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SYMPOSIUM ON CHEMICAL APPLICATIONS OF TOPOLOGY AND
GRAPH THEORY APRIL 18-22 1983(U) GEORGIA UNIV ATHENS
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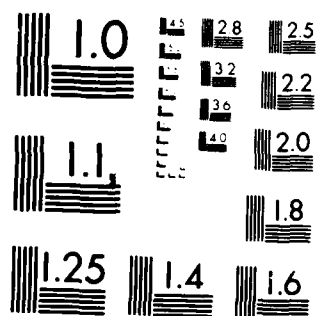
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SYMPOSIUM ON CHEMICAL APPLICATIONS OF TOPOLOGY AND GRAPH THEORY

Georgia Center for Continuing Education

University of Georgia

Athens, Georgia 30602, U.S.A.

April 18-22, 1983

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SYMPOSIUM ON CHEMICAL APPLICATIONS OF TOPOLOGY AND GRAPH THEORY

PROGRAM

Monday, April 18, 1983

R. B. King, presiding

9:00 AM Opening remarks

Dr. Robert C. Anderson, Vice-President for Research, University of Georgia
and President, University of Georgia Research Foundation

Dr. W. J. Payne, Dean, College of Arts and Sciences, University of Georgia

9:30 AM J. Dugundji, "Qualitative Stereochemistry"

10:30 AM Coffee Break

*11:00 AM O. Sinanoğlu, "Algebraic and Topological Structure of Quantum Chemistry
and of Chemical Kinetics"

12:00(noon) P.J. Plath and E. C. Hass, "Logic of Chemical Ideas"

12:30 PM Lunch, Georgia Center for Continuing Education

W. C. Herndon, presiding

2:00 PM R.E. Merrifield and H. E. Simmons, "Finite Point-Set Topology and Molecular
Structure"

3:00 PM R. F. W. Bader, "A Theory of Molecular Structure"

4:00 PM Break

4:30 PM P. G. Mezey, "Reaction Topology: Manifold Theory of Potential Surfaces
and Quantum Chemical Synthesis Design"

5:30 PM Adjourn for dinner

7:30 PM Wine and Cheese Party, Taylor-Grady House, Prince Avenue, Athens, Ga.

Tuesday, April 19, 1983

E. Wegman, presiding

8:30 AM F. Harary, "Some Graph Theoretic Models in Theoretical Chemistry"

9:30 AM K. Balasubramanian, "Symmetry and Spectra of Graphs and their Chemical
Applications"

10:00 AM Break

10:30 AM M. Randić, "On Ordering of Graphs and Structures and their Properties"

11:30 AM A. C. Day, R. B. Mallion, and M. J. Rigby, "On the Use of Riemannian Surfaces
in the Graph-Theoretical Representation of Möbius Systems"

12:00(noon) D. M. Walba, "Stereochemical Topology"

12:30 PM Lunch, Georgia Center for Continuing Education

D. Nelson, presiding

2:00 PM W. C. Herndon, "Canonical Labeling and Isomorphism of Graphs: Applications to Descriptors of Chemical Compounds"

*3:00 PM M. Barysz, G. Jashar, R. S. Lall, V. K. Srivastava, and N. Trinajstić, "On the Distance Matrix of Molecules Containing Heteroatoms"

3:30 PM Break

4:00 PM D. H. Rouvray, "Should We Have Designs on Topological Indices?"

5:00 PM V. R. Magnuson, D. K. Harriss, and S. C. Basak, "Topological Indices Based on Neighborhood Symmetry: Chemical and Biological Implications"

5:30 PM Adjourn

Wednesday, April 20, 1983

C. Holland, presiding

8:30 AM H. G. Othmer, "The Global Dynamics of Certain Classes of Reaction Networks"

9:30 AM R. Thomas, "Logical versus Continuous Description of Systems Comprising Feedback Loops"

10:30 AM Break

11:00 AM B. L. Clarke, "Qualitative Dynamics and Stability of Chemical Reaction Networks"

12:00(noon) Lunch, Georgia Center for Continuing Education

R. B. King, presiding

1:30 PM O. E. Rössler and J. L. Hudson, "Higher Chaos in Simple Reaction Systems"

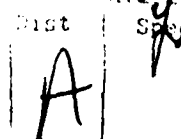
2:30 PM R. Larter, "The Use of Sensitivity Analysis in Determining the Structural Stability of Multi-parameter Oscillators"

3:00 PM Break

*3:30 PM H. Degn, "Periodic Perturbations of Next Period Functions"

4:00 PM L. Peusner, "Electrical Network Representations of n-Dimensional Chemical Manifolds"

4:30 PM C. Trindle and R. Givan, "A LISP Program for the Manipulation of Chemical Graphs"



5:00 PM Adjourn technical sessions for the day

7:00 PM Symposium barbecue, Pinecrest Lodge

Thursday, April 21, 1983

E. Wegman, presiding

8:30 AM E. C. Hass and P. J. Plath, "The Multi-Dimensional λ -Model. A Graph Theoretical/Algebraic Approach to Describe Mechanistic Aspects of Complex Chemical Reactions"

9:00 AM P. H. Sellers, "The Classification of Chemical Mechanisms from a Geometric Viewpoint"

9:30 AM S. H. Bertz, "The Modeling Molecular Complexity"

10:00 AM G. A. Jones and E. K. Lloyd, "The Automorphism Groups of Some Chemical Graphs"

10:30 AM Break

11:00 AM D. J. Klein and W. A. Seitz, "Graphs, Polymer Models, and Excluded Volume Effects"

12:00(noon) L. V. Quintas, "A Volume Function for Water Based on a Random Lattice-Subgraph Model"

12:30 PM Lunch, Georgia Center for Continuing Education

D. Nelson, presiding

2:00 PM R. B. King, "The Bonding Topology of Polyhedral Molecules"

3:00 PM A. G. Turner, "Topological Properties of Sulfur Nitrogen Compounds"

3:30 PM M. J. McGlinchey and Y. Tal, "The Shapes of Main Group Clusters: A Topological Approach to Skeletal Electron Counting"

4:00 PM Break

4:30 PM H. M. Martinez, "Dynamics of RNA Secondary Structure Formation"

5:00 PM S. Swaminathan, "Topological Aspects of Enzyme-Substrate Recognition"

5:30 PM Adjourn for dinner

Friday, April 22, 1983

R. B. King, presiding

9:00 AM Informal discussion on Future Directions for Research on Chemical Applications of Topology and Graph Theory

11:00 AM End of Symposium

*)Abstract not available in time to include in this collection.

