

The Theory of Conjugate Reactions in the Context of Modern Ideas

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Abstract

Various types of possible interactions between reactions are discussed. Some of them are united by the general idea of chemical reaction interference. The ideas on conjugated reactions are broadened and the determinant formula is deduced; the coherence condition for chemical interference is formulated and associated phase shifts are determined. It is shown how interaction between reactions may be qualitatively and quantitatively assessed and kinetic analysis of complex reactions with under-researched mechanisms may be performed with simultaneous consideration of the stationary concentration method. Using particular examples, interference of hydrogen peroxide dissociation and oxidation of substrates is considered.

Keywords

Conjugation, Interference, Determinant, Initiation

1. Introduction

Mechanisms of various chemical reactions were studied in depth in the twentieth century. This contributed to the creative development of the theory of conjugate processes. Thus a series of papers [1]-[6] was devoted to the development of this “half-forgotten branch of chemical kinetics of the past”, where “according to N.A. Shilov the concept of interference of chemical reactions is a natural generalization and nontrivial development of the idea of conjugate oxidation reactions” (from the foreword to the monograph by O.M Poltorak [1]).

However, there is a recent paper [7], claiming development of the theory of conjugate processes, where the “conjugation of elementary stages through general intermediates as a universal phenomenon” is taken as a basis.

This view contradicts one of the basic principles of chemical kinetics—about independence of the course of elementary stages. Therefore, there is a need to

consider the main principles of the theory of conjugate reactions in the kinetic aspect. These principles are as following: only gross reactions carried out in open systems can be conjugated, and only they may have common highly active intermediate substances (intermediates) [8]: while such basic principles of chemical kinetics as the law of the masses and the independence of the course of elementary reactions are fulfilled and retain their inviolability.

Energy aspect of the conjugate processes is discussed in [9] in the framework of thermodynamics of irreversible processes.

Despite the fact that the basics of conjugate reactions were formulated at the beginning of the 20th century, nowadays they have found their “second wind” as part of the creation of innovative technologies that mimic useful functions of the processes occurring in nature (in particular, enzymatic catalysis). It should be considered that despite the fact that the theory of conjugate reactions was developed at the time when there was almost no information about detailed mechanism of chemical reactions, it nevertheless remains true on its fundamental basis. However, the old theories “cannot be revived to life in their literal interpretation”.

Characteristic features of the conjugate reactions formulated by N.A. Shilov in his monograph [8] consist of following regulations:

- an exergonic reaction performs useful work for the flow of another—endergonic—reaction, *i.e.* a loss of free energy in a primary reaction fully covers an increase in free energy in a secondary reaction;
- communication channels between conjugate reactions are established through common intermediate compounds;
- conjugate reactions necessarily occur in open systems;
- conjugated reactions must be complex.

We have added to this list a number of classical regulations of chemical kinetics.

It is necessary to add new regulations as Shilov’s monograph [8] was published in 1905, when such highly active intermediate substances as free radicals, active complex compounds, etc. were not known. Undoubtedly, in the kinetics of conjugate reactions along with the law of masses, the fundamental chemical postulate of the independence of elementary reactions is unbreakable.

Possibility of occurrence of conjugate reactions only in open systems is associated with the requirement of the system to have a constant mass exchange with external environment. This regulation radically distinguishes conjugate reactions from initiated, catalytic, autocatalytic and polymeric processes that can occur in close systems.

The fact that conjugate reactions must necessarily be hindered is explained by the fact that only they (because of their complexity) may have common highly active intermediate particles. Here it is necessary to clarify why ordinary elementary stages involved in reaction mechanisms cannot be conjugated to each other: elementary stages of a mechanism of any complex chemical reaction never interfere in each other’s flow (otherwise it would contradict the independence of

their course); in this case all complex reactions known in chemistry would be conjugate (which is absurd). Only the part of the complex reactions that have common highly active intermediate particles (intermediates) can be conjugate.

The main subject of this article is discussion and terminological clarification of fundamental issues related to the kinetics of interaction of the complex reactions (chemical interference).

However, it is necessary to demonstrate differences between various synchronous (*i.e.*, simultaneously occurring) reactions—parallel, sequential, parallel-sequential, conjugate and coherent-synchronized reactions (see **Figure 1**).

Where $A \rightarrow B$ is the primary reaction; $A \rightarrow C$ is the secondary reaction.

As can be seen from the diagram, the most significant distinguishing feature of conjugate and coherently synchronized reactions from other reactions is their coherence (consistency).

It is necessary to consider the regulations stated below in order to understand these differences:

- the secondary (target) non-induced reaction is a non-spontaneous or self-induced reaction, which is difficult to realize due to kinetic and thermodynamic order;
- during induction, type of the target (secondary) reaction is transformed from non-spontaneous to self-induced and, under realizable conditions, it flows without difficulty;
- a gross equation of the secondary reaction is already formed in its induced form, *i.e.* in a transformed form;
- in contrast to parallel, sequential and parallel-sequential reactions, an induced (secondary) reaction cannot be carried out separately from the primary reaction;
- the spontaneous target reaction can also be modified under influence of induction and under certain conditions proceed with a high rate;
- the reaction system, in which chemical induction is realized, contains two or more components.

The concept of chemical interference is put forward by us, as a phenomenon consisting in the fact that reactions occurring synchronously in a chemical system, can mutually strengthen and weaken, and in this state they are necessarily coherent [1]-[6].

