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CCA-2804 *Essay*

Mathematical Chemistry*

Nenad Trinajstić[a,**] *and Ivan Gutman*[b]

[a] *The Rugjer Bošković Institute, P. O. Box 180, HR–10002 Zagreb, Croatia*

[b] *Faculty of Science, University of Kragujevac, P. O. Box 60, YU–34000 Kragujevac, Yugoslavia*

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A brief description is given of the historical development of mathematics and chemistry. A path leading to the meeting of these two sciences is described. An attempt is made to define mathematical chemistry, and journals containing the term *mathematical chemistry* in their titles are noted. In conclusion, the statement is made that although chemistry is an experimental science aimed at preparing new compounds and materials, mathematics is very useful in chemistry, among other things, to produce models that can guide experimental work to a target by the shortest possible route.

Key words: roots of chemistry, roots of mathematics, mathematical chemistry, mathematical chemistry journals.

".. every attempt to employ mathematical methods in the study of chemical questions must be considered profoundly irrational and contrary to the spirit of chemistry..."

Auguste Comte (1798–1857) in 1830.

* Dedicated to Professor Milan Randić on the occasion of his 70th birthday.

** Author to whom correspondence should be addressed. (E-mail: trina@rudjer.irb.hr)

PROLOGUE

The special issue of this journal, entitled *Mathematical Chemistry* and dedicated to Professor Milan Randić, the foremost mathematical chemist of our times, calls for some words to be said about the relationship between mathematics and chemistry. The present article is in part based on an earlier essay by one of us (N. T.).[1] In that essay, the relationship between mathematics and chemistry was said to be well described by the words of Erich Maria Remarque (1899–1970) (taken from *Shadows in Paradise*) "*They're two separate things, like wind and water; they move each other, but they don't mix*".

INTRODUCTION

Chemistry is one of three fundamental natural sciences; the other two being physics and biology. Chemical processes have continuously unfolded since shortly after the Big Bang and are probably responsible for the appearance of life on the planet Earth.[2–4] One might consider that life is the end-result of an evolutionary process in three steps:[5] (i) Physical evolution (the formation of chemical elements); (ii) Chemical evolution (the formation of molecules and biomolecules); and (iii) Biological evolution (the formation and development of organisms).

Chemical processes are ever present in our lives from birth to death because without them there is neither life nor death.[4] People are made of molecules; some of the molecules in people are rather simple whereas others are highly complex.[6] In fact, without chemistry and chemical products no human activity is possible. Pauling (1901–1994), the only scientist to date who has won two unshared Nobel prizes (one for chemistry (1954) and one for peace (1962)), summarized such ideas in his 1984 Priestley Medal address in the following words:[7] "*Every aspect of the world today – even politics and international relations – is affected by chemistry*". Another Nobel Prize winner, Arthur Kornberg (who shared the Nobel Prize for medicine with Severo Ochoa in 1959) stated:[8] "*Life, after all, is only chemistry, in fact, a small example of chemistry observed on a single, mundane planet*".* Pauling, of course, refers to chemistry and chemical technology whilst Kornberg to chemical processes that unroll in nature. Because of this kind of thinking, some refer to chemistry as the *central* science.[9] By similar reasoning and considering the above three evolutionary steps, one can label physics as the *first* science and biology as the *final* science.

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* This statement, of course, represents an over-simplified view. It is clear that life involves chemical processes, but they alone are not sufficient to create life.

Mathematics is not usually categorized as a natural science; it is a product of an intelligent mind. This could also be restated as that nature, that is, physical, chemical and biological processes, were before people, but people were before mathematics. However, physics, chemistry and biology, sciences that describe the physical, chemical and biological processes in nature, are also products of an intelligent mind. Of course, there are also other opinions on the nature of mathematics, such as that mathematical objects do exist and mathematicians simply discover them.[10]

It appears that the objects defined by mathematicians are abstract and can never be actually encountered in any way except *via* human imagination. Nevertheless, mathematics models nature unreasonably well, as the Nobelist Eugene P. Wigner (1902–1995), who shared the Nobel Prize for physics with Maria Goeppert-Mayer (1906–1972) and J. Hans D. Jensen (1907–1973) in 1963, remarked many years ago.[11] He also stated in the same article "*...that the enormous usefulness of mathematics in the natural sciences is something bordering on the mysterious and that there is no rational explanation for it*". This sounds like an echo from the times of Pythagoras, who was magically fascinated by mathematics and believed that "*everything is arranged according to number*".[12]

Some form of mathematics, *e.g.*, counting, was used by early peoples. Mathematics appears to be almost as old as humankind and also permeates all aspects of human life, although many of us are not fully aware of this fact. Similarly to chemistry, also mathematics has experimental roots.[13] In spite of this, mathematics and chemistry did not meet formally until the last century. Since that time, however, mathematics has strongly affected chemistry; chemistry has also occasionally stimulated advances in mathematics. Nowadays, chemical techniques may be used to solve mathematical problems, *e.g.*, a system of chemical waves can be set up in a labyrinth and then time-lapse images employed to construct a vector field that may be used to determine the shortest path between any two points.[14] Similarly, the feasibility of carrying out computations at the molecular level, that is, making use of the tools of molecular biology, has been demonstrated in the case of the directed Hamiltonian path problem.[15]

THE ROOTS OF MATHEMATICS

In a very general sense, mathematics can be described as the science of numbers and space. However, mathematics can be more properly regarded as a form of language, developed by people in order to exhange ideas about abstract concepts pertaining to numbers and space.[16] Mathematics is also the most economical language for formulating theories in natural sciences.

If it were not, humans would construct another and better language. It also enables the appearance of theories as elegant,[17–19] since "...*elegance is always worth something*", as Patrick Fowler once remarked.[20]

The roots of mathematics go back to the earliest civilizations.[21] The origins are, however, to a great extent unknown because the beginnings of mathematics are older than writing. It is usually assumed that early mathematics in the form of counting arose in response to practical human needs, *e.g.*, counting the domestic animals.[22,*] In a general way, counting may be regarded as the process of matching the objects to be counted with some familiar set of objects such as fingers, toes, pebbles, sticks, *etc*. Counting as described in this way has also found use in the modern computer-assisted enumeration schemes of chemistry where the matching is between mathematical objects (*e.g.*, numbers) and chemical objects (*e.g.*, structural isomers).[23] However, anthropologists have suggested other origins, namely that counting arose in connection with primitive religious rituals.[24] During the ritual, it would be necessary to call the participants to the scene in a specific order and perhaps some kind of counting was invented to take care of this problem. In the first case, *e.g.*, the counting of animals, importance accrued to the total count; that is, it was important for a shepherd to know how many animals were in the flock, and in the second case, *e.g.*, the religious ritual, importance accrued to the order of appearance; that is, it was important for the participants in the ritual to know their places in an ordered sequence of appearances at the altar. The former case may be the origin of cardinal numbers and the latter of ordinal numbers. The ritual origin of numbers also points to division of the integers into odd and even, the former being regarded as male and the latter as female. Such distinctions were known to all primitive societies and myths regarding the male and female numbers have been remarkably persistent.[21] The concept of natural number thus appears to be one of the oldest concepts in mathematics. Since these early days, people have been continually interested in numbers and number theory is one of the few areas of mathematics where the works of both amateurs and professional mathematicians have had considerable impact on the development of the entire field.[22]