QUALITATIVE STEREOCHEMISTRY

J. Dugundji

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The outline of a unified treatment of Stereochemistry, applicable to all molecules, flexible or not, will be presented. It is based on joint work with Ugi/Marquarding/Kopp, expressing the viewpoint that Stereochemistry cannot be treated adequately by considering the molecular geometry separately from the molecular chemistry; it is the interaction of these two features that is fundamental. This interaction is shown to be expressible by a group, called the chemical identity group of the molecule. Various stereochemical phenomena are described directly by this group and its properties. For example, the number of chemically distinct isomers in a family of permutation isomers can be determined and representatives of those isomers exhibited; chirality phenomena can be explained and predicted; the notion of an isomerization can be formulated precisely, and the possible intermediates or mechanisms can be determined.

The approach does not use energy considerations, being qualitative in the sense that all the theoretically possible outcomes of a stereochemical experiment are determined, thereby narrowing the possibilities deserving further experimental consideration.

Abstract

LOGIC OF CHEMICAL IDEAS

P.J. Plath⁺, E.C. Hass⁺⁺

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⁺⁺Institut für Physikalische Chemie, Freie Universität Berlin,
Takustraße 3, D-1000 Berlin 33

Based on the graph-theoretical formulation of several mechanisms, which might be possible using chemical structure theory, the applied chemical ideas have been analyzed logically. To illustrate our analysis we take examples of rearrangements within transition states of carbo-cations, as we can observe in the Demjanov-rearrangement as well as in acid-catalysed isomerisations within zeolite cavities. It can be shown that the declaration of any chosen mechanisms destroy the holistic character of an unprejudiced description of the whole reaction. The orthomodular lattice of propositions concerning the holistic description of the reaction has to be reduced to a boolean sublattice by declaring one of the mechanisms.

It can be shown that different conceptions on the molecular structure of carbo-cations corresponds with the introduction of special pre-assumptions, which cut out the boolean sublattice out of the reaction lattice.

Introducing a norm on such a boolean lattice one get the possibility for probabilistic interpretation within the scope of the chosen presupposition.

Key-words:

Lattice-theoretical investigation of chemical reaction mechanism;
graph-theoretical description of chemical formulae.

FINITE POINT-SET TOPOLOGY AND MOLECULAR STRUCTURE

R. E. Merrifield and H. E. Simmons

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and Company, Wilmington, Delaware 19898

A topological description of molecular structure has been developed which derives from the one-to-one correspondence between transitive digraphs on n vertices and finite topologies on n points. The two possible transitive orientations of a bipartite graph lead to a unique topology-cotopology pair associated with any alternant molecule. A similar pair of spaces is associated with a nonalternant (whose graph may have many or no transitive orientations) via its duplex, which is the graphical conjunction with K_2 and is necessarily connected and the only homeomorphic spaces are those of stereoisomers. The structure of these molecular spaces can be analyzed quantitatively by a variety of combinatorial measures. The cardinality of the molecular topology is a measure of structural complexity which increases with branching and decreases with cyclization. A topological correlate of delocalization in π -electron systems is the degree to which an atom or adjacent pair of atoms approximates a disconnected subspace of the molecular space. The patterns of free valences and π -bond orders given by this measure are in excellent agreement with molecular orbital theory.

A THEORY OF MOLECULAR STRUCTURE

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A theory of molecular structure has been developed which demonstrates that the concepts of atoms and bonds may be rigorously defined in terms of the topological properties of the observable distribution of charge for a molecular system. As a consequence of these definitions, one in turn obtains a definition of structure and a predictive theory of structural stability. The theory is linked to quantum mechanics by demonstrating that the atoms so defined represent a class of open quantum subsystems with a unique set of variationally defined properties. The definition of structure associates a given structure with an open neighbourhood of the most probable nuclear geometry, and removes the need to invoke the Born-Oppenheimer approximation for the justification or rationalization of structure in a molecular system. By defining all possible structures for a given system, the theory shows that a change in structure must be an abrupt and discontinuous process, one which is describable in terms of the mathematical theory of dynamical systems and their stabilities.

The application of the notion of structural stability to the topological study of the molecular charge distribution leads to a partitioning of the nuclear configuration space into a finite number, ℓ , of non-overlapping regions, the structural regions $W_i (i=1, \dots, \ell)$, each of which is characterized by a unique molecular structure. These structural regions form a dense open subset of the nuclear configuration space. A point which belongs to the union of the W_i belongs to some structural region, and is called a regular point. A nuclear configuration belonging to the complementary of the set of regular points is called a catastrophe point. The catastrophe set is the union of the boundaries of all the ℓ structural regions W_i .

We distinguish two types of catastrophe points. This distinction arises as a corollary of a theorem on structural stability first stated by Palis and Smale. The immediate consequence of the theorem is that a structural instability can be established through either of two mechanisms: in the bifurcation mechanism the charge distribution exhibits a degenerate critical point, while the conflict mechanism is characterized by the non-transversal intersection of the stable and unstable manifolds of pairs of critical points in the charge density. Catastrophe theory may be used to provide a mathematical model for structural changes in the neighbourhood of a bifurcation point, through the analysis of the universal unfoldings associated with singularities of particular kinds.

REACTION TOPOLOGY: MANIFOLD THEORY OF POTENTIAL SURFACES AND QUANTUM CHEMICAL SYNTHESIS DESIGN

PAUL G. MEZEY

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ABSTRACT

In the last decade the development of advanced quantum chemical methods and the related applied mathematical techniques, as well as the spectacular improvement of the available computer hardware and software, made quantum chemistry an important complement of experimental chemical research. In the foreseeable future it will be economically feasible to carry quantum chemical model studies on a variety of possible synthetic pathways before the actual synthesis of a new compound is attempted. Reaction topology and manifold theory of quantum chemical potential energy hypersurfaces of reacting chemical systems are proposed for the global and local analysis of the set of all reactions of all molecules composed from a given set of N nuclei and k electrons.