Mathematical apparatus of the chemical interference and, in particular, coherent-synchronized reactions

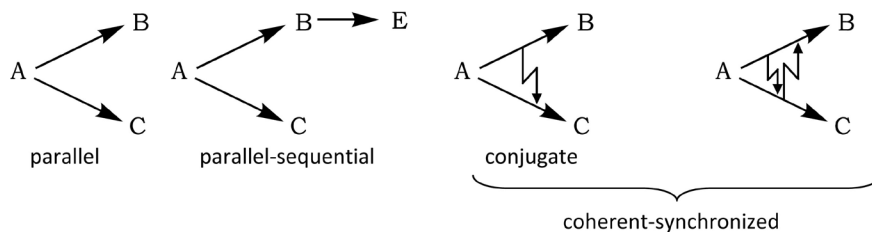
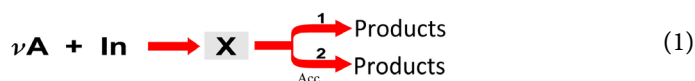


Figure 1. Synchronized chemical reactions.



(where A is an actor, In is an inductor, Acc is an acceptor and X is a highly active particle) consists of the determinant equation [1]-[6]:

$$D = \nu \left(f_{A_1} / f_{Acc} + f_{A_2} / f_{Acc} \right)^{-1} \quad \text{или} \quad D = \nu \left(r_{A_1} / r_{Acc} + r_{A_2} / r_{Acc} \right)^{-1} \quad (2)$$

(where r_{A_1}, r_{A_2} are the rates of the primary—1 and the secondary—2 reactions, f_{A_1} and f_{A_2} are the actor consumption in the primary and secondary reactions) and the coherence ratio:

$$\frac{1}{\nu} f_A = f_{In} = f_{A_1} + f_{A_2} = f'_{A_1} + f'_{A_2} = f''_{A_1} + f''_{A_2} \quad (3)$$

On the basis of these equations, a determinant scale was compiled. It is easy to determine in the reaction medium the nature of an intervention of one reaction into another (chemical interference) using this scale:

$D = 0 \div \nu$ is the area of chemical conjugation; $D > \nu$ is the area of other inter-related interfering reactions.

The scheme shows that the synchronous reactions which are not coherent, but one interferes with another, can be present in the chemical system (for example, initiated, catalytic and autocatalytic reactions, etc.).

A kinetic study of the chemical system where an interaction of reactions takes place, allows us to make a choice between various types of interfering chemical reactions on the basis of experimental data. Therefore, the study of chemical interference may be useful in an investigation of mechanisms of complex reactions.

In this respect, a determinant equation is an easily adaptable kinetic apparatus for solving complex chemical problems.

Thus, the determinant equation and a scale of chemical interference built on its basis make it easy to distinguish conjugate and coherent synchronous reactions from catalytic, initiated, free-radical reactions, autocatalytic and other reactions, which is practically difficult to do.

2. Chemical Interference-Intervention of One Reaction into Another

Simple and complex stoichiometric reactions with no interference are at the central position of the scheme (5) with $D = \nu$. Such complex reactions include parallel, sequential and parallel-sequential reactions. To the left of this position, when $D < \nu$, there are conjugate reactions that are part of coherently synchronized reactions.

With chemical induction, the secondary conjugate reaction can never be monomolecular. This is explained by the fact that the intermediate product of the primary reaction, being a reagent of the secondary reaction, is consumed in it, which naturally leads to a gross equation with participation of more than one component. The majority of biochemical oxidation processes is conjugate or

coherently synchronized catalytic (enzymatic) reactions. Therefore, it is very important to distinguish a catalyst from an inductor, because any error in this matter may lead to an incorrect interpretation of the chemical mechanism of reactions occurring in the biological system. For example, a catalyst of redox reactions is often taken as an inductor.

Is there a fundamental difference between conjugate and coherent-synchronized reactions? In fact, they are described by almost the same chemical equations, but with one distinctive feature. This feature is clearly shown in **Figure 1**. The conjugacy of synchronous reactions in this scheme is shown using an arrow indicating unilateral influence of the primary reaction on the secondary one. While in coherent-synchronized reactions, both reactions affect each other, which indicate the presence of feedback. It is the bilateral nature of interaction of synchronous reactions that is responsible for the interference pattern—the primary reaction accelerates the secondary one, which in turn slows the former one down. This coherent and dynamic chemical interference is uniquely described by consistent kinetic patterns of both reactions. The term inductor retains its universal meaning in both cases. Essentially, conjugate reactions are a reflection of coherently synchronized reactions in the forward direction and therefore they can be considered as a special case of coherently synchronized reactions with a simple mathematical apparatus (3) and (4).

It should be emphasized once again that an actor in the conjugate reactions is consumed as much as it participates at the stage of formation of an inducing intermediate (bifurcation center) in the primary reaction, which is distributed to the formation of final products of the primary and secondary reactions (bifurcation occurs) (**Figure 2**).

However, there is an unsuccessful attempt in the recent article [7] to prove that in the system of conjugate reactions elementary stages are actually interfaced. On the basis of this position, they reject one of the basic postulates of chemical kinetics about independence of elementary reactions.