Like counting, also geometry had its beginnings in prehistoric times. Various neolithic peoples produced drawings and designs rich in symmetry and spatial relationships that show a knowledge of elementary geometry. On the other hand, Herodotus (*ca.* 484 – between 430 and 420 B.C.) and Ari-

* However, some form of primitive counting was probaly employed even at the earlier stages of human development because the early people, in order to survive, needed to identified times of the year associated with the various seasons, to know how many there were in a group, to count distances to hunting grounds, *etc*.

stotle (384–322 B.C.) placed the origin of geometry in the period of Egyptian civilization. Herodotus believed that geometry originated in Egypt because of the practical need to survey the river valley after the annual flooding of the Nile. Aristotle thought that it was the existence of a priestly class in Egypt with a lot of leisure time that had prompted the pursuit of geometry. Herodotus and Aristotle had opposite views on the beginnings of mathematics: either practical needs or leisure and ritual were the driving force. One cannot confidently contradict either Herodotus or Aristotle on the motive that led us to mathematics, but both of these great men might have underestimated the time for the beginning of geometry (and mathematics).* Counting and geometry clearly go back to unknown prehistoric times. The motivation behind the attempts by early peoples to design drawings with distinct geometric features is not known, unless it was the urge to produce beautiful forms. But this is the same motive that often stimulates the artists, mathematicians and scientists of today to produce beautiful paintings, theorems or theories. This need for beauty is deeply rooted in human psyche and does not depend on any particular historical period. Thus, prehistoric people and modern people show an equally intense need to create beautiful things and enjoy them.

Sometimes a question is raised that should perhaps not be asked at all, namely, does mathematics predate people? This question raises some doubt as to the veracity of the statement made in the introductory part of this chapter where it was emphasized that mathematics was invented by people. Accordingly, our answer to this question has to be negative: There was no mathematics before people. We also stated above that physical, chemical and biological processes predate people. However, the sciences of physics, chemistry and biology are also mental constructs as is mathematics.[25]

The hand was indisputably the earliest calculating device used by humans.[26] Not surprisingly, the number five has always been fascinating people.[27,28] The decimal (or the decadic) system that is used today is founded in the practice of counting in tens. This counting system is the result of counting using the fingers of both hands, although the counting system based on the number five (or the quinary system) was also used by early peoples. Even today, the latter system is still found in a South American Arawakan language (called Saraveca) in which counting uses solely the base five.[29] It may be that the use of the decimal counting system was much simpler than the use of the quinary system for most practical purposes and, consequently, the former system has since developed almost exclusively. There was also

* However, if one demands more mathematical content of geometry, then it might be argued that Herodotus and Aristotle were largely correct.

quite a problem to accept zero as a number.[30] Even one was not easily accepted as a number; there was a long struggle to recognize one as a number.[31] Additionally, the development of language to cover abstractions such as numbers was rather slow. The difficulties in producing numerical verbal expressions were probably smallest in the case of the number system with base 10 and this perhaps also favored the decimal system.[32] Possibly, this is the reason why modern languages are built almost uniformly around the decimal system.

One point should be emphasized here: the subsequent development of mathematics from the earliest days of the subject was almost always dualistic. That is to say it was initiated either by practical needs of the society or by the curiosity of mathematicians concerning certain problems that at first sight appeared to be without any practical use (but which have eventually shown themselves to be of utmost practical value for science). However, the historical development of mathematics has shattered our belief that mathematics offers absolutely certain knowledge.[33] One of the first people to do this was Kurt Gödel (1906–1978).[34–38] His incompleteness theorem demonstrated that, in any deductive scheme constructed from a finite number of axioms, there would be well-formulated statements that could not be proven true or false within the scheme itself. Therefore, there are questions in mathematics that can never be answered, at least not within the axiomatic system under consideration.

From a philosophical point of view, most mathematicians may be classified as:[39–41] (i) Platonists, (ii) formalists, (iii) logicians, (iv) intuitionists, or (v) constructivists. Platonists consider ideas to be eternal and the only truth. Formalists only manipulate systems according to arbitrary rules. To the logicians, all of mathematics is a branch of logic. Intuitionists believe that no final proofs of anything can be given and human intuition rather than logic is at the bottom of everything. Finally, constructivists insist that things must be constructed to show that they exist. One may add a *sixth* class of mathematicians: pragmatists. Pragmatists represents a class of applied mathematicians which includes mathematical physicists, mathematical biologists, and now mathematical chemists.

The aim of the philosophy of mathematics is to explain the activity of mathematicians and the concepts they study.[40,41] Consequently, the most important question for the philosopher of mathematics is simply: "*What is mathematics*?" Quite clearly there is no simple answer to this question. Futhermore, it appears that there is no generally accepted answer to this question beyond the statement that "*Mathematics is nothing more and nothing less than what mathematicians do*".[42] It seems it is much easier to answer the question: "*What mathematics is not*?" We wish to end this section with the definition of mathematics that is most to our liking and is quoted by Hamming:[39] "*Mathematics is nothing but clear thinking*".

THE ROOTS OF CHEMISTRY

Chemistry can be broadly defined as the science of (material) substances and their transformations. In a somewhat narrower sense, chemistry is the science of molecules and their transformations.[43] Chemistry also concerns some collective features of matter (as in thermodynamics) that arise from the simultaneous interactions amongst many, many molecules.

In contrast to mathematics, chemical processes are older than people. The appearance of life and people on our planet Earth is most probably the end-result of specific chemical processes. Chemical processes have been present in the lives of people from the dawn of history until the present time.[44–47] Initially, these processes were beyond control, *e.g.*, the fermentation of fruit juice, the rotting of meat and fish, the burning of wood, *etc.*, but later on people learned to control chemical processes and to use them to prepare a variety of different products, such as food, metals, ceramics, leather, *etc.* In the development of chemistry, four periods may be distinguished: prehistoric chemistry, Greek chemistry, alchemy, and scientific chemistry.