The topological model of potential energy hypersurfaces leads to some simplifications in the actual quantum chemical calculations. It forms a rigorous quantum chemical basis for a topological definition of molecular structure and reaction mechanism. Intersection graphs of topological open sets of a manifold, replacing the concept of the conventional nuclear configuration space, lead to a global quantum chemical reaction network model, which network can be utilized in computer-aided synthesis planning.

SOME GRAPH THEORETIC MODELS IN THEORETICAL CHEMISTRY

Frank Harary

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Abstract

The best known graph theoretic model in theoretical chemistry, and perhaps the first one, is the representation of a molecule M by the graph $G = G(M) = (V, E)$ in which the point set V of G is the collection of atoms in M , and two points of G are adjacent whenever the corresponding atoms of M have a chemical bond joining them. Of course G is permitted to be a multigraph to allow for multiple bonds joining two atoms as in an unsaturated hydrocarbon. This model has been most useful for the determination of the number of isomers of tree-like molecules and others; the original formulas by Cayley were extended by Pólya in a general enumeration theorem, simplified by Otter, and also studied by Balaban. However it required additional methods to resolve the enumeration of chiral and achiral alkenes. These methods used the Power Group Enumeration Theorem to count 2-dimensional achiral plane trees, and were easily modified to handle 3-dimensional achiral alkenes.

Although the phrase 'the topology of a molecule' M always means the graph of M , the present decade has seen the synthesis of molecules with graphs homeomorphic to both of the prototypical nonplanar graphs of Kuratowski: the toroidal graph K_5 and the smallest mobius ladder $K_{3,3}$, the latter constructed by Walba.

Another graph theoretical model involves the expression of chemical reactions in terms of two different graphs with the same degree sequence. This model motivated the chemist, Senior, to characterize for the first time those graphical degree sequences which belong to exactly one graph. The graphs known as polyhexes constitute the table of contents of the classical books on organic chemistry by Clar. The square-celled and triangular-celled animals have also been mentioned in the chemical literature.

The spectrum of a graph, consisting of the nonincreasing sequence of the (real) eigenvalues of its adjacency matrix has a genuine chemical signifi-

cance. However the spectrum does not uniquely determine the graph of the molecule, contrary to chemical rumors which had been widely circulated. Spectral considerations also do not settle the celebrated Reconstruction Conjecture of graph theory although this assertion has been claimed in the chemical literature. The matching polynomial of a graph has been utilized by the Yugoslav chemist, Gutman, leading to a joint paper which generalized it, using line graphs. Finally, electronegativity considerations tell the strength of a chemical bond, suggesting undirected networks as a numerical rather than strictly topological model.

Symmetry and Spectra of Graphs and Their Chemical Applications

K. Balasubramanian

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The use of pruning methods and other graph product methods for the symmetry and spectra of graphs will be outlined. It will be shown that symmetry groups of several graphs of chemical interest can be expressed as generalized wreath product groups. Applications of these methods to dynamic NMR spectroscopy of non-rigid molecules will be considered. Spectra of weighted trees will be obtained using a tree-pruning method. These methods will be applied to NMR spectroscopy and chemical kinetics since graphs with weighted couplings (coupling constants in the case of NMR) play an important role in these areas.

M. Randić^a, G. Kraus^b and B. Džonova Jermon-Blažić^c

Ordering of Graphs as an Approach to Structure-Activity Relationships

We consider molecular graphs which are represented by sequences $(p_1, p_2, p_3 \dots p_4)$, where p_i counts the number of paths (self-avoiding walks) of length i . The path numbers p_i are constructed in a novel way (without a use of a computer) suitable when family of structures having different substituent are considered. In particular we consider a number of derivatives of phenanthrene carbinol, including a few structures reported in the literature as illustrations of "compounds that don't fit" the widely used QSAR approach of Hansch, which is essentially a multiparametric regression scheme using empirical parameters. The compounds are showing variable degree of antimalarial activity. As a consequence of the established partial order among the structures when the most potent autimalarials are taken as standards we were able to make predictions on the most likely derivatives of phenanthrene carbinol which may be expected to exhibit high antimalarial potency. Synthetic work is in progress on one such compound.

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ON THE USE OF RIEMANNIAN SURFACES IN THE GRAPH-THEORETICAL REPRESENTATION OF
MÖBIUS SYSTEMS

A. C. DAY¹, R. B. MALLION^{2*}, and M. J. RIGBY³

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ABSTRACT

Möbius systems have been studied by a novel graph-theoretical method involving non-planar graphs that may be embedded without crossing on a two-sheeted Riemannian surface. In this formulation, negative entries in the resulting adjacency-matrices arise quite naturally from the mathematics of the Riemannian surfaces, without the necessity of recourse to more-intuitive physical considerations. It is further emphasised that the provisions of the Perron-Frobenius theorem on non-negative matrices do not apply to the adjacency matrices of Möbius graphs, and the consequences of this fact for the eigenvalues and eigenvectors of such graphs are discussed.

* Presenter of the paper.

STEREOCHEMICAL TOPOLOGY

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In 1961 Edsel Wasserman coined the term chemical topology to describe certain novel isomerisms which may occur in macrocyclization processes. Chemists thus began consideration of the topology of molecular structures in the context of stereochemistry. We consider the bond graph as the construction composed of the nuclei (points) with adjacency determined by whether the atoms are considered bonded or not. Adjacency is thus arbitrary to some extent. However, for most molecules, construction of such a molecular bond graph is straightforward. Stereochemical topology deals with extrinsic properties of this bond graph deriving from embedding in three-space. We define stereochemical topology as the synthesis and characterization of stereoisomers which are topologically distinct in three-dimensional space. Such novel constructs as catenated rings, knotted rings, and molecular Möbius strips belong in the realm of stereochemical topology. We have recently developed efficient methodology for construction of molecular ladders composed of two polyether chains connected by double bonds. The chains are functionalized such that they may be connected end to end, thus generating cylindrical products. When the number of rungs in the starting molecular ladder is three or more, the products formed upon macrocyclization are homeomorphic with either prisms, or Möbius ladders. (Möbius ladders are graphs defined by Harary and Guy.) Because of the embedding in three space, unique molecular cylinders (prisms) with n vertices may, of course, possess either zero or an even number of $\frac{1}{2}$ twists, while the molecular Möbius ladders possess an odd number of $\frac{1}{2}$ twists. By cleavage of the double bonds of these novel molecules, molecular knotted rings and linked rings, including multiply looped catenanes, may be prepared. Discussion will focus on the novel topological properties of these products, and on general criteria for topological enantiomerism and diastereoisomerism. Topological enantiomers must be non-planar, either defining a non-planar graph (the Möbius ladder with six vertices is homeomorphic with $K_{3,3}$) or a knot or link which is non-planar by virtue of its embedding. In addition, there may be no presentation with an improper axis of symmetry. Interestingly, these criteria are necessary, but not sufficient for topological chirality. For topological diastereoisomerism, at least one of the isomers must be non-planar.

