

Combinatorics of NMR and ESR Spectral Simulations

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Combinatorial techniques which provide information on intensity and signal patterns for NMR and ESR spectra are reviewed. It is shown that these techniques can be applied to both ^{13}C and proton NMR of molecules as well as to predict the hyperfine pattern in the ESR spectra of complex polyatomic radicals.

I. INTRODUCTION

While combinatorial techniques have been applied extensively to the enumeration of chemical structures and isomers, their applications to the prediction of spectra are somewhat latent and more recent. It has been shown recently¹⁻⁷ that combinatorial techniques have important applications in NMR and ESR. Furthermore, these techniques can be computerized and, thus, provide automated algorithms for spectral simulation. Of course, combinatorial techniques cannot provide any information on signal positions and thus do not provide global spectral simulation. Nevertheless, they provide some important information on signal patterns and intensities that a practicing chemist seeks and when coupled with the work of Randić¹ on signal positions can lead to overall spectral simulation of some classes of compounds.

The objective of this article is to review some of the recent developments in this field. We focus on combinatorial techniques for NMR and ESR since these are far more developed compared to other spectra.

II. BASIC COMBINATORIAL TECHNIQUES

There are several computational techniques for constructing equivalence classes of nuclei in a molecule. These are described in the section on NMR. The basic computational technique for the enumeration of the equivalence classes of nuclei is based on Pólya's theorem and has been implemented on a computer by the author.²⁰ Hence we describe this method first briefly. The formalism described below is from ref 1.

Suppose D is a set of nuclei of the same kind in a molecule (radical). Let R be a set containing just two elements. Let G be the point group or the permutation-inversion group of the molecule or radical under consideration. Since G is the set of all permutational and composite permutation-inversion operations a $g \in G$ induces permutations on elements in D . Consider a set F of all maps from D to R . Every $g \in G$ acts on the elements of F as follows:

$$gf(d) = f(g^{-1}d) \text{ for every } d \in D \quad (1)$$

Two maps f_i and $f_j \in F$ are equivalent if

$$f_i(d) = f_j(gd) \text{ for every } d \in D \quad (2)$$

All maps in F that are equivalent are grouped into the same equivalence class. Consequently, the group G partitions F into equivalence classes. We restrict ourselves to those maps in F which have the following structure, since these are the relevant maps for NMR and ESR hyperfine structure patterns. Let the elements of the set R be denoted by α_1 and α_2 . Label the elements of D by d_1, d_2, \dots, d_n , with $n = |D|$. Consider a

subset F_w of F with every $f_i \in F_w$ defined as

$$\begin{aligned} f_i(d_j) &= \alpha_1 \text{ if } i \neq j, d_j \in D \\ &= \alpha_2 \text{ if } i = j \end{aligned} \quad (3)$$

It can be seen that two nuclei d_i and d_j are magnetically equivalent if f_i is equivalent to f_j . Thus, the equivalence classes of F_w are the magnetic equivalence classes of nuclei in the set D . All nuclei in a class would have the same ESR hyperfine constant or the same chemical shift in the case of NMR.

If a weight $w(r)$ is assigned to an element r in R to count the number of times any $r \in R$ occurs in a function, then the weight of any function $f \in F$ is defined as the product of the weight of its images. Symbolically, the weight of f , $W(f)$, is

$$W(f) = \prod_{d \in D} w[f(d)] \quad (4)$$

Since any $f_i \in F_w$ takes all $d_j \in D$ to α_1 except when $i = j$, the weight of any f_i in F_w is w , if 1 is the weight associated with α_1 and w is the weight assigned to α_2 .