Prehistoric Chemistry

The early beginnings of chemistry were clearly motivated by the practical needs of people. The discovery of fire offered prehistoric people the first opportunity to carry out controlled chemical processes. They learned how to prepare objects made of copper, bronze and other materials that were readily available to them. Since the use of chemical processes by these early people predates writing, there are no written records of their chemical skills. One can judge their chemical abilities only from the archaelogical discoveries of various artifacts. What has been found clearly indicates that practical needs influenced the early development of chemistry, as it was the case of the early development of mathematics. But, chemistry and mathematics probably did not interact at this early stage. If they did, there is no record to prove it.

Greek Chemistry

Greek chemistry was mainly based on speculation rather than on experiment. This was a common trait of all Greek science in antiquity. It should be also pointed out that the Greek scientist of antiquity was in fact the Greek philosopher.[48] Therefore, it is not suprising that the Greeks were much more interested in contemplating than in experimenting. Actually, most Greek philosophers seldom performed experiments outside of the thought experiment.* This was a good approach for mathematics but hardly one to be recommended for physical, chemical or biological sciences. Nevertheless, since the Greeks thought a lot about the nature and structure of matter, they can be considered the creators of the first chemical theories.

Greeks introduced the concept of the element and proposed four elements. Thales (625?–547 B.C.), from the city of Miletus in Asia Minor, thought that all things were formed from one elementary substance and that was water. Anaximenes (*ca.* 585 – *ca.* 528 B.C.), also from Miletus, accepted the idea of one element, but he believed that the single element from which all things were made was air. Heraclitus (*ca.* 540 – *ca.* 480 B.C.), from the city of Ephesus in Asia Minor, who thought that the fundamental characteristic of the universe was continuous change, regarded fire as the element that embodied perpetual change. Empedocles (*ca.* 490 – *ca.* 430 B.C.), from the Greek city of Akragas in Sicily, abandoned the idea of a single element and introduced the principle of four elements: water, air, fire and earth, and the two forces of attraction and repulsion operating between them. Empedocles is also known for his experimental proof that air is a material body.[44]

The term element was first used by the greatest of all philosophers and writers, not only of Greece, but of all times, Plato (428–347 B.C.),** who assumed that the particles of each element have a specific shape, even though such particles are too small to be seen. Thus, the smallest particle of fire has the shape of a regular tetrahedron; of air a regular octahedron; of water a regular icosahedron, and of earth a cube (or regular hexahedron). The regular tetrahedron, the regular octahedron, the regular icosahedron and the cube are regular polyhedra and there are five of them in all; the fifth regular polyhedron is the regular dodecahedron.[49] In the regular polyhedra, the surfaces are bounded by congruent regular polygons and their vertices are symmetrically equivalent to one another. Theaetetos (*ca*. 380 B.C.), a mathematician and a pupil of Socrates (*ca*. 470–399 B.C.) and Theodoros of Cyren, a friend of Plato, discovered the regular octahedron and the regular icosahedron. Theaetetos was also the first to write about the five regular polyhedra.[50]

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* However, there are Greek philosophers, *e.g.*, Empedocles, Aristotle, Archimedes, Ptolemy, Aristarchus of Samos, whose work was strongly grounded in detailed observations and experiments.

** One of the reviewers (we had four reviewers for this essay) does not agree with this statement. In his rather lengthy review he wrote "*...the authors describe Plato as the 'greatest of all philosophers', though I believe a number of people (including myself) would grant this description (amongst Western philosophers) to Aristotle or Socrates*".

According to Plato, fire is the smallest, most pointed and lightest among the elements because it can easily attack and destroy everything. It appeares to be a natural choice that the regular tetrahedron (which consists of four regular triangles) be taken as the shape of fire, since it is the smallest and most pointed among the regular polyhedra. Water is the largest, smoothest and heaviest, because it always flows smoothly into the valleys of the earth. Therefore, it appeared to be the natural choice that the regular icosahedron composed of 20 regular triangles be taken as its shape. Air is between fire and water and so it appeared natural to take the regular octahedron (which consists of eight regular triangles) as the shape of air. The regular octahedron has the same faces, *viz*., regular triangles, as the regular tetrahedron and the regular octahedron. Its number of faces is between the number of faces of those two. From the fact that the tetrahedron, octahedron and icosahedron could be decomposed into regular triangles that could be reassembled to form the other polyhedra, Plato concluded that fire, air and water can also be mutually transformed, that is, water can be transformed by fire into air whereas when air loses fire in the upper atmosphere it becomes water in the form of rain or snow. The last element was earth, which is heavy and stable and is assumed to take the shape of a cube, composed of six squares. Also, the cube is the only regular polyhedron that can be packed together in a (dense) space-filling manner. Since it was not possible to reduce the cube into regular triangles, but only into squares, Plato concluded that earth could not be transformed into fire, air or water. This is discussed in Plato's dialogue *Timaeus*.[51] In the dodecahedron, because its volume approaches that of the sphere most closely of all regular polyhedra, Plato saw the outer shape of the universe. The *Timaeus* contains also a discussion on the composition of organic and inorganic bodies and may be considered a rudimentary treatise on chemistry.[44] At this point, it should be perhaps emphasized that Plato taught us that the Idea, the form, was the truly fundamental pattern behind phenomena, that is, Ideas are more fundamental than objects.[52]

Plato's description of the shapes of the four elements is perhaps the first mathematical model used in chemistry, since regular polyhedra are mathematical objects. The regularity that exists between the numbers of their vertices V, edges E and faces F, was discovered by Léonard (or Leonhard) Euler (1707–1783) and is thus called Euler's theorem.[53] It states that:

$$F - E + V = 2$$

and is considered by some to be the second most beautiful mathematical theorem.[18] It is of some interest to speculate why the Greeks did not discover Euler's theorem. Perhaps the simplest explanation is that Greek mathematics was two thousand years away from topology.

A generalization of the above ideas of elements was put forward by Aristotle (384–322 B.C.). He accepted the idea of four elements, but introduced the concept of the transmutation of elements. Aristotle thought that the elements could be obtained by combining the pairs of opposing fundamental properties of matter. These properties were hotness, coldness, moistness and dryness. Thus, the combination of hotness and dryness gave fire. The combination of hotness and moistness produced air. Moistness and coldness gave water and, similarly, coldness and dryness produced earth. Aristotle added the fifth element – quintessence (ether). The sky and heavenly bodies were supposedly made up from this fifth element. Aristotle defined an element as a simple body that other bodies can be decomposed into but that is not itself capable of being divided into simpler bodies. He classified several chemical processes, was the first to mention mercury and was familiar with the technique of distillation. Aristotle's ideas dominated science for almost two thousand years.