According to Ostwald and Shilov [8], only the complex reactions can conjugate, and not the elementary stages that constitute mechanisms of the primary and secondary reactions. In the primary reaction, due to the elementary stage, a highly active intermediate particle is generated into the system, and then consumed through two channels (the primary and secondary reactions). This elementary

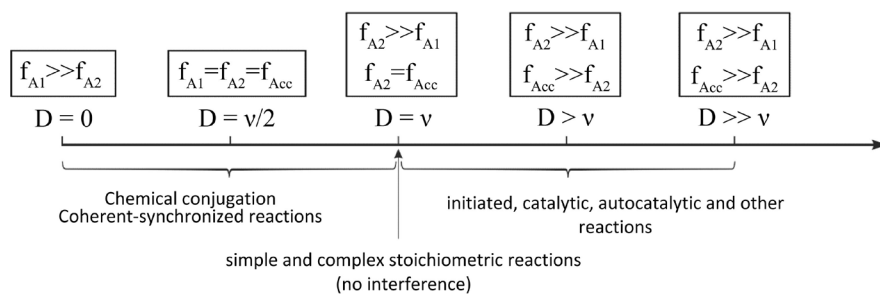


Figure 2. The scale of the determinant of chemical interference.

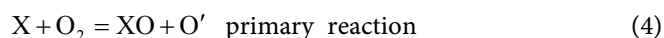
stage must necessarily be present in the stage mechanisms of both gross reactions. Hence, only complex reactions can have common highly active intermediate particles (intermediates) as centers of bifurcation; therefore, they can be conjugated according to Shilov, and not their elementary stages, as stated in [7].

A similar erroneous statement in [9] was expressed by Rakovsky A.V.: "... the phenomenon of the transfer of reactivity from one reaction to another is called chemical induction ... Obviously; in this case we are dealing with deviation from the principle of independence of reactions". However, in the textbook by Emanuel N.M. and Knorre D.G., p. 234 [10], the following idea is clearly and precisely expressed: "An elementary reaction cannot be induced by another reaction. This follows from the regulation on the independence of elementary reactions, according to which rate constants of an elementary reaction do not depend on whether other chemical processes occur simultaneously in the same system".

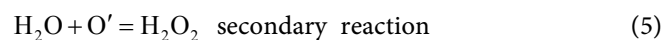
A common elementary stage in conjugate reactions cannot perform the function of a bifurcation center, only a highly active intermediate particle can.

Therefore, this is another reason why the statement about the conjugation of elementary stages, being a distortion of the concept of chemical conjugation itself, is not permissible.

The authors of [7] on p. 2016 gave the scheme and added the following "in the absence of the stage of product P2 formation from X, *i.e.* the primary reaction, an essence of the CP phenomenon with chemical induction is preserved". The reason why this is a completely erroneous statement is the following: if a highly active intermediate X is not a bifurcation center, *i.e.* subsequently it forms only the products of the secondary reaction. Thus, in the absence of the end products of the primary reaction a stoichiometric complex reaction with the determinant $D = \nu$ is observed in the reaction system. Only the presence of the final products of the primary reaction allows us to consider them as conjugate and their determinants are always $D < \nu$. All this is described in sufficient detail in the monographs [1] [4] [5]. At the time of writing of Shilov's book in 1905 [8], the nature of highly active intermediate compounds (free radicals, active complex compounds, forms of ions, etc.) were not known. Stable intermediate compounds of sequential reactions were often mistaken for intermediates. The reaction of water oxidation by oxygen to hydrogen peroxide (the secondary reaction), allegedly predicted by Shilov, was cited in [7], as an example. "Since the oxidation of H_2O to H_2O_2 cannot proceed arbitrarily and is accompanied by energy absorption, then, according to this theory, the H_2O_2 formation itself already represents the case of two conjugate processes with simultaneous flow where antozone is an intermediate product" [8]:



antozone



Reaction (6) and (7) are essentially sequential elementary reactions and anto-

zone is not a common intermediate particle (intermediate) and therefore these reactions cannot be conjugated in the conventional sense.

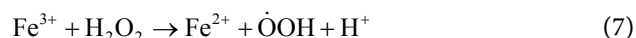
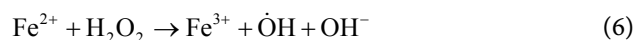
Further, according to Shilov [8], “Traube in 1884 received a patent for the production of H_2O_2 by introducing water into the flame, formed by burning CO , H_2 , water gas, etc.”

“... At the temperature below 900°C , H_2O_2 in equilibrium exists in trace amounts.”

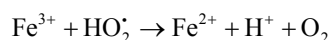
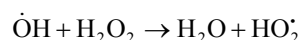
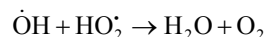
The scheme in [7] is absolutely incorrectly taken as the basis of their understanding of the theory of conjugate reactions, which is illustrated by the following statement: “A classic example of a process with chemical induction is the oxidation of benzene to phenol, which proceeds in conjunction with the oxidation of Fe^{2+} by hydrogen peroxide (Fenton’s system)”.

This reaction system is classical and is considered in many textbooks and monographs as a vivid example of conjugation of two gross reactions—oxidation of Fe^{2+} by hydrogen peroxide (Fenton reaction) and oxidation of benzene to phenol by hydrogen peroxide.

Fenton reaction: Ions of iron (II) in the liquid phase are oxidized by hydrogen peroxide to Fe (III) ions, which are later converted back to iron (II) affected by hydrogen peroxide [11]:



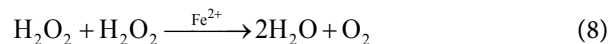
It follows from the reactions (8) and (9) that Fe^{2+} and Fe^{3+} ions are the catalysts for the decomposition of H_2O_2 with the formation of water and O_2 :



Thus, Fenton’s reagent generates hydroxyl radicals into the system. The Fe^{2+} ion is a catalyst for this reaction and cannot perform useful work in the system to induce and accelerate another secondary reaction associated with it (Shilov p. 10 [8]).

