied to Category I-type, well-defined nanoparticles. This produced 12 proposed nano-element categories that were classified into six hard particle and six soft-particle nano-element categories. Chemically bonding or assembling these hard and soft nano-elements leads to hard:hard-, soft:hard-, or soft:soft-type nano-compound categories, many of which have been reported in the literature. Based on the discrete, quantized features associated with the proposed nano-elements and their compounds, an abundance of nano-periodic property patterns related to their intrinsic physico-chemical and functional/application properties have been observed and reported in the literature [2].
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soft–hard-particle-type nano-compounds. Both the nano-elements and their nano-compounds are widely recognized to exhibit new emerging properties and nano-periodic property patterns [2]. At least three unique core–shell nano-compound category types may be formed by combining appropriate soft and hard nano-elements as illustrated in Figure 1.17. For example, combining [S-1]-type dendrimers with other dendrimers has been shown to produce precise, stoichiometric [S-1:(S-1)]n core–shell-type nano-compounds (Figure 1.19), whereas [H-4]-type fullerenes reacted with [S-1]-type dendrimers to give [S-1:(H-4)]n core-shell-type nano-compounds and finally [S-1]-type dendrimers were found to react with [H-1]-type metal nano-clusters to yield stoichiometric [H-1:(S-1)]n core-shell-type nano-compounds. Leading literature references to these nano-compound types and others in the three combinatorial nano-compound libraries (Figure 1.17) are described in greater detail elsewhere [2].

1.8.1 Dendrimer–Dendrimer [S-1:(S-1)]n Core–Shell-Type Nano-compounds

Saturated-shell nano-compounds such as dendrimer–cluster compounds (Figure 1.20) are prepared by a two-step approach that involved, firstly, self-assembly of an excess of carboxylic acid terminated dendrimers (i.e., shell reagent) around a limited amount of amine-terminated dendrimer (i.e., core reagent) in the presence of LiCl. This was followed by covalent amid bond formation between the core and dendrimer shell reagents using a carbodiimide reagent [52–54]. The resulting nano-compounds (i.e., saturated core–shell tecto (dendrimers), referred to as megamers) are prime examples of precise poly-dendrimer cluster structures as shown in Figure 1.20.

The stoichiometries of these structures may be predicted mathematically by the Mansfield–Tomalia–Rakesh equation.
CHEMICAL BOND FORMATION/VALENCY AND STOICHIOMETRIC BINDING RATIOS WITH DENDRIMERS TO FORM NANO-COMPOUNDS

Figure 1.19. A soft nano-element combinatorial library indicating possible soft–soft-type nano-compounds. Highlighted dendrimer–cluster compounds \([S-1: (S-1)_n]\) and the tobacco mosaic virus \([S-6: (S-1)_{2130}]\)-type or \([S-6: (S-5)]\)-type nano-compounds.

Figure 1.21 [1, 55] and are dependent upon the relative diameters of dendrimer core reagent relative to dendrimer shell reagent. The predicted stoichiometric limits \((N_{\text{max}})\) are determined by the core–shell spheroid ratios that are shown in the far-right column. These predicted stoichiometries have been unequivocally verified by experimental mass spectrometry, gel electrophoresis, and atomic force field microscopy (AFM) [1, 52, 54, 56]. It is interesting to note that when the core and shell have identical diameters to produce a spheroidal core–shell ratio of one, as is the case for all core–shell, metal nanoclusters, one should expect a core–shell stoichiometry of \((N_{\text{max}}) = 12\) (Figure 1.14). This is exactly what is predicted according to the Mansfield–Tomalia–Rakesh equation (Figure 1.21).