The idea of the Greeks' four 'elements' may be, perhaps (as suggested by Douglas J. Klein),[54] better described in modern terms to correspond to four phases of matter: solid, liquid, gas and plasma corresponding to the Greeks' earth, water, air and fire. This would make the Greeks' view less naive than many otherwise take it to be.

Another theory of the structure of matter was put forward by Greek thinkers. This was concerned with the divisibility of matter. The first Greek philosopher to think about this problem appears to have been Leucippus (*ca.* 470–420 B.C.) from Miletus. He came up with the proposition that the matter cannot be divided endlessly, imagining that in the process of dividing matter one will sooner or later come to a piece that will not be divisible into smaller parts. His pupil Democritus (*ca.* 460 – *ca.* 370 B.C.), from the city of Abdera, continued to develop the ideas of Leucippus. He named these ultimately small pieces of matter ατομοσ (atomos), meaning indivisible. This is the origin of our term atom. The concept of the atom is the basis of the atomistic theory of the structure of matter and the philosophy of materialism. Most Greek philosophers, and particularly Aristotle, did not accept the atomistic teaching of Leucippus and Democritus. Atomism, however, did not die out because Epicurus (*ca.* 342–270 B.C.) made atomism part of his philosophy and Epicureanism won many followers in the next few centuries. One of the followers was the Roman poet and philosopher Titus Lucretius Carus (*ca.* 96 – *ca.* 55 B.C.), known simply as Lucretius, who wrote a fine didactic poem entitled *De Rerum Natura* ("On the Nature of Things"), in which he expounded the atomistic teaching of Democritus and Epicurus. Most of the works by Democritus and Epicurus are lost, but Lucretius's poem has survived intact and served as the vehicle that conveyed the atomistic teaching of the Greeks to modern times.

The philosophy of idealism and the philosophy of materialism were opposed throughout history. From the chemical point of view, the philosophy of materialism affords the basis for an understanding of the structure of compounds. However, the collective properties of compounds, such as their smell or color or taste, can also be interpreted in terms of Plato's ideas.[52] An important point to stress is that Plato's ideas are particularly well-suited to studying the mathematical properties of chemical structures.[55,56] If we link the philosophy of materialism with experimental work in chemistry and likewise the philosophy of idealism with theoretical work, it is clear that both philosophies as well as both experiment and theory are needed to advance chemistry. This is of course also true of other sciences.

Alchemy

Alchemy is the type of chemistry that existed from about 300 B.C. until the second half of the 17th century. This is a less interesting period for our purposes, since alchemists were 'practical' people who did not care much for theories and mathematics. Alchemists had two main objectives:[46,47] (i) to turn base metals into gold (the "Great Work"), and (ii) to discover the elixir of life. Both goals are usually considered to be impossible and futile. However, if we re-state them as: (i) to turn inexspensive and easily available materials of low quality into expensive, high-quality products, and (ii) to produce substances that can cure diseases, improve and extend human life, then we may say that the efforts of alchemists and the modern-day chemists are not dissimilar. It should also be mentioned that nuclear physics made the transmutation of base metals into gold possible (though the process is far from inexpensive). We now realize that the main reason why alchemists failed is that they used low-energy experimental techniques (mainly heat, of the order 0.1 eV), contrary to nuclear physicists who employ energies of the order 10^6 eV or higher.

Alchemists believed that the Great Work could be accomplished by means of something called 'Philosopher's stone'. Nobody knew exactly what this was, but the majority seem to have understood that this was a kind of material substance (perhaps what we call a 'catalyst'). Some alchemists, however, maintained that the Philosopher's stone was a prayer or a magic spell (or both), perhaps combined with certain laboratory operations, perhaps done at a convenient moment, perhaps done by a properly prepared person. A few alchemists were of the opinion that the Great Work was based on certain mathematical operations. For instance, Michael Maier, a physician at the court of Rudolf II of Bohemia in Prague,[57] in his book *Atalanta Fugiens* (1618) wrote: "*Make a circle of male and female, then square, from that triangle; make a circle, and thou shalt have the philosopher's stone*".

(Here 'male' and 'female' stand for two substances of opposite chemical behavior, possibly a metal and a non-metal.)

Alchemists used mathematics for magical purposes; it seems that they never attempted to develop a mathematical model of any real chemical phenomena. The mathematical apparatus used by alchemists consists almost exclusively of arithmetic and geometric constructions. This should not be surprising in view of the fact that at their time arithmetics and geometry were the only well-developed fields of mathematics.

The origins of alchemy can be traced back to the ancient Egyptians. There was a lot of magic involved in the work of alchemists and their symbols have proved difficult to decipher.[58] However, the coding systems used by various alchemists are really cryptograms and as such possess a mathematical basis.

Chemistry as a Science

It is important to stress that chemistry as a science started only in the second half of the 17th century when alchemy was gradually transformed into the science now known as chemistry following the appearance of the book *The Sceptical Chymist or Chymico-Physical Doubts & Paradoxes* (London, 1661) by Robert Boyle (1627–1691). With this book, Boyle announced a rigorous critical approach that is characteristic of chemistry as a science. The transition period from alchemy to chemistry lasted more than a century. It started with Boyle's book and ended with the book *Traité élémentaire de chimie* ("Elementary Treatise on Chemistry", Paris, 1789) by Antoine-Laurent Lavoisier (1743–1794). It was during this period that the first unifying chemical theory, that is, the phlogiston theory appeared.[44,45] The term phlogiston is derived from the Greek word φλογιστοσ which means flammable.

In the development of the phlogiston theory, one can identify five chronological and thematic parts:[59] (i) The roots of the phlogiston theory given in the book *Physica subterranea* (Frankfurt, 1669) by Jochann Joachim Becher (1635–1682), (ii) The phlogiston theory of Georg Ernst Stahl (1660–1734), first introduced in his book *Zymotechnia fundamentalis* (Halle, 1697), and the idea of phlogiston as the principle of burning, (iii) The phlogiston theory after Stahl and the idea of phlogiston as a special substance, (iv) The combination of the phlogiston theory and the antiphlogiston theory before the publication of the fundamental work *Traité élémentaire de chimie* by Lavoisier, and (v) The abandonment of the phlogiston theory. Lavoisier's exact experiments led to the discovery of the role of oxygen in combustion and the phlogiston theory was abandoned. It is interesting to note that the first scientist who carried out experiments similar to those of Lavoisier was the Russian polymath Mikhail Vasilievich Lomonosov (1711–1765).[60,61] His research was published in Russian and in Latin and remained unknown in Western Europe. However, some authors[62] have stated that Leonardo da Vinci (1452–1519) discovered the role of air in combustion almost three centuries before Lomonosov and Lavosier. It is also noteworthy that the phlogiston theory was abandoned from the teaching at the University of Zagreb in 1798, though it had never been fully accepted at this institution.[59]