Pólya's²¹ theorem generates the equivalence classes of F from a structure known as the cycle index of a group. Suppose any $g \in G$ generates b_1 cycles of length 1, b_2 cycles of length 2, etc. when it acts on D ; then we can associate a cycle representation $x_1^{b_1}x_2^{b_2}\dots$ with g . The cycle index of G , P_G is defined as

$$P_G(x_1, x_2, \dots) = 1/|G| \sum_{g \in G} x_1^{b_1}x_2^{b_2}\dots \quad (5)$$

Pólya showed that a generating function (GF) for the equivalence classes of F is given by the following substitution in the cycle index:

$$\text{GF} = P_G(x_k \rightarrow \sum_{r \in R} [w(r)]^k) \quad (6)$$

The coefficient of w in GF gives the number equivalence classes of nuclei in D .

The coefficient of w in the above GF is interpreted differently in different applications. In the case of NMR it gives the number of NMR signals attributed to the particular set of nuclei chosen in the set D . For ESR this information will have to be coupled with the actual set of possible nuclear spin functions to generate the actual ESR hyperfine structure. We will consider this in a subsequent section.

Numerous illustrations have been provided in ref 1, demonstrating how the GF method is useful in enumerating both ^{13}C and proton NMR of different molecules. The readers are referred to this reference for further details.

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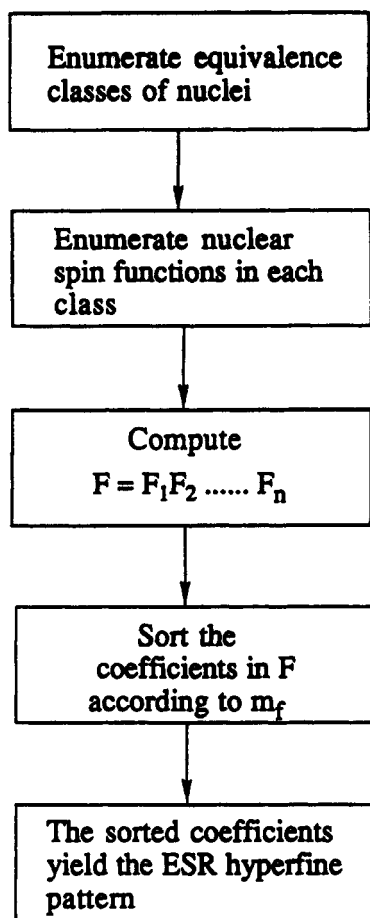


Figure 1. Schematic illustration of various steps in ESR spectral simulation.

III. GRAPH THEORETICAL CONSTRUCTION OF NMR SIGNAL AND INTENSITY PATTERNS

Liu et al.^{5,6} have considered different techniques for the computer-assisted graph-theoretical construction of NMR signal and intensity patterns. Algorithms called vertex-parti and list-generator were constructed and computationally implemented. It was shown that these algorithms worked satisfactorily for graphs possessing isospectral points and regular graphs. In a subsequent paper Liu et al.⁶ critically compared vertex-parti/list-generator algorithms with the Morgan algorithm, the Shelley-Munk modification of the Morgan algorithm, the principal eigenvector algorithm, etc. found in refs 8–19. At present, most of these algorithms work satisfactorily for several graphs. However, highly transitive regular graphs containing large numbers of vertices still pose special problems. By definition, vertex transitive graphs contain a single automorphism partitioning set, and hence the final outcome of correct algorithms is a trivial result. However, the transitive nature of such graphs often leads to slow convergence or nonconvergence in some cases. Application of these techniques to transitive graphs of carbon clusters such as C₁₂₀, C₂₄₀, etc. would certainly be interesting. Further research is called for in this direction.

IV. APPLICATIONS TO ESR

Combinatorial prediction of ESR hyperfine patterns consists of several steps, delineated in Figure 1. The first step is to enumerate the equivalence classes of nuclei which was considered before. The second step is to enumerate possible nuclear spin functions in each equivalence class. Subsequently, nuclear spin functions with the same total m_f quantum num-

ber (projection of nuclear spin above the z-axis) are sorted. The sorted information yields the hyperfine pattern. These steps are described below with examples (see also Figure 1).