Combinatorial libraries of these \([S-1: (S-1)_n]\); core–shell-type nano-compounds can be readily synthesized by simply combining various dendrimer generations according to this protocol. Furthermore, various dendrimer families (i.e., PAMAM, PPI, etc.) may be used to produce a variety of dendrimer cluster-compositional copolymers. As shown in Figure 1.22, using a \(G = 7\); PAMAM dendrimer as a core reagent and \(G = 5\); PAMAM dendrimers in excess as the shell reagent produces a core–shell nano-compound (i.e., \([S-1: (S-1)_{13}]\) with a stoichiometry of 1:13. Many examples

Figure 1.20. The saturated-shell-architecture approach to covalent megamer synthesis. All surface dendrimers are carboxylic acid terminated [53].
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FIGURE 1.21. (a) Symmetry properties of core–shell tecto(dendrimer) structures, when $r_1/r_2 < 1.20$. (b) Sterically induced stoichiometry (SIS) defined shell capacities ($N_{\text{max}}$), based on the respective core and shell radii, when $r_1/r_2 < 1.20$. (c) Mansfield–Tomalia–Rakesh equation for calculating the maximum shell filling value (capacity)($N_{\text{max}}$), when $r_1/r_2 > 1.20$ [1, 31, 55]. It should be noted that when the core spheroid radius equals the shell spheroid radius, as in metal nano-clusters (see Figure 1.15), then the ($N_{\text{max}}$) = 12 as shown above. Metal nano-cluster image reprinted [44] with permission of Elsevier.

of these well-characterized core–shell nano-compounds are described in detail elsewhere [53].

1.8.2 A Quest for Synthetic Mimicry of Biological Quasi-equivalence with [S-1]-Type Amphiphilic Dendrons

As early as 1992, Percec et al. [57] compared the similarity of supramolecular nano-cylinders obtained from his amphiphilic dendrons to the supramolecular assembly of protein subunits to produce the cylindrical viral capsids that surround RNA in tobacco mosaic viruses (TMVs). More recently, Percec [58] reviewed the historical inspiration provided by Klug’s seminal Nobel Prize work on the structure of TMV [59, 60]. Percec was able to show unequivocally that dendrons behave much like protein subunits to produce a rich variety of cylindrical and spherical supramolecular dendrimers that exhibit quasi-equivalency much as is noted in many viral capsids. Based on accelerated design strategies involving synthetic amphiphilic dendrons, Percec et al. [61–64] were able to demonstrate the quasi-equivalent mimicry of biological systems by using retrostructural analysis [64] of their periodic and quasi-periodic supramolecule dendrimer assemblies as outlined in Figure 1.23. This remarkable comparison corroborates and documents many dendron libraries and other examples of dendron/dendrimer-based protein mimicry [65–67].

1.8.3 Tobacco Mosaic Virus: Compelling Example of a Supramolecular Core–Shell-Type Nano-compound Exhibiting Well-Defined Stoichiometry: Self-Assembly of Protein Subunits [S-4] around a [S-6]; ssRNA Core to Produce [S-6][S-4]$_{2130}$

More than three decades ago, important stoichiometric, self-assembly relationships were noted by Klug et al. [59, 60, 68] between the ss-RNA core and the self-assembling protein.
subunits in the formation of tobacco mosaic viruses (TMVs). The stoichiometric relationship between the viral core and the viral capsid was carefully documented by x-ray studies. This work rigorously demonstrated that exactly 2130 protein subunits assembled to form a viral capsid shell around a ss-RNA core to produce TMV with diameter = 18 nm, length = 300 nm, and helical symmetry. Elucidation of this self-assembly process together with the unprecedented characterization of this viral assembly by x-ray analysis, garnered the Nobel Prize for A. Klug in 1982. In the context of the systematic, nano-periodic concept [2], this viral construct may be viewed as a supramolecular, stoichiometric core–shell \( [S-6;(S-4)_{2130}] \)-type nano-assembly as described in Figure 1.24.