GRAPH THEORETICAL CHARACTERIZATIONS OF MOLECULAR GRAPHS
APPLICATIONS TO DESCRIPTORS OF CHEMICAL COMPOUNDS

William C. Herndon

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Graph theoretical characterizations of molecular graphs can be used for two principal purposes. One is to provide an alphanumeric description or code to aid in the processing or retrieval of chemical structures. It is desirable to have a unique code for any given molecular structure (including stereochemistry), and this requirement is related to problems of graph isomorphism for which many solutions have been proposed. A unique labelling of a molecular graph gives a solution for the unique coding problem. Following the work of several previous investigators, we have recently proposed a method for uniquely denoting polynuclear cluster compounds. The method begins with an algorithm for canonically numbering the molecular graph, and then converts this numbering into a compact linear form of a complete labeled adjacency matrix. The algorithm uses the concept of extended connectivity and a perturbation method to label the graph. The explicit ordering of the final listing completely specifies stereochemical configuration at stereo-centers in the cluster. The procedure is easily carried out hand, and if two molecular graphs have identical notations isomorphism is established. The canonical labelling procedure has been extended to several graphs which are highly resistant to many other canonical numbering methods.

Graph theoretical properties of molecular graphs also give rise to numerical indices derived from the structure which can be used for correlation with physical or chemical properties. This is a well-known and worthwhile application of graph theory to chemistry with many reported successful correlations. Many of these topological indices have also been proposed to be useful in solving graph isomorphism questions, especially when several indices are combined into a single "super-index". However, no combination of topological indices can be shown to be sufficient to establish isomorphism and a canonical labelling procedure would seem to be a more useful approach to questions of this type.

SHOULD WE HAVE DESIGNS ON TOPOLOGICAL INDICES?

D. H. Rouvray

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Over the past three decades it has become increasingly clear that many of the physicochemical properties of substances are determined primarily by the underlying topological structure of the molecular species of which they are constituted. The topological structure of a given species can be formulated in mathematical terms by means of a topological index which reflects not the metric properties of the species but rather its overall shape and size. To date, some 20 different topological indices have been devised and correlations with physicochemical parameters have been obtained for most of them. Although differing indices vary in their sensitivity to characterize molecular branching, the correlations found for a wide range of parameters have, in general, been good to excellent. Topological indices can thus now be regarded as a valuable predictive tool for chemists and others.

After tracing their early historical evolution, we enumerate here all of the major topological indices which have been postulated so far. The mathematical relationships known to exist between various indices are also exhibited and it is concluded that virtually all of the indices are inter-related. The manifold new areas of potential application of such indices in the future are explored under three main headings: bibliographical species classification, physicochemical parameter evaluation and pharmaceutical drug design. It is pointed out that the indices are likely to become increasingly important for the prediction of species behavior in both inanimate and living systems. Novel pharmaceutical and medical applications in particular appear to warrant further study. The question posed in the title of the paper can thus be answered in the affirmative: designs on the utilization and exploitation of topological indices in several as yet uncharted domains are certainly admissible.

TOPOLOGICAL INDICES BASED ON NEIGHBORHOOD SYMMETRY: CHEMICAL AND BIOLOGICAL APPLICATIONS

V.R. MAGNUSON, D.K. HARRISS and S.C. BASAK

Chemistry Dept., University of Minnesota, Duluth, Duluth, Minnesota, 55812, (USA)

One of the current trends in chemistry and molecular pharmacology is the progressive use of topological molecular descriptors in the correlation of physicochemical and biological properties of molecules. One of the more interesting approaches in this area is the development of information-theoretic invariants. The essence of the approach is to partition the appropriate set of elements derived from the molecular graph into disjoint subsets on the basis of a selected equivalence relation, construct a probability scheme and calculate the structural complexity (information content) using Shannon's formula.

Like atoms in a molecule may possess quite different physical and chemical characteristics depending upon the number and nature of their neighbors. To account for this phenomenon, we have developed a formalism where the equivalence relation is constructed to partition the atom set according to their zero, first and higher order neighbors in the total molecular graph. For a vertex v in the graph G , an open sphere, $S(v,r)$, is defined as

$$S(v,r) = \{u: d(u,v) < r\} \quad (1)$$

where r is any non-negative real number. $S(v, e+1)$ can be expressed as the union of the disjoint neighbors $\tau^i(v)$, ($i=0,1,\dots,e$), where e is the eccentricity of the vertex v . One can then construct all such open spheres, $S(v,r)$, where v runs over the entire vertex set $V(G)$ and these form a neighborhood system for the vertices of G . An equivalence relation is then defined to achieve zero, first and higher order partitioning of $V(G)$. Subsequently, Shannon's formula is used to calculate the various order information contents (IC_v) of the graph.

The utility of IC_v and other derived indices is demonstrated by correlating these molecular descriptors with the aqueous solubility of 51 alkanols and the narcotic action of a group of thirteen barbiturates. The relative efficacy of these newly formulated indices vis-a-vis other topological indices, viz., Wiener number (W), molecular connectivity ($^1\chi$, $^1\chi^v$), information indices on the distance matrix (I_D^w , I_D^w), and partition coefficient ($\log P$, octanol-water) is also analyzed for barbiturate narcosis.

THE GLOBAL DYNAMICS OF CERTAIN CLASSES
OF REACTION NETWORKS

Hans G. Othmer
Department of Mathematics
University of Utah
Salt Lake City, UT 84112

One aspect of chemical kinetics concerns the prediction of the qualitative dynamics of a reacting mixture based on information about the topology of the reaction network and the dependence of the rates on the concentration of the various species. A graph-theoretic approach is natural for such problems because it leads to a factorization of the equations of change in which the effects of stoichiometry, network structure and reaction rate phenomenology can be studied separately. This in turn leads to a classification of the steady states and an algorithm for systematically determining which, if any, of the various types exist in a given network. This approach also leads to a complete description of the global dynamics of a subset of what are called vertex-controlled networks. In particular, one can show that the equations for such networks always have exactly one steady state that is globally-asymptotically stable, and if such networks are periodically-forced, the system always relaxes to a periodic solution with period equal to that of the driving function.

