

THEORETICAL CHEMISTRY
Periodicities in Chemistry
and Biology

VOLUME 4

Edited by

HENRY EYRING/DOUGLAS HENDERSON

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Preface

In a sense, theoretical chemistry has existed as long as scientists have tried to understand chemical phenomena. However, it has been only recently that theoretical chemistry has grown into a mature field. Three developments, all relatively recent, have spurred this growth. First, at the end of the nineteenth century the foundations of statistical mechanics were laid. As a result, the bulk properties of chemical systems could be calculated from their microscopic dynamics. Second, during the first third of the twentieth century, quantum mechanics was developed, giving a satisfactory theory for the microscopic dynamics of chemical systems. Finally, in the past two decades, fast electronic computers have made accessible the full richness of quantum and statistical mechanics for the theoretical description of complex chemical systems.

Despite the maturity of theoretical chemistry, there are very few journals or review series devoted to all aspects of this field. It is hoped that this serial publication will fill, in part at least, this gap. Articles concerning all aspects of theoretical chemistry will be published in these volumes. Articles concerning experimental chemistry which pose or answer questions of theoretical interest may also be published from time to time.

In this volume a multisided phase of periodicity is presented. Winfree is concerned with the principles that relate the geometry of the visible activity patterns to the less obvious geometry of reaction kinetics. His procedure is analogous to Gibbs geometrizing of thermodynamics. He is chiefly concerned with biological periodicities. Field is concerned with chemical periodicities and how they arise and gets explicitly involved with a variety of chemical mechanisms. Troy is concerned with the mathematical approach to nerve impulse transmission and to an interpretation in depth of several other chemical reactions.

Hess and Chance give a historical introduction to a variety of biological periodicities controlled by enzymes and then develop models of glycolytic

oscillations in more detail. They classify the enzyme functions in the latter case into promotion of four processes.

1. An input supplying the substrate
2. The primary oscillator enzyme
3. A feedback function
4. A sink

From DeHaan and DeFelice we get an in-depth picture of heart behavior together with an interpretation of this behavior at the molecular level. Ortoleva provides a very general overview of periodicities and shows they are wide ranging throughout nature. Finally, Oster and Ipaktchi treat the ecological problems associated with population growth and stability and illustrate the complexity of the matters requiring attention.

HENRY EYRING
DOUGLAS HENDERSON

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Stably Rotating Patterns of Reaction and Diffusion

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I. Introduction

During my first summer of graduate school, 12 years ago, I had the good fortune to work in Robert DeHaan's laboratory in the Carnegie Institute of Embryology in Baltimore. More than whatever I learned about heart cells, I remember Bob's recurrent enquiry: "What question are you asking?" That question never failed to stop frantic agitation, whether of tongue or of hands, dead in its tracks. What question *am* I asking? It is particularly important to answer clearly at the outset of this particular essay, which is less closely tied than I would like to either to quantitative experiment or to rigorous mathematics.

The question concerns a new class of phenomenon: a persistent rotating mode of activity in media that can alternatively lie stably inactive, except for giving a pulselike response to occasional stimuli. Such media include nerve membrane, heart muscle, the smooth muscle of stomach and gut, certain primitive embryos, and, since 1970, a feverishly studied inorganic chemical reaction.

And what am I asking about these self-organizing patches of rotary activity? At this stage, nothing rigorously quantitative, nothing steadfastly reductionistic, but something fuzzier, something like "How can we begin to think about them? What principles relate the geometry of the visible activity patterns to the less obvious geometry of reaction kinetics? How can such geometric principles be made at least compatible with physical chemistry? How can they be maneuvered to show us how rotors come about and how they cease to exist? What alternative modes of spatially self-organizing chemical activity can be anticipated?"

With mathematicians everywhere busily geometrizing everything from relativity theory through thermodynamics to classical mechanics, it would seem at least sporting to have a go at chemical dynamics (e.g., see Oster and Perelson, 1974). Perhaps the game will enrich its flavor by assimilating the rotating waves of chemical activity first discovered by Zhabotinsky (1970).

The question posed here, then, is "What aspects of the observed chemical oscillations and rotating structures can be understood, at least qualitatively, in geometric terms adaptable to a variety of underlying molecular mechanics?" In attempting an answer, we come upon a principle of potentially wider application in Section III,B,2. I use it only heuristically, but I suspect more rewarding sequelae await its proper mathematical development. The principle stems from Poincaré's introduction of "phase portraits" (Section II,A), which catalyzed deeper understanding of ordinary differential equations, and therefore of dynamics in well-stirred reactors. No comparably intuitive and general method has emerged to save us from *partial* differential equations, such as inevitably arise in spatially distributed reac-

tions. And there are good reasons why not. Convection and turbulence, surface absorption, electrostatic effects of ion concentrations, and so on, really do make the subject of reaction *morphology* a fairyland of mathematically complicated special phenomena [e.g., see Aris' book on reaction and diffusion interactions (1975)].