The function of highly active intermediate substance is performed by $\dot{\text{O}}\text{H}$ radical—a product of the primary reaction of H_2O_2 catalytic decomposition (see reaction 1). In this respect, the Fenton reaction is considered in the monograph (pp. 243-254 [4]) as a reaction inducing the secondary reaction.

Essentially, Fenton’s reagent in the system of conjugate reactions is associated with the formation of $\dot{\text{O}}\text{H}$ radicals in the reaction of H_2O_2 decomposition:

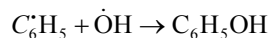
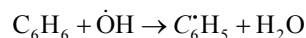
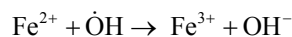
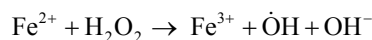


The first elementary reaction of a complex reaction (10) is a stage (8), where Fe^{2+} catalyst is oxidized to Fe^{3+} , and then Fe^{3+} is reduced (9) to Fe^{2+} , thereby closing the catalytic cycle. Naturally, this catalyst, like any other, cannot have an

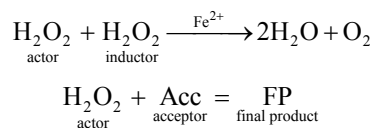
inducing effect (to be a power source for a secondary reaction). In addition, the elementary reaction (8) cannot cause and accelerate another elementary reaction of the secondary reaction, since this contradicts the basic principle of kinetics—the elementary reactions proceed independently from each other; otherwise, the rate constant of elementary reactions would always be a variable value.

Shilov (pp. 10-12 [8]) states: “... since the catalyst does not change during the process, it cannot serve as a power source and, therefore, does not change the driving force of the reaction. The catalyst, not being a power source, causes only those processes that can proceed arbitrarily at least with very little speed”. Thus, the catalyst can never be taken as an active intermediate substance. According to Shilov, “A general task in studying conjugate reactions is determining the nature of intermediate products that serve as a link between the primary and secondary reactions (p. 16 [8])”.

Let us consider an oxidation reaction of benzene with hydrogen peroxide in the Fenton system as a classic case. In the textbook on kinetics [10] as well as in [7], during the oxidation of benzene to phenol, in the presence of Fe^{2+} ions (Fenton’s reagent), oxidation of benzene to phenol and the oxidation of Fe^{2+} by hydrogen peroxide are considered as conjugating reactions:



It follows from this mechanism, that the oxidation of Fe^{2+} and C_6H_6 is carried out with the participation of a common intermediate— $\dot{\text{O}}\text{H}$ free radicals. $\dot{\text{O}}\text{H}$ free radical is a common intermediate, which is involved not only in this reaction, but also in many other oxidation reactions. Fe^{2+} ion is usually a catalyst for the decomposition of H_2O_2 and in the Fenton system it cannot perform useful work for the secondary reaction. Therefore, the oxidation of Fe^{2+} cannot be considered as a conjugating factor in the oxidation of benzene: a flow of the reaction of H_2O_2 decomposition to $\dot{\text{O}}\text{H}$ with the participation of the Fe^{2+} ion as a catalyst (Fenton Reagent) is necessary. The decomposition of H_2O_2 under the action of the catalyst Fe^{2+} to H_2O and O_2 (primary reaction) is conjugated with the secondary oxidation reaction of benzene with hydrogen peroxide. In this case, the free radical $\dot{\text{O}}\text{H}$ is a carrier of the inducing action of H_2O_2 (inductor) on the secondary reaction:

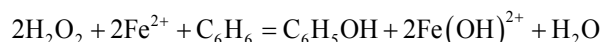


This scheme “describes a process of the chemical conjugation in the oxidation reactions with hydrogen peroxide not only in the gas phase, but also in the liquid phase” [1]-[6] as well as in the presence of various catalysts in both conjugate

reactions. Summing up these arguments, we see the fallacy of the statement in [7] that the oxidation reaction of benzene to phenol proceeds in conjunction with the oxidation of Fe^{2+} with hydrogen peroxide. Moreover, the catalyst can be neither an actor nor an inductor, since the inductor and the actor should be consumed during the reaction [8].

It is noted in [7] that the actor consumption in the conjugate reactions is determined by the stoichiometry and the number of products of the primary and secondary reactions, *i.e.* the material balance of the process, and not by how much of it is consumed in the primary reaction during the formation of the key intermediate X (p. 47 [4]). There is no denying the fact that the material balance of the process determines the flow rate of the actor and the inductor. Moreover, guided by this in [1]-[6], the conjugate reactions are considered in general form according to the scheme (2).