LOGICAL vs CONTINUOUS DESCRIPTION OF SYSTEMS COMPRISING FEEDBACK LOOPS

R. Thomas, Laboratoire de Génétique, Université Libre de Bruxelles, Belgium

Looped systems comprising multiple non linear interactions can be described in terms of differential equations, as used for instance in chemical kinetics. However, unless the number of variables is very low, these systems cannot be treated analytically, and such essential qualitative properties as the number and quality of the attractors have often to be ascertained from numerical identification of steady states, for more or less arbitrary chosen values of the parameters.

The usefulness of a logical description, i.e. a description in which variables can take only a limited number of values (usually two), has been realized for many years, and solutions proposed (see Rashevsky, 1954 ; Sugita, 1963 ; Kauffman, 1969 ; Glass, 1975). A method called since "Kinetic Logic" has been introduced some ten years ago (Thomas, 1973 ; Thomas and Van Ham, 1974). Its characteristic features are as follows :

1. To each relevant constituent (i) of a system we associate two logical elements : a logical variable (α_i) describing the concentration (or more generally the presence of the element, and a logical function (a_i) describing its rate of synthesis (or more generally, its production).
2. Time is not discretized. Rather, we associate with each couple (α_i, a_i) two (occasionally more) time delays ; switching on the function ($a_i=1$) normally results in the appearance of the product ($\alpha_i=1$) after a characteristic delay t_{α_i} and switching off the function ($a_i=0$) normally results in the disappearance of the product ($\alpha_i=0$) after a characteristic time delay t_{α_i} . This ensures a fully asynchronous, yet perfectly practicable, treatment.
3. Each system is described by a set of logical equations of the form $\alpha_i = f_i (\alpha_1, \alpha_2, \dots, \alpha_i, \dots, \alpha_n)$, a description which permits self input. The set of equations generates a state table which gives the values of the logical functions for each set of values of the logical variables. From the state table one can generate a graph of the sequences of states which permits the identification of the attractors (stable, periodic, ...) and the pathways towards them.

R. Thomas (continued)

4. The conditions which impose the various pathways can be studied "analytically", this is without any prior assignement of numerical values to the time delays. In particular, one can perform a logical stability analysis of cyclic pathways.

A recent description of this method can be found in Thomas (1983).

In this talk I plan to discuss various aspects of the relation between my logical equations and differential equations using sigmoid interactions (as proposed e.g. by Goodwin (1965) and by Glass and Kauffman (1972)). In particular, we will see :

1. How one can infer from the logical description of a system the number and nature (stable steady states, limit cycles, ...) of the attractors of a homologous differential system (using sigmoid interactions).
2. How one can reverse the logical procedure so as to use it in an inductive way (instead of deducing the possible behaviours from the structure, we build a structure, as simple as possible, which will display a desired behaviour)
3. (A more recent development).
How one can relate the parameters of the continuous description to the delays of the logical description.

QUALITATIVE DYNAMICS AND STABILITY OF CHEMICAL REACTION NETWORKS

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This paper presents concepts and computer algorithms that should enable a beginner to discover the qualitative dynamics of an ordinary reaction network. The algorithms supplied will run on an IBM personal computer. The paper begins with the practical aspects of setting up a network that faithfully represents that dynamics of a system on the time-scale of interest. Then it carries the reader through the analysis of a typical network and examines various theoretical questions of relevance along the way. A major topic is the structure of the manifold(s) of steady states, for these bear on the question of the existence of multiple steady states, the possibility of explosions and other exotic dynamics. The question of whether the steady states are globally attracting is treated using Lyapunov functions. Networks that have simple Lyapunov function are easily identified by tests that can be made by the computer algorithms supplied. The paper goes on to discuss how network structure can cause a breakdown of a simple type of qualitative dynamics and lead to more exotic dynamics. The latter part of the paper treats a number of questions: the effect of cycle length on instability, Lyapunov functions that can show that networks with exotic dynamics have their trajectories confined within a finite volume of dynamical space, and how the structure of networks can produce chaotic dynamics, and evolution.

HIGHER CHAOS IN ABSTRACT KINETICS

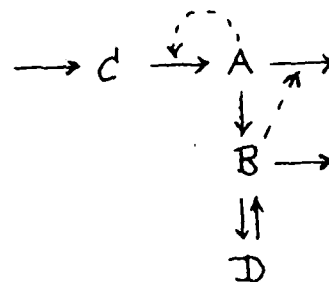
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ABSTRACT

BIFURCATION PARAMETERS THAT ARE TURNED INTO SLOW VARIABLES BY MAKING THEM DEPENDENT ON ONE OF THE VARIABLES OF THE SYSTEM PROVIDE A POWERFUL MEANS TO GENERATE NONTRIVIAL HIGHER-DIMENSIONAL BEHAVIOR [1]. FOR EXAMPLE, LETTING A 2-VARIABLE SUBSYSTEM GO THROUGH A HOPF BIFURCATION, VIA A SLOW THIRD VARIABLE COUPLED TO ONE OF THE 2 VARIABLES, EASILY GENERATES CHAOS (ESPECIALLY SO IF THE HOPF BIFURCATION LEADS TO A LARGE-AMPLITUDE LIMIT CYCLE SOON) [2]. ANALOGOUSLY, LETTING A 3-VARIABLE SUBSYSTEM GO THROUGH A CHAOS-GENERATING BIFURCATION (OR BIFURCATION SEQUENCE, RESPECTIVELY), VIA A SLOW FOURTH VARIABLE COUPLED TO ONE OF THE 3 VARIABLES, EASILY GENERATES HIGHER CHAOS (ESPECIALLY SO IF THE BIFURCATION LEADS TO A LARGE CHANGE IN AMPLITUDE). AND SO ON. AS AN EXAMPLE, CONSIDER THE FOLLOWING ABSTRACT REACTION SCHEME:

HERE A, B IS THE WELL-KNOWN TURING OSCILLATOR [3]. THE ADDITION OF THE (DURING PART OF ITS OPERATION) SLOW VARIABLE C LEADS TO CHAOS (CF. [2]). THE ADDITION OF THE FURTHER SLOW VARIABLE D LEADS TO HIGHER CHAOS. NOTE THAT THE WHOLE SYSTEM ($A+B+C+D$) IS A SIMPLIFIED VERSION OF THE BELOUSOV-ZHABOTINSKY REACTION [4,5].