Suppose the radical whose ESR is under consideration consists of n_1 nuclei with spin I_1 in the first class, n_2 nuclei with spin I_2 in the second class, ... n_m nuclei with spin I_m in the m th class. Note that the number of possible projections of any nuclear spin in the i th class is $2I_i + 1$. Hence the number of nuclear spin functions in the i th set is $(2I_i + 1)^{n_i}$. The total number of nuclear spin projections of all nuclei in all classes is given by

$$\prod_i (2I_i + 1)^{n_i} \quad (7)$$

Let us associate a symbol with each spin projection. For example, the standard symbols are $\alpha(m_f = +1/2)$ and $\beta(m_f = -1/2)$ for the two projections of the hydrogen nucleus. Similarly for the three-spin projections of the nitrogen nucleus, the symbols $\lambda(m_f = 1)$, $\mu(m_f = 0)$, and $\nu(m_f = -1)$ are used.

Spin projections of different equivalence classes are not equivalent since they will not yield the same hyperfine interaction energies. Hence to differentiate these we use suffixes 1, 2, ... in the order of occurrence for a given type of nucleus. For example, consider a system containing multinuclear equivalence classes of the type {P₁, P₂}, {P₃, P₄}, {N₁, N₂}, where P stands for proton and N stands for nitrogen. Then the nuclear projections for any nucleus in the first class are α_1 and β_1 ; those in the second class, α_2 and β_2 ; and those in the third class, λ_1 , μ_1 , and ν_1 . Let us denote $p_i = 2I_i + 1$ for convenience. Then possible spin functions of n_i nuclei in an equivalence class with nuclear spin I_i with projection represented by, say, f_1, f_2, \dots, f_{p_i} are enumerated by the multinomial expansion

$$F = (f_1 + f_2 + \dots + f_{p_i})^{n_i} \quad (8)$$

The coefficient of a term $f_1^{a_1} f_2^{a_2} \dots f_{p_i}^{a_{p_i}}$, such that $\sum_i a_i = n_i$ gives the number of possible spin functions spanned by n_i nuclei, among which a_1 nuclei have spin projection f_1 , a_2 nuclei have spin projection f_2 , ..., a_{p_i} have spin projection f_{p_i} .

Consider a radical containing one class with four nitrogen atoms. The generating function for possible nuclear spin functions for such a radical is given by

$$F = (\lambda + \mu + \nu)^4 \quad (9)$$

or

$$F = \lambda^4 + 4\lambda^3\mu + 4\lambda^3\nu + 6\lambda^2\mu^2 + 6\lambda^2\nu^2 + 12\lambda^2\mu\nu + 12\lambda\mu^2\nu + 12\lambda\mu\nu^2 + \mu^4 + 4\mu^3\lambda + 4\mu^3\nu + 6\mu^2\nu^2 + \nu^4 + 4\nu^3\lambda + 4\nu^3\mu \quad (10)$$

The coefficient of $\lambda^{a_1}\mu^{a_2}\nu^{a_3}$ enumerates the number of spin functions containing $a_1\lambda$'s, $a_2\mu$'s, and $a_3\nu$'s. For example, there are 12 possible spin functions containing two λ 's, one μ , and one ν . The total generating function F for the radical under consideration is given by

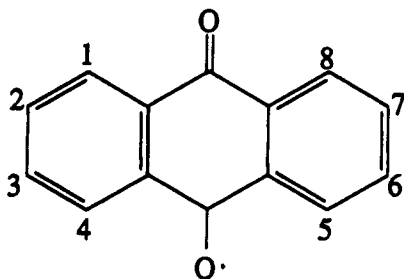
$$F = F_1 F_2 \dots F_m \quad (11)$$

where

$$F_i = (f_1 + f_2 + \dots + f_{p_i})^{n_i} \quad (12)$$

where f_1, f_2, \dots, f_{p_i} are the possible projections of a nucleus in the i th class and $p_i = 2I_i + 1$.