Viral capsids were included in the original list of six soft nano-element categories. These entities consist of a large group of well-defined nano-assemblies/objects that are known to be very well-defined as a function of their CNDPs. They are derived from the self-assembly of protein subunits (i.e., [S-4]-type nano-elements) and fulfill our criteria for their designation as [S-5]-type soft nano-elements. Similarly, RNA and DNA structures (i.e., designated as the [S-6]-type nano-element category) also fulfilled this criteria and were included on this list. As such, it is noteworthy to point out

![Figure 1.22](image1.png)

**FIGURE 1.22.** A size comparison of TEMs for Tomalia-type PAMAM dendrimers; \( G = 5–10 \). Covalent synthesis of a core–shell tecto (dendrimer) by combining a dendrimer; \( G = 7 \) core reagent with an excess of dendrimer; \( G = 5 \) shell reagent to produce the dendrimer cluster with a stoichiometry of 1:13.

![Figure 1.23](image2.png)

**FIGURE 1.23.** Dependency of self-assembly patterns leading to tertiary and quaternary dendron assemblies based on primary structure controlled dendron CNDP’s such as (a) size, (b) shape, (c) surface/apex chemistry, and (d) flexibility [46]. Copyright 2009 American Chemical Society.
A PROPOSED TAXONOMY AND CLASSIFICATION STRATEGY FOR WELL-DEFINED, SOFT-MATTER NANOSCALE BUILDING BLOCKS

FIGURE 1.24. Tobacco mosaic virus (TMV). An example of a well-defined nano-compound \([S-6]:(S-4)\) consisting of an ss-RNA(core):protein subunits (shell) that has nano-dimensions of diameter 18 nm, length 300 nm, and helical symmetry \([68]\). Adapted with permission from Scientific American.

that in the case of TMV, precise stoichiometries are observed for the protein to genome constituents. For example, the protein \([S-4]\) to RNA \([S-5]\) stoichiometry is 2130:1, whereas the viral capsid \([S-5]\) to RNA \([S-6]\) is 1:1.

Similarly, the M13 bacteriophage virus is derived from a single-strand DNA (ssDNA) that is 6407 nucleotides long. This genomic core is encapsulated with \(\sim 2700\) protein subunits to produce a filament-like cylinder with a diameter of 6.6 nm and length of 880 nm. This viral-type nano-compound exhibits a protein \([S-4]\) to DNA \([S-5]\) stoichiometry of 2700:1. Recent work has shown that these nano-compound building blocks can be self-assembled to produce a wide variety of higher hierarchical organizations that conserve and communicate their CNDPs well into the micron-scale region \([69]\).

It will be interesting to note whether all classified viruses exhibit precise and well-defined stoichiometries between their genomic and protein constituents. If this is the case, then all viruses may be viewed as nano-compounds in the context of our nano-periodic system.

Inspired by Klug’s work on TMV, the Percec group synthesized and analyzed innumerable libraries of self-assembling amphiphilic dendrons (Figure 1.25) \([70, 71]\). For each library, the dendron primary structures were compared to the tertiary structures of the self-assembled supramolecular dendrimers and the quaternary structure of the crystal lattices. A sampling of these libraries reveals primary dendron structures derived from \(AB_2; 3.4, AB_3; 3.5, AB_4; 3.4,5\)-dendrons, to mention a few \([46]\). A typical library for an \(AB_4; 3.4\)-disubstituted biphenyl \((Bp)\) dendron family is characterized as a function of dendron CNDPs such as generation \((n)\), surface/apex chemistry, and shape and flexibility as shown in Figure 1.26. These analyses clearly reveal important dendron parameters such as \((a)\) the molecular solid angle \((\alpha')\) of the dendron, \((b)\) morphology (shape) of the supramolecular dendrimer, and \((c)\) aggregation number \((\mu)\) \((i.e., supramolecular dendrimer stoichiometry)\) varied in a predictive manner to reveal important self-assembly patterns as a function of dendron generation. It should be noted that very precise reproducible stoichiometries were observed for these dendron self-assemblies as evidenced by their discrete aggregation numbers, namely, \([S-1]\), (see Figure 1.26). For example, these library analyses revealed interesting patterns such as: Increasing the generation number causes a change in molecular solid angle \((\alpha')\) and typically a transition from lamellar to columnar and spherical assemblies. Increasing the generation number does not necessarily increase the diameter of the supramolecular dendrimer \((D)\), but generally reduces the aggregation number \((i.e., \mu)\) or number of dendrons required to form a supramolecular sphere or the cross section of a supramolecular column. Deviations from these patterns usually indicate the formation of hollow core