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PAPER TO BE PRESENTED AT THE MATHEMATICAL CHEMISTRY CONFERENCE (B. KING, ORG.), ATHENS, GEORGIA, APRIL 18-22, 1983.

THE USE OF SENSITIVITY ANALYSIS IN DETERMINING THE STRUCTURAL STABILITY OF MULTI-PARAMETER OSCILLATORS

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ABSTRACT

The use of sensitivity analysis for the study of models of oscillating reactions is discussed. It is shown that linear sensitivity coefficients for oscillating systems almost always contain secular terms; this makes a physical interpretation of the sensitivity information very difficult. A new sensitivity method which eliminates the secular terms via a uniformly valid expansion is derived. A method for extracting the modified sensitivity coefficients from the ordinary sensitivity coefficients is proposed and illustrated by application to the Lotka-Volterra oscillator.

ELECTRICAL NETWORK REPRESENTATION OF
n-DIMENSIONAL CHEMICAL MANIFOLDS

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A planar network representation, which utilizes lumped parameter elements connected by Kirchhoff's laws, is used to represent the Riemannian metric of chemical energy manifolds. Thus, the consideration of primary concepts of chemistry -- e.g., molecular structure, reaction mechanism, stability, etc. -- which can be analyzed by using quantum mechanical, kinetic, or thermodynamic energy hypersurfaces reduces to the consideration of planar graphs. The input currents in the network correspond to the contravariant components of the tangent vectors in the directions of the manifold coordinates at a given point (e.g., reaction rates) while the conjugate voltages correspond to the covariant components (e.g., affinities). Tellegen's theorem and the introduction of linear resistances, which are constant over a differential range, lead to the typical Riemannian distance element. Schwarz's inequality translates into a parameter which measures optimum dynamical efficiency and the elemental local volumes (or higher dimensional measure of content) determined by the manifold coordinates can be measured by looking at the efficiency of chemical energy conversion along various paths which start at the same point on the energy hypersurface. Because the distance element measured by using the port variables is equal to sums of square of variables inside the resistive network (the power provided by the inputs equals the sum of powers dissipated by the network resistances), the network construction is equivalent to embedding the n-dimensional (non-orthogonal) manifold in a higher dimensional (orthogonal) frame of reference of dimensionality $d \geq n(n+1)/2$. Vibrations in the transitions between two states in the chemical manifold can be introduced by the additions of inductive and capacitive elements which store energy as a function of a path parameter. The topological and metric properties of the network lead to Lagrange's equations, geodesic equations and stability requirements equivalent to a generalized Le Chatelier principle.

Abstract for Georgia Symposium on Chemical Applications of
of Topology and Graph Theory

Title: A LISP Program for the Manipulation of Chemical Graphs

Authors: Carl Trindle and Robert Givan, Department of Chemistry
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The representation and manipulation of chemical graphs is awkward in most familiar programming languages. LISP, the Esperanto of artificial intelligence research, makes possible a representation of chemical structural formulas which is much more nearly analogous to the chemist's use of such graphs. This is a considerable computational advantage as well as convenience for the user.

We will describe a "functional fragment" representation of structural formulas, applicable to any molecule, which will resolve a chemical graph into a list of fundamental fragments. Exploiting the property feature of LISP and the distance geometry algorithms of Crippen, we will recover Cartesian coordinates for each atom, suitable for input to molecular mechanics programs or ab initio systems.

A method for recovering a chemical graph and Cartesian coordinates from an IUPAC name will be outlined as well.

E. C. HASS and P. J. PLATH

The Multi-Dimensional λ -Model. - A Graph Theoretical / Algebraic Approach to Describe Mechanistic Aspects of Complex Chemical Reactions.

Abstract

Based upon (1) the concept of the reaction lattice, generated by graphs of the reaction, (2) a graph theoretical description of bonding symbols, and (3) the model of a continuous structural change of reactants into products by means of reaction parameters (λ -model), correlation diagrams are derived which lead to conclusions about the course of chemical reactions. Using this formalism, closed analytical formulae are derived for the Woodward-Hoffmann Rules for concerted pericyclic reactions. Special emphasis is given to multi-dimensional approaches in order to describe mechanistic aspects of complex organic reactions.

THE CLASSIFICATION OF CHEMICAL MECHANISMS FROM A GEOMETRIC VIEW-POINT

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ABSTRACT

A systematic method is introduced here for determining all mechanisms for a given chemical reaction, which are possible from a combinatorial viewpoint. Every mechanism is represented by a polyhedron in a real vector space. Every lower-dimensional face of such a polyhedron represents a submechanism, all of whose elementary steps advance in the same direction as those of the original mechanism. The vertices or zero-dimensional faces of the polyhedron correspond to the mechanisms, called direct mechanisms, which have minimal sets of steps. The fact that this polyhedron can be characterized by its set of vertices leads to the conclusion that every mechanism is reducible to a set of direct mechanisms connected in parallel. The method is illustrated by examples from chemistry which are sufficiently complex to be inaccessible without a mathematical approach such as this one.

MODELLING MOLECULAR COMPLEXITY

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ABSTRACT

A mathematical model of molecular complexity based on concepts from graph theory and information theory has been developed (see JACS 1981, 3599, CC 1981, 818) and is being applied to analyze organic syntheses. Plots of complexity vs. number of steps are used to estimate probable efficiency (JACS 1982, 5801). Changes in complexity upon breaking bonds in a target help locate strategic bonds in retrosynthetic analysis. Reactions can be rated according to the increase in molecular complexity they produce. The principle of convergence is clarified by considering symmetry in molecular graphs and synthesis graphs.

THE AUTOMORPHISM GROUPS OF SOME CHEMICAL GRAPHS

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In recent years many authors have used graphs for a variety of purposes in chemistry, in particular various "reaction graphs" have been studied in which the vertices represent chemical species and the edges chemical processes which interconvert the species. Some interest has been shown in determining the automorphism (symmetry) groups of reaction graphs. In general this is a hard problem, but many reaction graphs are highly symmetrical and since such graphs are comparatively few in number it is inevitable that some of those appearing in the chemical literature are ones which have already been discovered by mathematicians in totally different contexts.