We will illustrate the above techniques using the example of *p*-anthrasemiquinone radical (Figure 2) considered before in ref 7. As shown in ref 7, application of Pólya's theorem

Figure 2. Structure of *p*-anthraquinone radical.Table I. Generating Function Coefficients and Hyperfine Pattern of *p*-Anthraquinone Radical (Figure 2)

term in GF	coeff	contribution to intensity ratio	term in GF	coeff	contribution to intensity ratio
$\alpha_1^4\alpha_2^4$	1	1	$\alpha_1^2\beta_1^2\alpha_2\beta_2^3$	24	24
$\alpha_1^4\alpha_2^3\beta_2$	4	4	$\alpha_1^2\beta_1^2\beta_2^4$	6	6
$\alpha_1^4\alpha_2^2\beta_2^2$	6	6	$\alpha_1\beta_1^3\alpha_2^4$	4	4
$\alpha_1^4\alpha_2\beta_2^3$	4	4	$\alpha_1\beta_1^3\alpha_2^3\beta_2$	16	16
$\alpha_1^4\beta_2^4$	1	1	$\alpha_1\beta_1^3\alpha_2^2\beta_2^2$	24	24
$\alpha_1^3\beta_1\alpha_2^4$	4	4	$\alpha_1\beta_1^3\alpha_2\beta_2^3$	16	16
$\alpha_1^3\beta_1\alpha_2^3\beta_2$	16	16	$\alpha_1\beta_1^3\beta_2^4$	4	4
$\alpha_1^3\beta_1\alpha_2^2\beta_2^2$	24	24	$\beta_1^4\alpha_2^4$	1	1
$\alpha_1^3\beta_1\alpha_2\beta_2^3$	16	16	$\beta_1^4\alpha_2^3\beta_2$	4	4
$\alpha_1^3\beta_1\beta_2^4$	4	4	$\beta_1^4\alpha_2^2\beta_2^2$	6	6
$\alpha_1^2\beta_1^2\alpha_2^4$	6	6	$\beta_1^4\alpha_2\beta_2^3$	4	4
$\alpha_1^2\beta_1^2\alpha_2^3\beta_2$	24	24	$\beta_1^4\beta_2^4$	1	1
$\alpha_1^2\beta_1^2\alpha_2^2\beta_2^2$	36	36			

yields two equivalence classes, each class containing four protons. These are {1,4,5,8} and {2,3,7,6}. The total generating function for this structure is given by

$$F = (\alpha_1 + \beta_1)^4 (\alpha_2 + \beta_2)^4 \quad (13)$$

where α_1 and β_1 stand for spin up and down in the first nuclear spin equivalence class while α_2 and β_2 stand for the corresponding spins in the second equivalence class. Table I shows the coefficients of various terms in the above generating function and the corresponding contribution to the intensity ratio in the hyperfine structure. The coefficients of various terms in Table I are obtained by using the binomial expansion of eq 13. The total number of hyperfine lines is also easily obtained as

$$(2 \times \frac{1}{2} \times 4 + 1)(2 \times \frac{1}{2} \times 4 + 1) = 25$$

These techniques are now computerized. For details the readers are referred to refs 1 and 5-7.

V. CONCLUSION

In this article we reviewed the development of important combinatorial techniques for NMR and ESR spectra. It was shown that computer-assisted combinatorial techniques can provide adequate information on NMR signal and intensity patterns for several molecules. However, these techniques do not provide any information on the signal positions. Several talks were presented in this symposium on locating signal

positions through databases or empirical and other fitting techniques. Randić and co-workers are also developing topological indices which correlate with NMR chemical shifts. While considerable progress has taken place in the computer simulation of ^{13}C NMR spectra, this is not the case with proton NMR. The simulation of proton NMR is complicated by the fact that stereochemistry and fluxional motions in molecules have to be taken into consideration for the simulation of proton NMR. We have developed combinatorial techniques for including both stereochemistry and fluxionality for proton NMR. However, this does not generate information on the signal position. Hence computer simulation of proton NMR including dynamical stereochemistry is an interesting problem for further research.