A role of intermediate X, which is common for conjugate reactions, is very clearly revealed in this scheme. The inductor is consumed in an amount that ensures consumption of A in both reactions. It clearly follows from the scheme (2): “how much actor is consumed in the primary reaction $\nu A + \text{In}$, which is the initial stage of X formation—the bifurcation center, where reaction 1 is responsible for the formation of the final products of the primary reaction and reaction 2 for the formation of the secondary reaction products”. In other words, the scheme (2) demonstrates a simple regulation that the actor is consumed exactly as much as it is necessary for the formation of X in primary reaction and this absolutely does not contradict the material balance. There is the following phrase in [7] “the reaction with H_2O_2 hinders the development of the chain process of H_2O_2 decomposition” that I was credited with, which is not found in the monograph [4]. Surprisingly, this phrase is given in brackets, thus it is difficult to figure out what is meant by the authors. Moreover, the use of dubious approaches for the approval of their own ideas leads authors [7] to the absurd. For example, “The final equation



which in fact, is the result of the addition of the twice-repeated first-stage reaction of Fenton and two stages involving benzene” is further stated in [8]. This final reaction includes a Fe^{2+} catalyst as a starting reagent. It follows that performing a useful work (free energy) it contributes to the formation of the final product of the secondary reaction—phenol. We have already discussed above that the catalyst cannot in principle be a power source and therefore the inclusion of the catalytic stage in the final gross equation of the secondary reaction is not correct.

The authors [7] consider that: “A conjugation of elementary stages through common intermediates as a universal phenomenon. Presence of common intermediates that ensure mutual influence and interconnection of rates and chemical affinity of successive adjacent stages of the mechanism, as well as the interrelation of the reactions of formation of various products (through different

routes), should be called kinetic conjugation”.

Concerning the validity of such statement, Shilov gives a rigorous explanation on pp. 1-2 [8]: “... the concept of conjugate processes is opposite to the well-known principle of coexistence of reactions, although it is possible that conjugation of reactions does not contradict this basic law of chemical dynamics, since the principle of coexistence means elementary reactions flowing without intermediate phases and in accordance with empirical equations; conjugation of reactions is possible only with complex processes that represent a sequence of individual reactions and lead to the formation of intermediate products”.

We have already expressed our attitude towards the term “conjugation of elementary reactions”, and as for the concept of “kinetic conjugation” proposed in [7], this expression in the context of the theory of conjugate reactions is meaningless.

The statement on p. 278 [7]: “Although a phenomenon of the kinetic conjugation in case of complex reactions is universal, only the stages having a common intermediate and included in a sequential chain of reactions have a positive effect on each other. The existence of a common intermediate in parallel reactions ...”. The concept of parallel reactions ultimately eliminates the presence of a common intermediate, and the presence of the latter is characteristic only of conjugate reactions.

Complex reactions can be in conjugation in the case when they have a common source substance-actor. However, this is a necessary but not sufficient condition. A sufficient condition is the presence of highly active intermediate common for these reactions. The combination of these two conditions fundamentally distinguishes conjugate processes from parallel and other complex reactions that have a common source substance.

Another expression from the same page: “The basic reaction (III) can proceed in parallel with the reaction (XVII) through a common intermediate”. Parallel reactions and the general intermediate reflect a continuous confusion that underlies the so-called “Kinetic conjugation”. There is a simple and clear trivial expression “kinetics of conjugate reactions” which does not allow such distortions in kinetic terminology.

“The sequential reactions (stages) mutually influence the flow rate of each other due to changes in the concentration of the common intermediate” (p. 281 [7]). Mutual influence of the successive stages through the “common intermediate” contradicts the concept of sequential reactions. The intermediate formed in the first elementary stage, as its final product, is the starting point for the second stage, etc. and their course obeys the principle of independence of the course of elementary stages.

The intermediate common for two conjugate reactions undoubtedly changes the mechanism of the secondary reaction and, naturally, this circumstance affects the kinetics and thermodynamics of the conjugated process [1]-[6].

Concerning the following expression on p. 281 [7] “... thermodynamic conjugation occurs in the case of simple parallel reactions”, it can be stated that simple

reactions take place in one elementary stage, and for this reason they cannot be conjugate, including simple parallel ones.

It is also stated on page 282 [7] that "... the kinetic conjugation of the stages is a characteristic feature of all complex reactions". According to the authors all known complex chemical reactions are conjugate, and their notion of "kinetic conjugation" leads to this false conclusion.

Their reasoning indicates that "The main feature of unbranched and branched chain processes is the kinetic conjugation of two or more routes ...", which leads to a complete confusion.

It is given on page 286 [7] that "... the flow of the parallel reactions, which do not have common with the main process reagents (parallel reactions always have one common reagent) and intermediates, does not make the endoergic process thermodynamically possible. It was shown above that interrelation of rates takes place only with the presence of common intermediates in sequential and parallel-sequential reactions (*i.e.*, with the presence of the kinetic conjugation)...".

We have already mentioned above that parallel, sequential, parallel-sequential, as well as conjugate reactions are completely independent kinetic concepts. They are considered within the framework of complex gross reactions and bringing them into one concept of "kinetic conjugation" is scientifically meaningless.

The authors [7] analyze another phrase from my book [1]: "For example, the first characteristic feature of conjugate reactions according to Nagiev ([4] p. 38) is as follows: '... the decrease in free energy in the primary reaction fully covers the increase in free energy in the secondary reaction.' As we have noted above, this situation is impossible in the classical scheme by Shilov, since the product of the primary reaction (I) P2 is not included in the final equation of the conjugate reaction."

However, according to Shilov ([8], p. 11) "... in view of the fact that an inducator enters a reaction that proceeds arbitrarily (the primary process) and undergoes chemical transformation, the free energy released by it can compensate for the formation of a substance that requires work input."