We look at some examples of reaction graphs. In each case we start with a small graph B which has vertices labelled $1, 2, \dots, n$ and we have some rearrangement rule which might consist of repositioning edges in the graph or of permuting the vertex labels. As we restrict our attention to degenerate rearrangements, the resulting graph is isomorphic to B but with the vertex labels redistributed. In the reaction graph Γ each vertex corresponds to a labelling and two vertices are joined by an edge if it is possible to interconvert the labellings by a single step application of the rearrangement rule. In most of our examples the automorphism group $\text{aut}\Gamma$ of Γ is the symmetric group S_n . We show that many reaction graphs are examples of what group theorists variously call suborbital, orbital or coloured graphs and this enables us to deduce that for such reaction graphs $\text{aut}\Gamma$ always contains S_n , though in some cases $\text{aut}\Gamma$ is much larger than S_n .

There is some information in the literature on suborbital graphs relevant to the question "when is a reaction graph connected?" and it is likely that there are other results which could be applied to reaction graphs.

*author presenting paper

GRAPHS, POLYMER MODELS, AND EXCLUDED VOLUME EFFECTS

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Simple graph-theoretical polymer models such as the random-walk for chain polymers or the Cayley-Polya tree models for branched alkanes do not account for volume exclusion—that is, the fact that two pieces of a molecule do not occupy the same region of space at the same time. Volume exclusion is accounted for in easily devised corrected graph-theoretical models, such as self-avoiding walks on a lattice for the case of chain polymers. However, as has long been realized, these corrected models seem to be much more difficult to deal with in an analytic fashion.

Here we discuss some generating function methods for both uncorrected and corrected models. This entails fractal dimension ideas, renormalization group approaches, and transfer matrix techniques. Via such methods it seems that excluded volume models can be attacked and useful properties deduced—in particular the mean spatial extent of the model polymer conformations.

Finally we also note that graph-theoretic problems similar to those occurring for models with volume exclusion also arise in a variety of other statistical mechanical models and wavefunction cluster expansions involving localized orbitals (or sites). Indeed volume exclusion features seem to occur frequently in all areas of science; for instance, branched structures seem most typically to exhibit such features, although neither the usual graph-theoretic trees nor the common branching process theory account for such features.

A VOLUME FUNCTION FOR WATER BASED ON A RANDOM LATTICE-SUBGRAPH MODEL

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ABSTRACT

It is shown how the following concept can be used to obtain a volume function for water.

If G is a connected r -regular labelled graph, let $RG(p)$ denote any subgraph of G having the same point set as G and line set defined by selecting or rejecting each of the lines of G with independent probability p or $q = 1 - p$, respectively. $RG(p)$ is called a random subgraph of G and is analyzed using the appropriate probabilistic considerations.

Here the graph G is taken to be homeomorphic to the ice lattice I and p , as a function of temperature, is associated with the hydrogen bonding probability of water molecules. Physical assumptions relating volume to bond and cycle formation lead to a volume function $V(p)$ which is qualitatively of the correct form. Additional assumptions, which match the bond percolation probabilities of certain subgraphs of $RI(p)$ with the phase transitions in water at 0°C and 100°C , yield a good numerical fit of $V(p)$ to empirical data. With respect to the latter it is noted that the lack and/or wide discrepancy of physical and mathematical numerical results in the literature is a serious handicap in all studies of water.

This work is presented in support of the continued use of random graph models in physical applications.

THE BONDING TOPOLOGY OF POLYHEDRAL MOLECULES

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This paper summarizes the topology of the chemical bonding in molecules based on polyhedra having atoms at each vertex. In such molecules delocalized bonding occurs when there is a mismatch between the vertex degree of the polygon or polyhedron and the number of internal orbitals (normally but not necessarily 3) provided by the vertex atoms. This analysis leads naturally to the concepts of two-dimensional aromaticity in planar polygonal molecules such as benzene and three-dimensional aromaticity in deltahedral molecules such as certain carboranes and metal clusters. Elementary graph theoretical considerations provide a basis for the $2n + 2$ skeletal electrons normally observed in delocalized deltahedral molecules without tetrahedral chambers. Electron-rich polyhedral cluster systems have $2n + 2$ skeletal electrons and form polyhedra having one or more faces with four or more edges, which may be regarded as holes in the topological sense. Electron-poor polyhedral cluster systems have less than $2n + 2$ skeletal electrons and form deltahedra having one or more tetrahedral chambers. Puncture or excision of closed deltahedra to form electron-rich open polyhedra having one or more holes may be considered as opposite or dual to the capping of closed deltahedra to form electron-poor larger polyhedra having tetrahedral chambers. Elementary polyhedranes are hydrocarbons of the stoichiometry $(CH)_{2m}$ and are based on polyhedra with all vertices of degree 3 and a localized carbon-carbon single bond along each edge. The localized polyhedrane polyhedra are thus the duals of the delocalized deltahedra of carboranes and metal clusters.

TOPOLOGICAL PROPERTIES OF SULFUR NITROGEN COMPOUNDS

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ABSTRACT

The general question of the electronic structure of the binary compounds formed from nitrogen and sulfur will be discussed. This group of electron rich molecules and ions possess structures wherein it is not always evident which atoms are bonded to which other atoms or how this bonding occurs. The discussion and analysis will be based upon the results of semiempirical molecular orbital calculation (ref. 1) and utilize the concepts of localized molecular orbitals (ref. 2) and density functional analysis (ref. 3). The discussion will include the species S_2N_2 , S_3N_2 , $S_3N_3^-$, the isomers of S_4N_2 , $S_4N_3^+$, $S_4N_4^{2+}$ and the molecule S_4N_4 (ref. 4).

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THE SHAPES OF MAIN GROUP CLUSTERS: A TOPOLOGICAL APPROACH TO SKELETAL ELECTRON COUNTING.