FIGURE 1.25. Amphiphilic dendron self-assembly libraries directed by the critical nanoscale design parameters (CNDPs): \((a)\) size, \((b)\) shape, \((c)\) surface chemistry, and \((d)\) flexibility. Copyright 2009 American Chemical Society \([70]\).
supramolecular dendrimers or other novel mechanisms of self-assembly. Generally AB$_2$; 3,4,5-trisubstituted libraries exhibit more spherical structures when compared to AB$_3$; 3,4-disubstituted dendron libraries.

Furthermore, it was shown by Percec et al. [46] that simply knowing the four CNDPs—namely, (a) size, (b) shape, (c) surface chemistry, and (d) flexibility of the primary dendron structure—one can predict self-assembly patterns leading to tertiary and quaternary structures with greater than 85–93% accuracy as shown in nano-periodic Table 1.1 (Figure 1.27).

1.8.4 First Nano-periodic Tables for Predicting Amphiphilic Dendron Self-Assembly to Supramolecular Dendrimers Based on the Critical Nanoscale Design Parameters

Like proteins, the primary structures of the amphiphilic dendrons determine their tertiary structure. As such, Percec has compared dozens of his AB$_2$- and AB$_3$-derived dendron libraries in an effort to determine trends or “nano-periodic self-assembly patterns” as proposed by others [2]. Percec’s seminal comparison produced the first three Mendeleev-like, predictive Nano-periodic Tables I for the self-assembly of aryl ether dendrons, which are described elsewhere [46]. One of these nano-periodic tables is as illustrated in Figure 1.27. These three nano-periodic tables summarize the tertiary and quaternary structures that are formed for similar primary dendron structures, however, using different dendron building blocks. They provide predictive nano-periodic tables that describe general trends in the sequence–structure relationship (i.e., primary→secondary→tertiary→quaternary structures). Furthermore, they identify clustered regions where specific structures will be found. The supramolecular dendrimer structures formed may be classified into lamellar, columnar, or spherical morphologies by analogy to β-sheets, helical structures of fibrillar proteins, and the pseudo-spherical structure of globular proteins. In all three
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TABLE 1.1. Proposed Linnaean-Type Taxonomy for Classifying Dendrimers

<table>
<thead>
<tr>
<th>Linnaean Taxa</th>
<th>Similarity Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kingdom</td>
<td>Picoscale, subnanoscale, nanoscale, micro-scale</td>
</tr>
<tr>
<td>Phylum</td>
<td>Synthetic, synthetic-biological, biological</td>
</tr>
<tr>
<td>Class</td>
<td>Linear, cross-linked (bridged), branched, dendritic</td>
</tr>
<tr>
<td>Order</td>
<td>Inorganic, inorganic-organic, organic</td>
</tr>
<tr>
<td>Family</td>
<td>Elemental/connectivity composition (i.e., PAMAM, PPI, PLys)</td>
</tr>
<tr>
<td>Genus</td>
<td>(a) Core-type (i.e., NH, EDA, DAB, etc.)</td>
</tr>
<tr>
<td></td>
<td>(b) Core/branch cell multiplicities (i.e., ( N_0 = 30N_4 ) = 2)</td>
</tr>
<tr>
<td></td>
<td>(c) Generation level (i.e., ( G = 4 ))</td>
</tr>
<tr>
<td>Species</td>
<td>(a) Terminal/surface chemistry (i.e., electrophilic, nucleophilic, etc.)</td>
</tr>
<tr>
<td></td>
<td>(b) Surface functionality (i.e., amine, hydroxyl, carboxyl, etc.)</td>
</tr>
<tr>
<td></td>
<td>(c) Terminal/surface valency (( Z )) (i.e., ( Z = N_0N_4^C = 48 ))</td>
</tr>
</tbody>
</table>

**Shorthand Nomenclature:** Core: \( \text{NH}_3^+; N_0 = 3 \rightarrow N_4 = 2; \text{dendrimer} \) (poly(amidoamine)-(NH\( \text{OH} \))\( \text{NH}_3^+; \), \( G = 4 \)) (PAMAM) dendrimer.