I.M. Emanuel and Knorre [9] stated in the textbook on chemical kinetics the following: "In order for the reaction to proceed with an increase in free energy, a source of power (free energy) is necessary. An inducing reaction can be such a source. The free energy released by an inducing reaction must be greater than the free energy absorbed by the induced reaction. The use of free energy released in chemical reactions for the implementation of other reactions associated with the first processes is crucial in biological systems".

The formulations given in [9], from a thermodynamic point of view, unambiguously indicate the fundamental role of "free energy released in the primary reaction to cover the free energy" of the endothermic reaction—so that the latter secondary reaction becomes spontaneous.

The main thesis of the authors against these formulations, including mine, is that "the product of the primary reaction is not included in the final equation of the conjugate reaction".

There is a complete misunderstanding in [7] of the fact that the highly active intermediate particle generated by the primary reaction, due to bifurcation, transforms the secondary thermodynamically obstructed reaction into a spontaneous one. At the same time, the stage mechanism of a complex secondary reaction always includes elementary reactions responsible for the formation of a common, highly active intermediate particle in the mechanism of the primary reaction. Thus, along with the common highly active particle, conjugate reactions have at least one common elementary reaction.

Interaction of reactions, as is known, occurs through a common highly reactive intermediate particle “or through the final product of a reaction, which is the catalyst of another reaction”. In the first case, in the framework of the theory of conjugate reactions, a non-spontaneous induced reaction is caused and amplified by an inducing spontaneous reaction through a highly active common intermediate, which, being consumed in the secondary reaction, transforms it into the category of spontaneous ones.

The second case relates to autocatalytic reactions, where the catalysis effect can enhance only a spontaneous reaction, while conjugation of reactions allows a non-spontaneous reaction to be carried out, due to the consumption of a highly active general intermediate synthesized in it by the primary reaction.

Thus, on page 286 [7] there are confused arguments on the following “in the presence of common intermediates in sequential or parallel-sequential, (*i.e.*, kinetic conjugation), a correlation of rates occurs ...”, which introduces formulations into chemical kinetics, that distort its basis.

Let us consider the mechanisms of sequential and parallel-sequential reactions, described in [7]:



where C, and D are the final products that can be isolated, *i.e.* quite stable compounds. Substance B is an intermediate stable product of sequential and parallel-sequential reactions, and not a highly active common intermediate, due to which the conjugation of reactions is carried out in the system.

If we assume that substance B in the reaction (12) is a highly active common intermediate, then it ceases to be parallel-sequential in the accepted sense, and becomes the stage of the conjugate primary reaction. In this case B is the link between the two conjugate gross reactions, and its bifurcation leads to the formation of the final products C and D. Thus there is no need to mention sequential and parallel-sequential reactions, as is done in [7].

Only gross reactions that have a common, highly active intermediate which is a bifurcation center that cannot be isolated from the reaction medium can be conjugated. We have already noted above that in order to form a new modified mechanism of the secondary reaction, elementary stages are taken from the mechanism of the primary reaction, leading to the formation of a common highly

active intermediate (bifurcation center) in the system. Because of the bifurcation mechanism, the initial form of the secondary reaction is transformed from a thermodynamically hindered reaction to a spontaneous one.

It is important to take into account the fact that common elementary stages of the primary and secondary reactions cannot functionally be a bifurcation center. The bifurcation center is their common intermediate, which is consumed in the subsequent stages of the conjugate reactions.

It is further stated in [7] that "... a decrease in free energy in the primary reaction fully covers the increase in free energy in the secondary reaction", this is impossible because the product of the primary (1)—P2 is not included in the final equation in the conjugate reaction (XVII). It is given in the textbook [12] and the monograph [13] that the joint occurrence of spontaneous ("conjugate", No. 2) and thermodynamically forbidden ("conjugate", No. 1) gross reactions, in the mechanism of which there is a common intermediate (or common intermediates), makes possible the flow of a thermodynamically forbidden process. Similar statements are given in [14] [15]. "These unsubstantiated statements (on the possibility of a situation arising when $A; R; <0$) apparently appeared for the first time in the monographs" [16] [17].

These considerations are summarized in [7] on page 287: "Thermodynamics of the primary exoergic reaction affects thermodynamic characteristics of the conjugate process only when a stoichiometric equation of the primary reaction fully enters a new final equation of the conjugate reaction along with an equation of the conjugate target reaction as a result of an occurrence of a chain of successive reactions".

In the first place, the primary reaction cannot fully enter the mechanism of the secondary reaction due to the fact that they are two independent gross reactions with their characteristic end products. Another thing is when the elementary stages of the primary reaction (see above) lead to the occasion when they participate in a transformation of a non-spontaneous secondary reaction into a spontaneous one with the help of the formed highly active intermediate substance (intermediate). Free energy of a chemical reaction is usually calculated from state of substances, in their initial and final states. Another way is when a stage mechanism of a complex reaction is known, wherein its free energy will be the sum of free energies of each elementary stage. This implies that the sum of the free energies of the elementary stages, which lead to the generation of a common highly active intermediate in the system, is added to the sum of the free energies of the subsequent stages, leading to the secondary reaction. Shilov, proceeding from the knowledge of his time (1905), justifiably believed that the free energy of the conjugating primary reaction should completely cover the free energy of the thermodynamically hindered secondary reaction. Based on today's knowledge, we see that both approaches lead to identical conclusions and the authors of [12] [13] quite rightly use Shilov's approach.

Thus, the final equation of the secondary reaction transformed into the spontaneous one should not include the final products of the primary reaction, as it is

not correctly suggested in [7].