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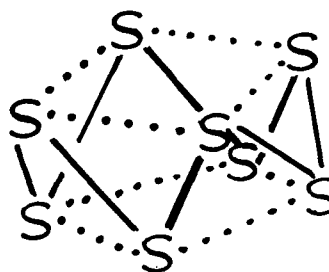
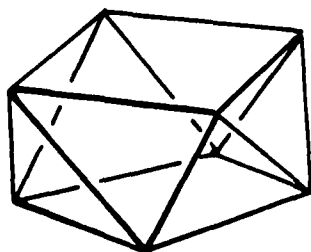
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ABSTRACT

A quantum topological approach, based on the topological properties of molecular charge densities is used to propose a symmetry hierarchy of molecular graphs. It is shown that the structures of a large number of cluster compounds may be predicted via a mapping of their molecular graphs onto a single polyhedron, the corresponding molecular graphs being constructed by a simple method of electron counting. The proposed model is exemplified through a detailed analysis of 5 through 8 atom clusters.

Typically, cyclo-octasulfur, S_8 , has 48 valence electrons and, subtracting an exo-skeletal electron pair (analogous to those in the exo-skeletal BH bonds of the boranes), one is left with 16 skeletal electron pairs to hold together the cluster. It remains merely to find the highest symmetry polyhedron having 8 vertices, 16 edges and (from Euler's theorem) 10 faces. This is the square antiprism which indeed leads to the overall geometry of the S_8 molecule.



DYNAMICS OF RNA SECONDARY STRUCTURE FORMATION

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ABSTRACT

We review the status of the RNA secondary structure problem and pose a new approach based on simulating the dynamics of the folding process. Constrained versus unconstrained models of folding are discussed as are methods for detecting common features in the population of equilibrium structures generated.

TOPOLOGICAL ASPECTS OF ENZYME-SUBSTRATE RECOGNITION

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ABSTRACT

Enzymes are compounds in the presence of which certain chemical reactions proceed at higher rates than would otherwise be the case. They are generally unchanged in amount and in their chemical properties after the reactions have occurred. Hence they belong to the class of catalysts; they are distinguished from other catalysts by the fact that they occur only as products of living organisms. A substance with which an enzyme reacts is called its substrate. All enzymes are functionally specific to varying degrees in their action on their substrates. An enzyme may act on one and only one substrate and the substrate molecule must be associated with the enzyme in a specific orientation. Thus there arises a problem of recognition in connection with the interaction of an enzyme with its substrate.

We describe a mathematical model for enzyme-substrate recognition. The foundations for this model were laid by L. Edelman and R. Rosen. Their theory rests on the following assumptions:

- (1) That substrates can be represented by continuous functions, which vanish outside some closed bounded region in $\mathbb{R}^3$, analogous to charge or mass distributions; i.e., substrates are represented by elements $F \in C(K)$, the space of all real-valued continuous functions on K , where K is a compact subset of $\mathbb{R}^3$ chosen to be large with respect to molecular dimensions.
- (2) That recognition of the substrate corresponds to the evaluation of a linear functional on $C(K)$ -- or what is equivalent:
- (2') That associated with a given enzyme is a function a in the dual space of $C(K)$, i.e., $a \in NBV(K)$, the space of all real-valued, normalized functions on K of bounded variation, and that recognition of a substrate F results from the evaluation of a Stieltjes integral of one form $\int F da$. (The equivalence of (2) and (2') is due to a theorem known as the Riesz Representation Theorem.)

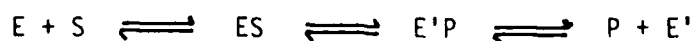
The recognition problem can also be analysed in its functional context as a characteristic feature of a system which responds to specific inputs to

S. Swaminathan (continued)

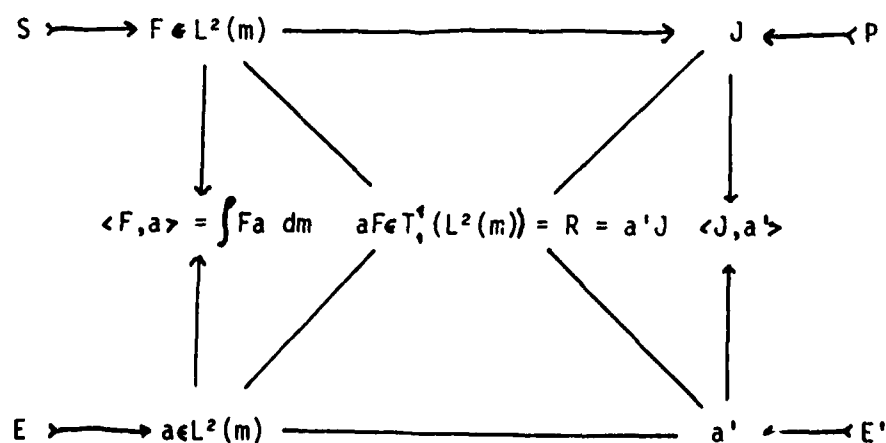
produce specific outputs. This point of view is explored by A.H.Louie, I.W. Richardson and S.Swaminathan [Journal of Theoretical Biology, 94(1982) 77-93]. The mathematical formulation of the concept of system response and the associated description of a system in terms of response lead directly to a metric calculus providing a quantitative measure for discrimination. Moreover the metric structure inherent in this phenomenology allows one to determine the functional relationship between the physical features used by the system to recognize an input (e.g., a substrate) and corresponding features possessed by the output (e.g., the product).

The system is divided into distinct, interacting subsystems, indexed by a finite set $\{i=1,2,\dots,m\}$. The set of causes imposed upon the system (i.e., the input) is given by various F_i belonging to some Hilbert space H . The system is characterized by a fixed set of constitutive parameters, a^i , which belong to the dual space H^* . The system dynamics is phenomenologically described by a response tensor given by the dyadic $R = a^i F_i$. It is postulated that R is invariant with respect to transformations of the representation, i.e., with respect to a change of parameters. In particular, R has an invariant dual representation.

In the model for enzyme-substrate recognition, the a^i 's represent enzymes and the F_i 's represent substrates. The recognition process is given by the evaluation $a^i(F_i)$, while the enzyme-substrate complex is represented by the response tensor $a^i F_i$. The dual representation is the mathematical analogue of the enzyme-product complex. The mechanism of enzyme-substrate interaction can be represented as



where ES is the enzyme-substrate complex, $E'P$ is the 'enzyme-product' complex, P is the product of interaction and E' the 'modified enzyme' from which the enzyme E can be recovered. The following diagram illustrates the model:



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