The 19th century produced a number of results that gave a scientific foundation to chemistry.[57,63] Here, we list only a few of these results, such as the atomic theory of John Dalton (1766–1844; in his book *A New System of Chemical Philosophy*, which appeared in 1808, Dalton put together the atomic theory and data from chemical experimentation. His book also contains one of the earliest depictions of molecular structure, in which the atoms in a molecule are spatially arranged in a specific fashion),[64] the molecule as the smallest unit in chemistry dating from 1811 (Lorenzo Romano Amedeo Carlo Avogadro (1776–1856); although the concept of molecule was conceived in 1811, it was accepted only after Stanislao Cannizzaro (1826–1910) drew it to the attention of the scientitific community in 1858 and successfully defended it in September 1860 at the First International Congress of Chemists, held in Karlsruhe, see *e.g.* Ref. 30); the breakdown of vitalism dating from 1828 (Friedrich Wöhler (1800–1882)); the concept of isomerism dating from 1830 (Jöns Jakob Berzelius (1779–1848); however, already in 1797 Alexander von Humboldt (1769–1859) suggested the existence of chemical isomers[65]); the concept of chemical valence dating from 1852 (Edward Frankland (1825–1899) who also introduced the term bond in 1866; however, already in 1797 von Humboldt used the word *Bindung* in his book on chemical processes in animals and plants[65]); the concept of chemical constitution dating from 1858 (Archibald Scott Couper (1831-1892) and Friedrich August Kekulé (1829–1896)); the graphical representation of a chemical bond and molecular structure dating from 1861 (Alexander Crum Brown (1838–1922); Joseph Loschmidt (1821–1895)); the concept of molecular structure and structural isomers dating from 1861 (Alexander Mikhailovich Butlerov (1828–1886)); the hexagonal formula of benzene dating from 1865 (Kekulé; Loschmidt anticipated a cyclic structure of benzene in 1861 while James Dewar (1842–1923) introduced in 1866 seven mechanical models for molecules consisting of six carbon and six hydrogen atoms (C_6H_6), one of which resembled the original model of Kekulé and one which is now called the Dewar structure); the periodic system dating from 1869 (Dmitry Ivanovich Mendeleev (1834–1907); his book *Osnovy khimii* (“Principles of Chemistry”), which appeared in 1869, was the first to use the Periodic Law as its organizing principle; Lothar Meyer (1830–1895) also discovered, simultaneously and independently, the periodicity of the physical and chemical properties of the elements and their atomic weights) and the three-dimensional structure of molecules dating from 1874 (Jacobus Hendrikus van't Hoff (1852–1911), Joseph-Achille Le Bel (1847–1930); however, Butlerov in 1862 and Emanuele Paterno (1847–1935) in 1869 anticipated ideas of van't Hoff and Le Bel, and even earlier Louis Pasteur (1822–1895) in 1848 showed that certain molecules, and specifically those of the strange-acting racemic acid, were composed of a combination of two twin molecules, one of which proved to be a non-superimposable mirror image of the other. Pasteur managed to split what was apparently a single substance into a 'right-hand' molecule and a 'left-hand' molecule, which are identical and indistinguishable except for the spatial aspect[66]). These achievements turned chemistry into a mature science, ready to be mathematized. This was fully realized only in the 20th century with the appearance of modern theoretical chemistry, which embraces both quantum chemistry and mathematical chemistry.[67]

Books by Boyle, Lavoisier, Dalton and Mendeleev, cited above, were selected by the panel of experts as the golden books of chemistry.[68] Only two more were selected as the golden books of chemistry: Jane Marcet's *Conversations on Chemistry* (London, 1806) and Linus Pauling's *The Nature of the Chemical Bond and the Structure of Molecules and Crystals* (Ithaca, NY, 1939). It was good to see, in the essay listing these and other important chemical books, that chemistry was mentioned as the central science.

MATHEMATICS ENTERS CHEMISTRY

The first attempt to mathematize chemistry is due to Crum Brown,[69] an underestimated person in the history of chemistry. His achievements were numerous and far ahead of his time. Crum Brown, in a pioneering paper that had no more than 19 lines, represented chemical substances as 'operands' and chemical processes as 'operators'. His approach to the classification of chemical processes was surprisingly modern, but it was only recently taken up by Bonchev, Temkin and their co-workers.[70–74]

An even earlier attempt to mathematize chemistry was done by Lomonosov. After his death, a manuscript (in Latin) entitled *Elementa Chimiae Mathematicae* was found among his papers, estimated to have been written in September of 1741.[61,75] It seems that Lomonosov, inspired by Isaac Newton's (1642–1727) *Principia*, intended to write a similar chemical treatise. The *Elementa* were, possibly, intended as an introduction to that (never written) book. Lomonosov wanted to do no less than outline all the existing chemical knowledge in an axiomatic manner. This, of course, was much too early (recall that in 1741 Lavoisier was not yet born), and the project had to be abandoned.

The first mathematicians to be interested in some aspects of chemistry were Arthur Cayley (1821–1895) and James Joseph Sylvester (1814–1897).[76–78] Cayley published a paper in *Berichte der deutschen Chemischen Gesellschaft*, then the leading chemical journal, on the enumeration of alkane isomers.[79] In this paper, Cayley enumerated the alkane isomers C_NH_{2N+2} and alkyl radicals C_NH_{2N+1} for N up to 13, though the numbers of isomers calculated for the C_{12} and C_{13} alkanes (357 and 799) were incorrect; the correct values are 355 and 802.[23] Similarly, Cayley's value (7638) for the $C_{13}H_{27}$ alkyl radicals was also wrong; the correct value is 7639.[23] Cayley's work provoked a deluge of contributions, especially from chemists, on various combinatorial problems in chemistry which, with the advent of computers, seems to be ever-increasing.[23] Cayley's mathematical work culminated in the classical theorem of Polyá, which offers the most powerful enumeration method available to chemists.[80,81] Although Polyá's method was predated by analogous results of Redfield (1927), it gave the first recipe for a systematic derivation of counting series by integrated use of symmetry properties of molecules, generating functions and weighting factors.[82–84]

The other direction of development in this area was constructive computer-assisted enumeration, that is, the direct counting of generated structures.[23] Combinatorial approaches have found use in many areas of chemistry, but they are especially important in medicinal chemistry.[85] Note that medicinal chemistry is the part of chemistry that deals with bioactive compounds and its aim is to discover compounds with desirable biological activities. Accordingly, combinatorial methods and techniques allowing parallel investigation of whole collections of substances are indispensable for the drug design research.