However, since the common intermediate is consumed in the secondary reaction, it is natural that the common initial substance of both conjugated reactions as an actor is included in the gross equation of this reaction.

Kinetic definitions in textbooks and monographs related to simple and complex parallel, parallel-sequential and conjugate reactions relate only to gross reactions, but not to the elementary stages of the mechanism of a separate gross reaction. These kind of obvious kinetic ideas are ignored in [7], and, therefore, the authors propose a new concept of “conjugation of elementary stages through common intermediates as a universal phenomenon” which has no scientific basis. Elementary stages that are part of the mechanism of the two conjugated reactions, as noted above, cannot influence and interact with each other due to the fundamental principle of chemical kinetics about the independence of their flow. As it has been mentioned above, they enter into the mechanism of the conjugate gross reaction because of the general highly active intermediate (bifurcation center). The interaction of the reactions can only be considered at the level of gross reactions, which are characterized by the use of terms parallel, sequential, parallel-sequential and conjugate reactions.

Moreover, it is stated in [7] that: “The final catalytic reaction of $R \Leftrightarrow P$ does not proceed independently of the stages leading to it, which are



and



This two-stage mechanism involves kinetic conjugation of two stages through a common MR intermediate, however the final reaction does not conjugate anything”.

The authors' claim that stages (a) and (b) have a common intermediate substance MR is very doubtful: for the stage (a) MR is the final substance, and for the reaction (b) it is the starting substance. So the question is: where is the general intermediate substance in this mechanism? It makes sense to speak of a common highly active substance in conjugated reactions only when it forms the basis of its bifurcation (it is the bifurcation center) [4] [5].

It is given on p. 287 [7], ... a number of other statements in the manuscripts [12] [13] seem very strange: ... that the TDS phenomenon can be considered for parallel stoichiometric reactions, *i.e.* stationary gross reactions, each of which is characterized by a certain chemical affinity (p. 332 of [13]).

Parmon V.N. correctly took the approach regarding conjugate processes, that only gross reactions can be conjugated [13]. It is surprising, that the authors of [7], on the one hand are categorical, and on the other hand, they reproach the authors [14] [15] for not justifying their statements, while upholding their false perspectives about the conjugation of elementary stages.

It is stated on p. 287 of [7] that: “As for the ‘synchronous’ reactions, the ‘chemical interference’ and the ‘coherence of chemical interference’ [1] [4] [6], it

should be noted that these concepts have no relation to the features of conjugate reactions or to the effect of thermodynamic conjugation. Pseudo-scientific terminology only obscures reasonably clear kinetic effects”.

Synchronous reactions are nothing but simultaneous reactions and it is not quite clear why it is impossible to use this expression in this sense. The term “chemical interference” means that the primary reaction interferes with the flow of the secondary reaction and thereby conjugates with it. The authors’ reaction [7] to this appropriate analogy is quite surprising. If I had used the expression “conjugate intervention of one reaction into the flow of another” instead of “conjugate interfering reactions” the authors [7] would not supposedly react negatively. It has already been noted that interfering (*i.e.* interfering into the flow of each other) reactions can be conjugate, initiated, catalytic reactions, etc.

The expression “coherence of chemical interference” means the consistency of chemical intervention of one reaction into the flow of another, and there is nothing unclear about it.

While claiming that “these concepts have no relation to the features of the conjugate reactions or to the effect of thermodynamic conjugation”, the authors of [7] obviously did not understand obvious things and therefore we are not able to figure out their motive when they claim these quite clear terms as “pseudoscientific”.

Based solely on their false notions that “Conjugation of the primary and secondary reactions according to Shilov is the kinetic conjugation of the elementary stages ...” the authors deny a validity of the existence of “thermodynamic conjugation” in “conventional understanding”.

Summarizing all the above, we recall once again that simple reactions, due to their elementary nature, can never be conjugated, however much they are covered by “pseudoscientific terms” (as stated by the authors of [7]) such as “kinetic conjugation”, “conjugation of elementary reactions”, etc. Therefore, the statement on p. 282 [7] that “Kinetic conjugation of stages is a characteristic feature of all complex reactions” means only one thing: almost all complex chemical reactions known in nature are conjugate, and this contradicts the existence of a huge number of complex reactions outside of the system of conjugate reactions.

I consider it my duty to bring to the reader’s attention that in 1994 and in 2000 I published two articles [2] [3] purely devoted to conjugate reactions in the journal *Physical Chemistry*. In addition, in 1989 a monograph [1] was published in “Nauka” publishing house, the editor-in-chief of which was the famous physicist-chemist O.M. Poltorak. He wrote in his preface the following: “The theory of conjugate oxidation reactions also belongs to the parts of chemical kinetics, which, undoubtedly, need to be paid attention to at the present time. However, traditional branches of science almost never manage to be revived to life in their literal interpretation. They can acquire modern sound only with their creative modification, only with ‘dialectical return’ built on the use of new ideas and methods. It seems to me this is what exactly was done by famous Azerbaijani physicochemical doctor of chemical sciences T.M. Nagiev [16] [17] [18] [19].

His concept of the interference of chemical reactions is a natural generalization and a non-trivial development of N.A. Shilov's idea of conjugate oxidation reactions". Only scientific practice will show whether the new concept of "interference of chemical processes" will be viable or not.