REFERENCES AND NOTES

- Balasubramanian, K. Computer-assisted Enumeration of NMR Signals. *J. Magn. Reson.* **1982**, *48*, 165.
- Balasubramanian, K. Applications of Combinatorics and Graph Theory to Spectroscopy and Quantum Chemistry. *Chem. Rev.* **1985**, *85*, 599.
- Randić, M.; Gerstein, B. C. Small Variations in Chemical Shifts for Atoms in Similar Environments. *J. Magn. Reson.* **1981**, *43*, 207.
- Grant, D. M.; Paul, E. G. Carbon-13 Magnetic Resonance. II. Chemical Shift Data for the Alkanes. *J. Am. Chem. Soc.* **1984**, *86*, 2984.
- Liu, X. Y.; Balasubramanian, K.; Munk, M. E. Computer-assisted Graph-theoretical Construction of ^{13}C NMR Signal and Intensity Patterns. *J. Magn. Reson.* **1990**, *87*, 457.
- Liu, X. Y.; Balasubramanian, K.; Munk, M. E. Computational Techniques for Vertex Partitioning of Graphs. *J. Chem. Inf. Comput. Sci.* **1990**, *30*, 263.
- Balasubramanian, K. Computational Methods in ESR Spectroscopy. *J. Magn. Reson.* **1991**, *91*, 45.
- Morgan, H. L. The Generation of Unique Machine Description for Chemical Structure—A Technique Developed at Chemical Abstracts Service. *J. Chem. Doc.* **1965**, *5*, 107.
- Wipke, W. T.; Dyott, T. M. Stereochemically Unique Naming Algorithm. *J. Am. Chem. Soc.* **1974**, *96*, 4836.
- Moreau, G. A Topological Code for Molecular Structures. A Modified Morgan Algorithm. *Nouv. J. Chim.* **1980**, *4*, 17.
- Golender, V. E.; Drboglav, V. V.; Rosenblit, A. B. Graph Potential Method and Ion Application for Chemical Information Progressing. *J. Chem. Inf. Comput. Sci.* **1981**, *21*, 196.
- Razinger, M. Extended Connectivity in Chemical Graphs. *Theor. Chim. Acta* **1982**, *61*, 581.
- Herndon, W. C. Canonical Numbering, Stereochemical Descriptors, and Unique Linear Notations for Polyhedral Clusters. *Inorg. Chem.* **1983**, *22*, 554.
- Herndon, W. C. Isospectral Molecules. *Tetrahedron Lett.* **1974**, 671.
- Herndon, W. C. The Characteristic Polynomial Does Not Uniquely Determine Molecular Topology. *J. Chem. Doc.* **1974**, *14*, 150.
- Davis, M. I.; Ellzey, M. L., Jr. A Technique for Determining the Symmetry Properties of Molecular Graphs. *J. Comput. Chem.* **1983**, *4*, 267.
- (a) Randić, M.; Davis, M. I. Symmetry Properties of Chemical Graphs. VI. Isomerization of Octahedral Complex. *Int. J. Quantum Chem.* **1984**, *24*, 69. (b) Randić, M.; Brissey, G. M.; Wilkins, C. W. Computer Perception of Topology Symmetry Via Canonical Numbering of Atoms. *J. Chem. Inf. Comput. Sci.* **1981**, *21*, 52. (c) Randić, M. On Canonical Numbering of Atoms in a Molecular and Graph Isomorphism. *J. Chem. Inf. Comput. Sci.* **1977**, *17*, 171.
- Shelley, C. A.; Munk, M. E. An Approach to the Assignment of Chemical Connection Tables and Topology Symmetry Perception. *J. Chem. Inf. Comput. Sci.* **1979**, *19*, 247.
- Munk, M. E.; Christie, B. D. The Characterization of Structure by Computer. *Anal. Chem. Acta* **1989**, *216*, 57.
- Balasubramanian, K. Computer Enumeration of Chemical Isomers. *Comput. Chem.* **1982**, *6*, 57.
- Pólya, G. Kombinatorische Anzahlbestimmung für Grupper, Graphen und Chemische Verbindungen. *Acta Math.* **1937**, *65*, 145.