1.9 PROPOSED LINNAEAN-TYPE TAXONOMY FOR SOFT-MATTER-TYPE NANO-ELEMENT CATEGORIES, THEIR COMPOUNDS AND ASSEMBLIES

A broad Linnaean-like template for classification of well-defined nanostructure/objects could involve a simple format such as is described in Table 1.1. For example, classification of an \([S-1]\)-type poly(amidoamine) (PAMAM) dendrimer might involve the following steps and operations: (a) First, this \([S-1]\)-type nanostructure could be broadly classified according to Linnaean principles, using the taxa shown down to the taxon-specificity of the order, namely, a nanoscale, synthetic, dendritic macromolecular structure, (b) the family is poly(amidoamine) PAMAM, and the genus consists of the core type, core/branch cell multiplicities, and generation level (\( G \)); and (c) the species can be described as possessing 48-nucleophilic, amine-terminal groups. Meanwhile, a shorthand nomenclature emerges from this classification, which utilizes these taxa and is further described in Figures 1.28–1.29 for various dendrimer families.

1.9.1 A Proposed Dendron/Dendrimer Shorthand Nomenclature

Dendrons and dendrimers have been widely recognized as critical pivotal building blocks in the dendritic state. Although several traditional organic nomenclature schemes have been proposed [74,75] to describe and classify the many reported dendron and dendrimer families, these terminologies have not gained wide usage due to their complexity [74,76]. Meanwhile, the evolution of a shorthand nomenclature scheme has become a “works in progress” based on the hybridization of contributions/suggestions extracted from a number of examples in the literature. This shorthand nomenclature involves associating specific dendrimer components.
with the well-known general mathematical expression defining the three major architectural components (i.e., core, interior and terminal groups) (Figure 1.28). These architectural components are in turn described systematically by indicating core $\rightarrow$ interior branch cell connectivity (i.e., $N_c \rightarrow N_b$ multiplicities), a stoichiometric value for number of terminal groups ($Z$) and a generation number as described below. Several well-known dendrimer families associated with their scientific originators can be described using this shorthand nomenclature as described with structures (a) and (b)[77] in Figure 1.29.

1.9.2 Classification of $[S-1:(S-1)_n]$-Type Nano-compounds Derived from Dendrimer/Dendron $[S-1]$-Type Nano-element Categories

The stoichiometry boundaries for combinatorial libraries of dendrimer nano-compounds $[S-1:(S-1)_n]$ derived from spheroidal dendrimers based on generational sizes are outlined and defined by the Mansfield–Tomalia–Rakesh equation as described in Figure 1.21. Other variations could involve combinations of different families of dendrimers. For example, combining a PAMAM dendrimer (S-1) with
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Dendrimer Architecture

Architectural Components

[Core] : [Interior] : [Terminal Groups] Z

Mathematically Defined Structure

(core: structure); (N_c → N_b); dendri{poly(repeat units)}; terminal groups Z

Shorthand Nomenclature

FIGURE 1.28. Association of dendrimer architectural components mathematical expression to define dendrimer structure, where $N_c$ is core multiplicity, $N_b$ is branch cell multiplicity, $G$ represents generation, $Z$ represents terminal groups, and proposed shorthand nomenclature is based on these parameters.