3. Conclusions

The strategy associated with imparting high efficiency and orderliness to chemical interference has proved itself:

- 1) The primary reaction runs with almost 100% conversion in the absence of the secondary reaction;
- 2) It approaches 100% selectivity for both reactions.

The study of chemical interference and its particular case of conjugated processes indicate that it may represent a simple prototype for similar systems realizable in biochemical systems.

First of all, realization of chemical interference is associated with the selection of those reactions that are capable of self-organization, *i.e.* to formation of complex reaction ensemble. The ensemble of molecules and, as a consequence, the ensemble of reactions is able to interfere, because the aggregation of molecules in ensembles somehow creates an algorithm for the realization of mutually agreed spontaneous reactions. Contrary to free molecules, the distinctive feature of an ensemble of molecules is the fact that structural organization of an ensemble of molecules allows running of both simple and complex reactions, chemical interference of which is vitally important for the living system activity. In this discussion we would like to indicate that chemical interference is the necessary property of biochemical systems. Note also that molecular ensembles may be differently organized structurally and, therefore, the type of ensemble from the same molecules is responsible for proceeding of one type of interrelated reactions or another (*i.e.* chemically interfering reactions).

The ensemble of reactions is self-organized through the intermediary of general highly active substances. These processes may be accelerated and effectively implemented with the help of catalysts similar to processes, which take part in the living systems.

Thus, self-organization of an ensemble of reactions capable of being intensified or weakened and, therefore, inducing chemical interference, may be suggested as the basis for the principle of organization of many enzymatic ensembles.

Of great interest is the creation of trigger reaction ensembles, which will not only change the interference picture but also the type of interacting reaction with respect to the action of temperature, pressure, medium pH and other important factors.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

References

- [1] Nagiev, T.M. (1989) Chemical Conjugation. Nauka, 216.
- [2] Nagiev, T.M. (1994) Interrelated Reactions and Chemical Interference. *Russian Journal of Physical Chemistry*, **68**, 456-460.
- [3] Nagiev, T.M. (2000) Conjugated Chemical Reactions. *Russian Journal of Physical Chemistry*, **74**, 2034-2042.
- [4] Nagiev, T.M. (2001) Interaction of Synchronous Reactions in Chemistry and Biology. Baku, Sabail, 404.
- [5] Nagiev, T.M. (2007) Coherent Synchronized Oxidation Reactions by Hydrogen Peroxide. Elsevier, Amsterdam, 325.
- [6] Nagiev, T.M. (2015) The Theory of Coherent Synchronized Reactions: Chemical Interference Logics. *Materials Sciences and Application*, **6**, 152-170. <https://doi.org/10.4236/msa.2015.62019>
- [7] Bruk, L.G. and Temkin, O.N. (2016) Conjugate Reactions: New Potentials of an Old Idea. *Kinetics and Catalysis*, **57**, 277-296. <https://doi.org/10.1134/S0023158416030022>
- [8] Шилов, Н.А. (1905) О сопряженных реакциях окисления. М: Типография Мамонтова, 304.
- [9] Раковский, А.В. (1938) Введение в физическую химию. 683.
- [10] Эмануель, Н.М. and Кнорре, Д.Г. (1969) Курс химической кинетики. М: Высшаяшкола. С. 233-289.
- [11] Sara, G., Dan, M. and Gidon, C. (1993) The Fenton Reagents. *Free Radical Biology and Medicine*, **15**, 435-445. [https://doi.org/10.1016/0891-5849\(93\)90043-T](https://doi.org/10.1016/0891-5849(93)90043-T)
- [12] Бажин, Н.М., Иванченко, В.А. and Пармон, В.Н. (2004) Термодинамика для химиков. М: Химия, КолосС, с. 416.
- [13] Parmon, V.N. (2010) Thermodynamics of Non-Equilibrium Processes for Chemists with a Particular Application to Catalysis. Elsevier, Amsterdam, 321. <https://doi.org/10.1016/B978-0-444-53028-8.00001-0>
- [14] Prigogine, I. and Defay, R. (1954) Chemical Thermodynamics. Longmans, Green, 533.
- [15] Prigogine, I. and Condepudy, D. (2002) Current Thermodynamics. From Heat Engines to Dissipative Structures. Mir, Moscow.
- [16] Nagiev, T.M. (2019) New Approaches to Simulation of Enzymatic Reactions: Mimetic Catalysis. *Journal of Chemistry: Education Research and Practice*, **3**, 1-2. <https://doi.org/10.33140/JCERP.03.02.01>
- [17] Nagiev, T.M. (2015) The Theory of Coherent-Synchronized Reactions: Chemical Interference Logics. *International Journal of Chemical Engineering and Applications*, **6**, 293-305. <https://doi.org/10.7763/IJCEA.2015.V6.500>
- [18] Nasirova, U.V., Gasanova, L.M. and Nagiev, T.M. (2010) Monooxidation of Ethylene with Hydrogen Peroxide on the Per-F $TPhPF_6^{3+}OH/Al_2O_3$. *Russian Journal of Physical Chemistry A*, **84**, 941-945. <https://doi.org/10.1134/S0036024410060099>
- [19] Gasanova, L., Mustafaeva, C., Nagieva, I., Abbasov, A., Magerramov, A., Ternier, J. and Nagiev, T. (2005) Selective Biomimetic Oxidation of Ethanol by Hydrogen Peroxide on Immobilized Ironporphyrincatalysts. *Russian Journal of Physical Chemistry A*, **79**, 382-388.