Cayley also made an important mathematical discovery, which he himself did not use in the chemical context. He discovered matrices, which proved to be essential for the development of quantum chemistry and mathematical chemistry, although Heisenberg rediscovered matrices while developing matrix mechanics. One can imagine how clumsy mathematical research in natural sciences must have been before the discovery of matrices.

Cayley published 967 papers. Sylvester was not so prolific an author; he published 342 papers! A mere two of these are directly related to chemistry.[86,87] However, both of these papers, which appeared in 1878, are important for the development of mathematical chemistry. Sylvester called this branch of chemistry 'algebraic chemistry'. In the first paper, published in *Nature*,[86] Sylvester introduced the term *chemicograph* and its shorter version *graph* (which has remained in use ever since) for chemical graphic notation. This notation was clearly inspired by Crum Brown's notation, which became better known after Frankland published (in 1866) an introductory text entitled *Lecture Notes for Chemical Students,* in which he extensively utilized Crum Brown's graphic notation for molecules.[88] In the second paper,[87] Sylvester pointed to the many parallels that exist between chemistry and algebra. He was so enthusiastic about this apparent similarity between mathematics and chemistry that he thought optimistically that these two disciplines could be united by the use of an appropriate mathematical formalism. This aim was never achieved and Sylvester's oft-quoted papers had hardly any impact on the later development of mathematical chemistry.

Platonic solids were discussed earlier. These polyhedra are widely used as versatile models in modern chemistry. Among them, the tetrahedron is especially important in organic chemistry. Van't Hoff and Le Bel independently used the tetrahedron to model the three-dimensional structure of carbon compounds. A carbon atom was placed at the center of the tetrahedron and its bonds were directed to the four corners of the tetrahedron. This is one of the most fundamental models in chemistry and represents the very basis of our understanding of the structure, properties and reactivities of organic compounds. Later on, Pauling rationalized the tetrahedral carbon model in terms of an sp^n-hybridization (n = 1,2,3) model.[89] The optimum direction for the four sp^3-hybrids of the carbon atom in methane CH_4 is toward the four vertices of the tetrahedron. The importance of the tetrahedron in organic chemistry is also stressed by adopting its name for titles of the leading international organic chemistry journals: *Tetrahedron* (founded in 1957 by the Nobel Prize winning organic chemist Sir Robert Robinson (1886-1975)), *Tetrahedon Letters* (founded in 1959) and *Tetrahedron: Asymmetry* (founded in 1990). The importance of polyhedra for inorganic and organometallic chemistry is similarly stressed by adopting the name *Polyhedron* for a major international inorganic chemistry journal (which appeared in 1982 as a successor to the *Journal of Inorganic and Nuclear Chemistry* (founded in 1955) and *Inorganic and Nuclear Chemistry Letters* (founded in 1966)).

Truncation and 'snubbing' of the Platonic solids produces Archimedean solids, which are semi-regular polyhedra; there are thirteen of these in all. The first surviving description of Archimedean solids is that by the Greek geometer Pappus of Alexandria who lived in the fourth century (around 320–340).[90] Pappus of Alexandria explicitly attributed the invention of truncated Platonic polyhedra to Archimedes (287–212 B.C.). Archimedean solids were rediscovered during the Renaissance by the painter and mathematician Piero della Francesca.[91] It was, however, Johannes Kepler (1571–1630) who cataloged the thirteen Archimedean solids in 1619 and gave them their now generally accepted names.[92] Kepler also discovered a class of nonconvex semi-regular polyhedra, now known as the Keplerian polyhedra. There is an interesting story about his fame that extends even to our times. Kepler was born in the township of Weil in Swabia, in a corner of southwest Germany between the Black Forest, the Neckar and the Rhine. The city of Weil was spared at the end of the Second World War because, when the advancing US Army was ready to bomb the city, the commanding officer discovered that this was Kepler's birthplace. In honor of Kepler, he decided to capture the township without first destroying it.[93]

Semi-regular polyhedra are polyhedra whose faces are regular but are comprised of different polygons and each of their vertices is symmetrically equivalent to every other vertex. The current interest in Archimedean polyhedra arose after the announcement made in 1985 by Kroto, Heath, O'Brien, Curl, and Smalley[94] that they had detected a pure carbon molecule consisting of 60 atoms, C_{60}, with the shape of a truncated icosahedron. They gave this molecule the rather poetic name buckminsterfullerene after the American architect Richard Buckminster Fuller (1895–1983). Buckminster Fuller developed the art of constructing buildings in the shape of geodesic (dome-like) polyhedra. Thus, for example, the pavillion that he constructed and which hosted the American exhibition at Expo' 67 in Montreal was in the shape of a geodesic dome, whose triangulated surface contained vertices where five and six faces met. Buckminsterfullerene appears to be the parent molecule of a family of carbon cages C_n ($n \geq 20$ for n = even, with one exception, namely, the cage with 22 atoms is not mathematically possible[95] and many more are chemically 'unreasonable') now called fullerenes, which represent the third allotropic (and also the first molecular) form of carbon. Fullerenes and the related buckytubes and nanostructures possess many interesting properties and offer great possibilities of making a diversity of carbon molecules with unusual shapes.[96]

WHAT IS MATHEMATICAL CHEMISTRY?

In this section, we undertake the difficult task of attempting to give a (working) definition of mathematical chemistry. It has been shown in the preceding section that the roots of mathematical chemistry go back to, at least, the 18th century. However, specialized journals that publish papers reporting advances in mathematical chemistry are of quite recent date. If we consider in this respect three basic natural sciences, that is, physics, chemistry and biology, then the *Journal of Mathematical Physics* was the first to appear in 1960. It is published by the American Institute of Physics and the first editor was the well-known mathematical physicist Elliot Montroll. The American Institute of Physics decided to start the *Journal of Mathematical Physics* in order to provide a common meeting gound for mathematicians and physicists, since the Institute felt that both groups of scientists had started to diverge, with hardly any interaction between them. The reader perhaps does not needs to be reminded that classical mathematics and physics were developed almost exclusively by the same group of people. Therefore, it seemed that their divorce would hamper the development of mathematical physics. The new journal was initiated to bridge the ever-widening gap between mathematicians and physicists.