PPI dendrimers (S-1)′ as in Figure 1.29a would produce large series of [(S-1):(S-1)′] nano-compounds. Of course, many other stoichiometries would be possible by changing the dendrimer shape (i.e., combining spherical with cylindrical shapes). That withstand, attaching dendrons or dendrimers to the surface of other well-defined spheroidal nanostructures or assemblies such as gold nano-clusters; (i.e., [H-1]-type) would be expected to produce combinatorial series of hard-soft [H-1:S-1]-type nano-compounds. Many of these nano-compounds have been reported in the literature [2, 31].

Using combinations of hard and soft nano-element categories, Mirkin and co-workers [72] recently reported the assembly of gold nano-clusters (i.e., [H-1]-type nano-elements) modified with complementary single-strand DNA (i.e., [S-6]-type nano-elements). These interactive nano-conjugates (i.e., nano-compounds) self-assembled to form libraries of 3-D nano-lattices that mimicked traditional inorganic salt structures. Furthermore, these 3-D, [H-1:(S-6)], hard-soft-type crystal lattices exhibited crystal structures that unequivocally mimicked elemental atoms and were confirmed by x-ray studies.

As such, it is proposed that systematic cladograms could be developed to classify these possibilities according to similarity principles and features. The development of taxonomies for these various nano-element combinations would be expected to lead to suitable specific nomenclatures as witnessed for other Linnaean-type taxonomies. Nomenclatures have evolved in the case of certain soft nano-element categories, such as [S-4], [S-5], and [S-6] which are associated with the stoichiometric (genomic:capsid) construction of viruses. These issues are described in the next section.

1.9.3 Classification of Nano-compounds (i.e., Viruses) Derived from Proteins [S-4] or Viral Capsids [S-5] and DNA/RNA [S-6]-Type Nano-element Categories

A comprehensive taxonomy based on similarity features for viral capsids and viruses was initiated as early as 1962. This hierarchical classification pioneered by A. Lwoff, R. Horne, and P. Tournier [23], classified viruses according to shared properties with a focus on the following four features:

1. Nature of the nucleic acid core (i.e., RNA/DNA).
2. Symmetry of the capsid.
3. Presence or absence of an envelope.
4. Dimensions of the virion and capsid.

This classification scheme leads to two rather comprehensive cladograms that are divided broadly according to their
FIGURE 1.29. Various dendrimer families: (a) Vogtle/Meijer/Mulhaupt-type poly(propyleneimine) (PPI) dendrimers. (b) Tomalia-type poly(amidoamine) (PAMAM) dendrimers. Reproduced with permission from Elsevier [77].

FIGURE 1.30. A virus classification scheme broadly dividing according to RNA/DNA core type, symmetries, envelope features and diameters, and so on. Image courtesy of http://www.nlv.ch/Virologytutorials/graphics/classificationtotal.jpg.
A second virus classification scheme was introduced by D. Baltimore [9], and it is based on the hypothesis that all viruses must generate positive-strand mRNAs from their genomes in order to produce proteins and replicate themselves. The precise mechanism is different for each virus family, thus leading to seven different strategies for their replication and hence seven different viral families as described in Figure 1.31 [79].

If all viruses could be viewed as stoichiometric nanocompounds derived from well-defined ratios of genomic and protein subunits, it is apparent that suitable cladograms could be developed which would be consistent with both the Lwoff and Baltimore taxonomies described above. Each of these classifications has produced appropriate virus nomenclatures for defining specific viral prototypes.

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PRESENTLY, VIRAL CLASSIFICATIONS ARE FOCUSED ON THE TAXON LEVEL OF FAMILIES DOWNWARD. MEMBERS WITHIN A VIRUS FAMILY ARE ORDERED WITH GENOMICS, THE ELUCIDATION OF EVOLUTIONARY RELATIONSHIPS—THAT IS, ANALYSES OF NUCLEIC ACID AND PROTEIN SEQUENCE SIMILARITIES. AS SUCH, ALL VIRUS FAMILIES HAVE THE SUFFIX VIRIDAE (E.G., CALICIVIRIDAE, PICORNAVIRIDAE, REOVIRIDAE, ETC.); WHEREAS, GENERA HAVE THE SUFFIX V-VIRUS. WITHIN THE PICORNAVIRIDAE THERE ARE FIVE GENERA: ENTEROVIRUS, CARDIOVIRUS, RHINOVIRUS, APHTHOVIRUS AND HEPATOVIRUS. DEFINING ACTUAL “SPECIES” IS THE MOST IMPORTANT BUT DIFFICULT CHALLENGE ASSOCIATED WITH VIRUS NOMENCLATURE. THERE IS AN ELEMENT OF SUBJECTIVITY IN THAT TASK UNDOUBTEDLY DUE TO SUBTLE MUTATION-BASED ABBERRATIONS IN ACTUAL PRACTICE [20].