Ten years ago the special case of unstirred isothermal reaction in homogeneous phase, without interfacial exchanges, without hydrodynamic transport, attracted the attention of few specialists, and then mainly for instabilities of the spatially uniform solution. Even this interest is lost if the reactants have nearly equal diffusion coefficients. But all that has changed since the oscillating reaction of Belousov (1959) was parlayed into a spatially self-organizing reaction by Zaikin and Zhabotinsky (1970). The experimental convenience and dramatic quality of these phenomena have unleashed an explosive proliferation of work, both experimental and mathematical, on what seemed previously an unpromising special case: isothermal, isodiffusive, hydrodynamically inert, without surface phenomena.

And, to get to the point, it is in precisely that case that Poincaré's phase portrait methods may once again provide a considerable aid to intuition, if introduced through the geometrical trick of Section III,B,2. I intend that to be the main point of this article, apart from its supportive context of allusions to specific models and experimental systems.

Let us begin with homogeneous reactions, involving only one point of physical space. We will quickly move to reactions distributed along a one-dimensional filament with molecular diffusion coupling adjacent volume elements. Then we consider new features that emerge if the filament is made into a ring, and finally fill in the ring to consider a two-dimensional disk of reacting medium. Geometry comes into its own with a vengeance in three-dimensional media, but this lovely subject goes beyond my ambitions for this volume.

II. Zero-Dimensional Situations

A. COMPOSITION SPACE

The chemical composition of any homogeneous solution can be described mathematically as a point in composition space. Composition space is the N -dimensional positive orthant of ordinary Euclidean space, with its N coordinate axes representing the positive concentrations of N chemical species involved in the pertinent reactions. To each composition there corresponds a net rate of synthesis, and degradation of each of the N substances. (These rates are obtained from the pertinent kinetic equations, including input and output conditions. In this discussion I regard all chemical systems

as thermodynamically "open," at least in this sense: they consume energy-rich species whose depletion need not concern us on the time scale of interest.) Thus, a little arrow at each point in composition space points the direction and rate of change of composition. Those arrows collectively describe a flow (Fig. 1) that propels the composition of a reacting mixture

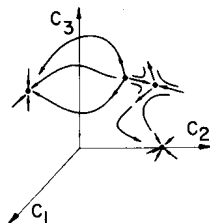


Fig. 1. Three concentration axes figuratively depict N -dimensional composition space. The origin represents concentration zero of each substance. The arrows sketchily evoke a flow in composition space, determined by the rates of change of all concentrations due to reaction, as a function of instantaneous composition. Several stagnation points of the flow (steady states of reaction and degradation of all substances) are depicted.

from almost any initial condition ultimately to some attractor. We say "almost" because every reaction must have at least one and may have more than one stagnant composition at which all the net rates of synthesis or degradation are zero (e.g., see Schmitz, 1975); and none of these need be an attractor (Wei, 1962). A stagnant composition *may* attract, in the sense that the flow arrows lead toward it from all nearby compositions. Such a point is stable against small perturbations of composition. Or it may *repel*, if there is at least one line along which a small perturbation will grow, i.e., if nearby arrows point outward in those directions. Mathematically, a point attracts if the real parts of all N eigenvalues of the linearized rate equations are negative. Otherwise, it repels (excepting the improbable case of purely imaginary eigenvalues).

Suppose the flow arrows not very far away on one side of an attracting stagnation point lead the composition initially farther away before turning around to funnel into the stagnation point (Fig. 2). Borrowing a term from

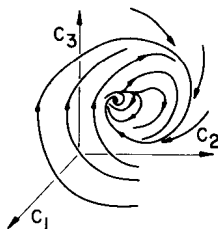


Fig. 2. As in Fig. 1, but the flow depicts an "excitable" reaction: an increase of C_3 or a decrease of C_2 from the attractor sets the system into a large excursion from the attractor.

physiologists, who have for a long time dealt with such models of biological excitability, such reactions are called "excitable." Nerve cells, for example, have an attracting steady state of ion balance across the cell membrane. It is stable to small perturbations, but a not-so-small perturbation results in an immediate and dramatic excursion further away from steady state before things settle down again (see chapter by Troy, this volume). At least one real chemical reaction in homogeneous solution has been found to exhibit excitable behavior, both in the laboratory and on paper (see Appendix, Rossler *et al.*, 1972, and chapter by Field, this volume). We will deal with the simplest geometrical caricature of this reaction shortly.