Some 14 years after the *Journal of Mathematical Physics*, the *Journal of Mathematical Biology* appeared in 1974. It was published by Springer-Verlag in Berlin. The Editors, H. J. Bremermann (Berkeley), F. A. Dodge (Yorktown Heights) and K. P. Hadeler (Tübingen), stated in their Editorial that the journal was started in order to increase the biologists' awareness of the potential of mathematics for research in biology. They also stated their editorial policy with the following words: "*The Journal of Mathematical Biology will accept papers on biological topics (including those which overlap into adjacent areas of medicine, chemistry and physics) in which nontrivial mathematics leads to a better understanding of biological problems*". Neither the first editor of the *Journal of Mathematical Physics* nor the first set of editors of the *Journal of Mathematical Biology* attempted to define either mathematical physics or mathematical biology, as if these terms were well understood.

Apparently, the chemical community-at-large is much more conservative than either the physical community or biological community, since the *Journal of Mathematical Chemistry* appeared only recently, in 1987. It was published by J. C. Baltzer AG, Basel (but it was taken over on May 1st, 2000 by Kluwer Academic Publishers as a result of the acquisition of Baltzer Science Publishers) and the first editor was the renowned mathematical chemist Dennis H. Rouvray. Rouvray, unlike the editors of the *Journal of Mathematical Physics* and the *Journal of Mathematical Biology*, attempted in his Editorial Foreword if not to define mathematical chemistry, at least to describe the field. In his own words: "*Mathematical chemistry concerns itself primarily with the* novel *application of mathematical methods in the chemical realm. The novelty is commonly expressed in one of two ways, viz. (i) the development of new chemical theory, and (ii) the development of new mathematical approaches which enable us to gain insights into or to solve problems of chemical interest. The type of mathematics employed is immaterial, its novelty in respect of the chemical problem under consideration is all important*". Rouvray was editor until the end of 1989. After Rouvray, the journal was under the joint editorship of Paul Mezey and Nenad Trinajstić until the end of 1993, and since then Mezey has been editor-in-chief.

Already before the appearance of the *Journal of Mathematical Chemistry,* a periodical entitled *Informal Communications in Mathematical Chemistry (MATCH)* was initiated in 1975 by Oskar E. Polansky (1919–1989). This journal has been continuously published to the present day, usually twice a year. Its present editor-in-chief is the well-known mathematician Adalbert Kerber. The title of the journal changed over the years first into *Communications in Mathematical Chemistry (MATCH)* and later into *Communications in Mathematical and in Computer Chemistry (MATCH)*.

Since 1991, *Mathematical Chemistry Series* has been published by Gordon and Breach Science Publishers. This *Series* is edited by Danail Bonchev and Dennis H. Rouvray and publishes topical review articles from mathematical chemistry. Six volumes have appeared so far. A volume dealing with the complexity of molecules and reactions is presently in preparation.

It is worth pointing out that the term *mathematical chemistry* itself is fairly new, although, as already stated, the first formal application of mathematics (beyond simple arithmetic and chemical stoichiometry) to chemistry dates back to the 19th century and the work of Crum Brown. In addition to Lomonosov's *Elementa Chimiae Mathematicae* (1741), we found the term *mathematical chemistry* in a paper by John Hasbrouck Van Vleck (1899–1980; shared the Nobel Prize for Physics in 1977) published in 1928.[97] He wrote: "*Is it too optimistic to hazard the opinion that this is perhaps the beginning of a science of 'mathematical chemistry' in which chemical heats of reaction are calculated by quantum mechanics just as are the spectroscopic frequencies of the physicist*?" However, this is the misuse of the term *mathematical chemistry* because what Van Vleck really was aiming at was *computational chemistry,* which was already anticipated by Louis Joseph Gay-Lussac (1778–1850) when he stated in 1809: " *I hope we are not far removed from the time when we shall be able to submit the bulk of chemical phenomena to calculation*".[98] Because of this statement, Gay-Lussac may be considered the forefather of theoretical (and computational) chemistry.

During a conversation on the subject which one of us (N. T.) had with Professor André Dreiding (of Dreiding models for chemical compounds fame and a co-editor of *MATCH* from the beginning) of the University of Zürich in the "Brasserie" of Hotel Intercontinental (now Hotel Opera) in Zagreb on February 17, 1989 during the meeting entitled *Chemical Modelling of Biologically Active Compounds: Application and Manufacture* (Zagreb: February 16–17, 1989), we debated whether whatever the definition of mathematical chemistry is going to be it should include the following words: "... *mathematical chemistry is a non-trivial application of mathematics to chem-*

ical problems..." These are, of course, words very similar to those used by the Editors of the *Journal of Mathematical Biology*. Apparently, Rouvray's attempt to give an explanation of what constitutes mathematical chemistry sparked off some debate and the practitioners of mathematical chemistry sought for other definitions. For example, soon afterwards one of us (I. G.), in 1992 (Ref. 99) in reviewing the *Proceedings of the Third International Conference on Mathematical Chemistry*, held in Galveston, Texas, March 5–9, 1989, concluded that "*there is no precise definition and commonly accepted definition of mathematical chemistry*".

Discussions about the nature of mathematical chemistry appear from time to time in the literature.[100] For example, Klein got involved in a discussion about the use of mathematics in chemistry after the 1985 Nobel prize for chemistry was given to Jerome Karle and Herbert A. Hauptman for their work on mathematical solutions to crystal structures. He described mathematical chemistry as concerning "*the development of mathematical methods for chemical applications*".[101] Ivar Ugi, who has been very active in the field of mathematical chemistry for many years, stated that the goal of mathematical chemistry is "*the mathematization of chemistry without the intermediary of physics and the direct solution of chemical problems by qualitative mathematical methods*".[102]

We give here a working definition of mathematical chemistry as follows: "*Mathematical chemistry is part of theoretical chemistry which is concerned with applications of mathematical methods to the chemical problems*". As can be seen, two words *new* (used by Rouvray in his definition) and *non-trivial* (mentioned above) have been left out of our definition. This demands a brief comment. The term *new* should not imply that the mathematics itself should be new. It may in fact be quite old. What should be new is its application in chemistry. This is so understandable that it need not appear in the definition. The other term *non-trivial* is rather vague. What is trivial to one person could be a laborious mathematical struggle to another. After all, research in chemistry itself can be trivial (and all too frequently is!), but chemists did not include this in the subject definition, merely accepting the rule of thumb that when the research is trivial, the results will not be interesting. Therefore, this word should not appear as a part of the definition of mathematical chemistry either.

A direction of research, closely related to what is above defined as "*Mathematical Chemistry*", should also be mentioned. Namely, problems and concepts occurring in chemistry may motivate mathematicians to introduce and elaborate mathematical objects, concepts and theories that are often much more general and much more abstract than what chemists immediately need, and are sometimes quite remote from their chemical origins.