1.10 CONCLUSIONS

In this account, we have reviewed the successful use of Linnaean-type taxonomies for micron-scale biological structure/organism classifications, as well as for picoscale, atomic element classifications as evidenced by the Mendeleev Periodic Table. Each of these taxonomies has led to very useful nomenclatures. Each of these taxonomy areas were based on either picoscale or micron-scale aufbau pathways (i.e., evolutionary intermediates) that were organized according to...
CONCLUSIONS

FIGURE 1.32. A brief comparison of nineteenth-century picoscale building blocks [51] (images reproduced with permission from Wiley–VCH Verlag GmbH & Co. KGaA) and twenty-first-century nanoscale building blocks [45].

“features of similarity.” This, in turn, led to appropriate cladograms and corresponding “trees of similarity.” Mendeleev’s Periodic Table of the atomic elements projected in a Niels Bohr format represents such a “tree of similarity for the elements.” These Linnaean taxonomy principles have been shown to be useful for classifying three biology-based soft nano-element categories; namely, proteins [S-4], viral capsids [S-5], and DNA/RNA [S-6]-type nano-element categories. These same principles are now proposed as first steps toward the development of a taxonomy and nomenclature for certain well-defined, non-biologically derived, soft nano-element categories and are summarized as follows:
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This is a first step toward the development of a taxonomy and nomenclature for well-defined soft nanomaterials (i.e., [S-1],[S-2],[S-3],[S-4],[S-5], and [S-6]-type nano-element categories).

Three of the six soft nano-element categories (i.e., [S-4],[S-5], and [S-6]) enjoy taxonomies/nomenclatures and are biologically based.

Diverse process strategies that produce the three “nonbiological” soft nano-element categories (i.e., [S-1],[S-2], and [S-3]) involved the construction of specific “macromolecular architectures”—namely, (I) linear, (II) cross-linked, and (IV) dendritic architectures—for example, (a) divergent/convergent dendritic amplification (Type IV) dendritic polymers (i.e., [S-1]), (b) micelle-templated polymerization (Type II) cross-linked (bridged polymers) (i.e., [S-2]), and (c) Grubbs-type catalyst (Type I) linear polymers (i.e., [S-3]). As such, initial steps for nonbiological, soft nano-element taxonomies based on “architectural types” should be considered.

In summary, the eighteenth and nineteenth century witnessed the successful development of Linnaean-based taxonomy systems for classifying vast libraries of micro-scale/macro-scale biological structures and organisms. Similarly, during the nineteenth century the chemistry field enjoyed the successful development of a useful Linnaean-like taxonomy system for classifying all of the atomic elements in the form of Mendeleev’s Periodic Table [7, 80]. This early classification system naturally defined and unified traditional chemistry with the emergence of a useful and versatile nomenclature. This present account is an effort to define a new taxonomy and nomenclature for well-defined soft nanomaterials in the context of a nano-periodic system (Figure 1.17, 1.18, and 1.32) derived from these same traditional first principles [2, 19, 31]. It should be considered a “works in progress.” However, there is now optimism that continued development and success will lead to a similar Linnaean-type classification system for well-defined soft-matter, nano-element categories and perhaps be extended to hard-matter, nano-element categories with the concurrent emergence of a useful and versatile nanomaterials nomenclature.

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