A slight local change in the flow field near the stagnation point turns the funnel trajectory into a closed loop (Fig. 3) (Franck, 1973, 1974). We then

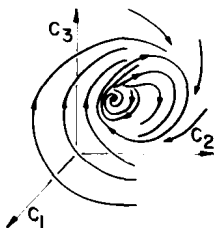


Fig. 3. As in Figs. 1 and 2, but the flow depicts a reaction that approaches a limit cycle along which its composition fluctuates regularly.

have a limit cycle: a cyclic change in composition that leads round and round periodically. In idealized reaction systems involving only two chemical species or only two reaction rates, this is quite a common situation. For example, if there is but one stagnation point and it repels, and if concentrations all decrease from arbitrarily high values as required in any reasonable chemical model, then there is not much else trajectories can do but to run in a ring circulating around the repelling stagnation point. Papers exhibiting such attracting limit cycles in two-dimensional composition spaces have become quite numerous (for reviews, see Higgins, 1967; Hess and Boiteux, 1971; Nicolis and Portnow, 1973; Goldbeter and Caplan, 1976).

Unfortunately, most chemically realizable reactions involve at least three independent variables. Limit cycles in such systems are much more difficult to exhibit analytically and have been exhibited in very few chemical models (e.g., Glass and Perez, 1974; Goldbeter, 1975; Hastings and Murray, 1975; Tyson and Kauffman, 1975; Cummings, 1976; Stanshine and Howard, 1976). A number of real systems are currently under intensive study for the likelihood that they would exhibit true limit cycles in a chemostat with suitable input of raw materials and overflow of product (see *Faraday Symp. Chem. Soc.* 9, 1974).

Trajectories of more subtle geometry can arise once we abandon the early

theorists' blue laws against having more than two variables. For example, in recent years an exciting literature has begun to blossom around the term "strange attractor" (Lorenz, 1963; Moore and Spiegel, 1966; May, 1976; May and Oster, 1976; Roessler, 1976a, 1976b, 1976c, 1977; Gilpin, 1977; Williams, 1977; Guckenheimer *et al.*, 1977). A strange attractor is a region of two or more dimensions in composition space that attracts trajectories and from which no trajectories emerge. But, within a strange attractor the kinetics almost defies description. It does not settle down to a stable periodicity, even of a complex sort, nor to stationarity. Several theoretical examples under current study (May, 1976; May and Oster, 1976; Rossler, 1976a, 1976b, 1976c, 1977; Guckenheimer *et al.*, 1977; Williams, 1977) seem to be perfectly feasible consequences of realistic kinetic equations: not at all mathematically pathological delicacies. The "origami" constructions of Rossler (1976a,b,c,d) make it all much more intuitively understandable, and even assist in deliberate construction of chaotic reaction schemes. Olsen and Degn (1977) give experimental evidence of a strange attractor in the reaction of H_2O_2 with peroxidase. Rossler and Wegmann (1977), and Schmitz, Graziani, and Hudson (1977) show what appears to be chaotic dynamics in the Belousov-Zhabotinsky reaction; Schmitz and Garrigan (1977) show the same in Pt-catalyzed H oxidation.

B. SKETCHING THE FLOW

One way to describe the complex kinetics of a reaction is to draw its trajectories as a flow in composition space. Such artwork is no substitute for understanding the mechanisms of molecular encounter and rearrangement. But neither does the molecular cause and effect description by itself tell us much about the dynamic behavior of a process involving many coupled reactions. This is what the flow diagram or "phase portrait" provides in one timeless glance. This geometric construction is a routine exercise for digital computer and plotter if the kinetic equations are known. But if they are not, as is more commonly the case in research, then the sketch must be made from fragments of data and anecdotal phenomenology.

In preparing such a sketch, the main questions to answer are as follows.

(i) How many independent variables (concentrations or reaction rates) are important in the sense that they all interact in the time scale of interest? This is the dimension N of composition space. (Quantities that change much more slowly may be treated as parameters affecting the rate laws, rather than as state variables.)

(ii) Does the reaction's composition stay on some lower dimensional surface embedded in the Euclidean N -space, except for negligibly brief transients? If so, what is the topology and shape of that surface? (See Feinn and Ortoleva, 1977.)

(iii) How many stagnation points (steady states) are there in addition to