Cayley's trees (a generalization of the molecular graphs representing alkanes), Polya's theory (a far-reaching generalization and solution of the isomer-enumeration problem) and the concept of the energy of a graph (obtained by extending an algebraic form occurring in the expression for the Hückel molecular orbital total π-electron energy to all graphs)[103] may serve as typical examples. Although these directions of mathematical research are not necessarily parts of Mathematical Chemistry (as defined above), they should not be fully disregarded by the mathematico-chemical community.

At the end of this section, we point out that there is, as yet, not a single book available on mathematical chemistry. There is, however, a book attempting to outline the entire mathematical apparatus of mathematical organic chemistry.[104] There is also a nice recent mathematics book by Kerber[105] with some discussion about the part of mathematical chemistry concerning isomer enumeration and chemical combinatorics. However, there has been a very large mathematical impact on chemistry by way of quantum mechanics – even numerous theorems have been established in this context, and many books have appeared dealing with this subject.

CONCLUDING REMARKS

Chemistry has come a long way along the route to mathematization since the days in 1786 when Immanuel Kant (1724–1804), in a review of the sciences of his time, gave chemistry a very low mathematical rating.[106] Starting from the premise that "*...jeder besonderen Naturlehre nur so viel Wissenchaft angetroffen werden könne, als darin Mathematik anzutreffen ist*", Kant came to the inevitable conclusion that "*... – so kann Chemie nichts mehr als Kunst oder Experimentallehre, niemals aber eigentliche Wissenschaft werden*".[107]

The most important chemical theory, the structural theory of chemistry, was and is a fertile ground for introducing mathematics into chemistry. It was through the structural theory that discrete mathematics entered chemistry. At first this included graph theory, and later topology and group theory. Graph theory is linked with the constitutional formulae (such formulae represent chemical, constitutional or molecular graphs).[108] The totality of infomation about the connectivity in the molecular graph is usually referred to as *molecular topology* although it has little in common with what *topology* means in modern-day mathematics. Group theory is the appropriate mathematical framework for formalizing symmetry,[109] which is important in practically every area of chemistry. Symmetry, dissymmetry and asymmetry became recognized as important features of molecules. Among other things, they are responsible for the presence or lack of the optical activity of molecules.[66] Coupling of group theory with topology has led to the concept of molecular chirality.[110] The introduction of the important mathematics-based concepts of molecular topology and molecular chirality into chemistry and the popularization of the concept of molecular graph are due to the Croatian-born Nobel Prize winner Vladimir Prelog (1906–1998) (who shared the Nobel Prize for chemistry with John Warcup Cornforth in 1975). This makes him perhaps one of the most important mathematical chemists in the 20th century, though he was primarily a first class synthetic chemist.

Graph theory, group theory and knot theory are parts of discrete mathematics.[111–115] They were initially especially important in the development of the structural theory of chemistry. However, the computer revolution made discrete mathematics an all-important tool for computer scientists, including computer chemists.[116–118] Besides, chemical objects are generally believed to be discrete objects. Thus, discrete mathematics appears to be a natural tool for studying chemical objects. One may even claim that most chemical objects are also at the same time three-dimensional realizations of mathematical objects.

Continuous mathematics entered chemistry through physical chemistry, chemical physics and quantum chemistry. It dominated the teaching of mathematics to chemists until very recently. This is perhaps the reason why Ralston entitled his article of 1986 *Discrete Mathematics: The New Mathematics of Science*.[111] This, however, is not quite so because, as we have shown, discrete mathematics has been extant in chemistry since the 19th century, though not recognized as such. Furthermore, even nowadays, many chemists and, what is worse, many theoretical chemists, do not seem to know the distinction between discrete mathematics and continuous mathematics and do not seem to be aware of the potentials of discrete mathematics. To our minds, there is no doubt that in modern chemistry discrete mathematics is equally important as continuous mathematics. We also expect that in the novel developments in chemistry which are now under way, such a computer-assisted preparative work and combinatorial chemistry, topological strategies and preparations of knotted molecules, nanostructures, molecular devices and the study of Möbius molecules, discrete mathematics will become increasingly important. Our prediction is that this will be reflected not only in pure and applied mathematical research, but also in the mathematical education of chemists.

In summary, one can say that chemistry today includes a great deal of mathematics (even new developments in mathematics such as fractal geometry[119] found almost immediate use in chemistry)[120–125] so that chemistry can now be considered a respectable science in the Kantian sense. A warning, however, should be sounded by paraphrasing William Thomson, Lord

Kelvin of Largs (1824–1907) that: "*It is as dangerous to let mathematics take charge of chemistry as to let an army run a government*".

Chemistry needs mathematics in order to rationalize its observations and experiments and sometimes even to be guided by mathematics in its development. In general, however, chemistry is an experimental science whose objects are as real as our world is real whereas mathematical objects are abstract, and merely serve as models for chemical (physical) objects, and for as yet unexplained reasons very effectively model chemical (physical) objects and processes.

Some final words again concern Milan Randić. The American Chemical Society – the Division of Chemical Information established in 1976 the Herman Skolnik Award to recognize outstanding contributions to and achievements in the theory and practice of chemical information science in areas such as design of new and unique computerized information systems, preparation and dissemination of chemical information, editorial innovations, design of new indexing, classification and notation systems, chemical nomenclature, structure-activity relationships, numerical data correlation and evaluation, *etc*. The Award is named in honor of its first recipient, Herman Skolnik (1914–1994). Skolnik founded the *Journal of Chemical Documentation* in 1960 and was its first editor. This journal changed in 1975 its name to the *Journal of Chemical Information and Computer Sciences*, which is today one of the most important international media for publishing mathematical chemistry papers, especially in the area of structure-property-activity studies. Randić was awarded the Herman Skolnik Award in 1996 in recognition of his work on the development and applications of the chemical graph theory. A part of the *Journal of Chemical Information and Computer Sciences* in 1997 (Vol. 4, issue no. 4) contained papers presented at the 1996 Herman Skolnik Award Symposium in honor of Milan Randić.

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SAŽETAK

Matematička kemija

Nenad Trinajstić i Ivan Gutman

Ukratko je prikazan povijesni razvitak matematike i kemije. Opisan je susret ovih dviju znanosti. Pokušano je definiranje matematičke kemije i prikazani su časopisi koji u svojim naslovima sadržavaju riječi *matematička kemija*. U zaključku je istaknuto da je kemija eksperimentalna znanost, kojoj je cilj priprava novih spojeva i materijala, ali da je matematika vrlo upotrebljiva u kemiji, kao npr. za izvođenje modela, koji mogu voditi eksperiment k cilju najkraćim mogućim putom.