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Resonance Interaction of the Protein Fragment of the Viral Capsid and the RNA Fragment in the Body Cell

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Abstract—Collaboration of scientists from different countries is a crucial tool for the development of science. Today's pandemic initiates the integration of the ideas of scientists around the world to study and combat the aggressive pathogen COVID-19. Under current circumstances, we are losing informal communication as one of the essential aspects of scientific progress. This situation seriously changes the paradigm of the development of scientific thought, reducing communication to formal things. Scientific discoveries occur just when thought goes beyond the framework. Thus, the pandemic poses a comprehensive threat to society. To date, the uncontrolled situation of the pandemic is associated with a multifaceted behavioral factor of the virus. The virus acts differently on different continents of the planet and within the same geographical area, which makes its symptoms somewhat arbitrary. This pushes to an entirely new, information-wave level of understanding of the virus. The penetration of virions into the cell is the transfer of information, in this case, foreign to it and damaging. The interaction of the "virtual signal" with the "information receiver" is evident, and the virion itself is considered a virtual genetic signal, which becomes real only when received by a cell with an adequate code. The nature of the information contained in viruses is essential for determining the formation of diseases. These may be purely functional disorders, inflammatory (regardless of their location), or other processes. All of the above is determined based on the vibration frequencies of the virus–organism system. Viruses, like other biological objects, are characterized by both systemic biological properties and purely physical ones. If we consider the human body from the standpoint of physical properties, there is no division between the body's internal environment and the external one. There is a single environment engulfed in cyclic, oscillatory processes, the characteristics of which are the same everywhere: in a person, in the movement of planets, on the Sun, and in interplanetary space. Throughout evolutionary history, both the virus and the organism are formed based on mutual environmental fluctuations. The formation of a specific oscillatory system, based on general physical considerations, ends when the oscillations of all system components are coordinated with each other. Thus, having information about the vibration frequencies of viral fragments, we can artificially select such a protein, the vibration frequency of which corresponds to the rhythm of the virus fragment. Such a protein could bind to the virus, preventing it from infecting healthy cells.

Keywords: RNA, virion fragment, vibration frequency

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INTRODUCTION

The coronavirus pandemic has made millions of people think about what science knows about the world of viruses, whether it can protect people, predict or prevent the next virus attack. The reproduction of viruses, especially RNA viruses, leads to the appearance of many mutations in their genomes, that is, errors in copying a nucleotide chain. First, this is explained by the low impact accuracy of viral RNA polymerases, the enzymes that synthesize daughter molecules on the genomic RNA matrix. Due to the inaccuracy of copying, the populations of such viruses are genetically heterogeneous. Some of the mutations that arise can drastically weaken the viability of viruses or even be deadly, but the population usually retains its main properties. Here natural selection occurs: carriers of harmful traits are less likely to survive or transmit these traits when copied. The stability of genomes is such that the populations remain almost identical even for viruses that have appeared over 30 years in different countries. The coexistence of viruses with diverse genomes helps a population survive if conditions change dramatically: with such a change (for example, when immunity is developed or a person begins to take antiviral drugs), viruses that accidentally already have the desired properties obtained by genetic errors survive. However, when viruses spread

within an organism or between organisms, they often encounter various barriers that single viral particles can overcome. By chance, these may be mutants with reduced viability. Paradoxically, their viability can be restored precisely due to the inaccuracy of copying, which creates, among others, favorable mutations. The virus has two ways to restore viability. One is to “fix” the damaged element, and another is to change another functional section to compensate for damage. In both cases, either this “correction” restores the main biological properties of the original viral population, or a new type of virus appears.

In addition to mutations, other changes, for example, reassortment (mixing of genome segments of different viruses) and recombination, may occur. Reassortment and recombination lead to abrupt rather than smooth changes in the biological properties of the virus. This variability is one of the critical factors in their ability to escape from human immunity. However, the mechanism of such changes is not fully known, nor the mechanism of virus mutation is fully understood. Therefore, the study of these issues from the standpoint of quantum chemistry is especially relevant today.

This work aims to study the frequency characteristics of the viral protein capsid fragment and the host RNA fragment.

METHOD OF CALCULATION

The studies were carried out within the framework of quantum chemical calculations using a wide range of quantum chemical programs [1]. Fragments of the RNA nucleotide sequences of the cell of the organism (host) and the protein capsid envelope of the virus were used as objects of research. To obtain the values of the vibrational characteristics, we first calculated the matrices of the second derivatives of the energy with respect to the coordinates of the atoms (matrices of force constants) of the n -atomic system, followed by diagonalization. The eigenvalues, considering the atomic masses, make it possible to obtain $3n-6$ frequencies of the system. First, we optimized the geometric characteristics with a search for the minima of the total energies of the system and then, for the found equilibrium configuration, calculated the oscillations taking into account the intrinsic angular momentum of the atomic nucleus.

RESULTS AND DISCUSSION

We studied a possible change in the isotopic composition of water and, consequently, its fundamental nature, and viruses, including COVID-19, were the instrument of adaptation of the body to such changes [2].

In this work, we continued to study the interaction of the protein fragment of the viral capsid and the RNA fragment of the body cell.

The coronavirus, entering the body, attaches to the angiotensin receptor on the cell surface and promotes the synthesis of angiotensin-converting enzyme 2, penetrating the cell with the help of this molecule. Angiotensin-converting enzyme 2 (ACE2, EC 3.4.17.23) is a membrane protein, exopeptidase, a zinc-containing metalloenzyme that catalyzes the process of reversible hydration of CO_2 , for example, by the “zinc–water” mechanism [3]:

ACE2 has an affinity for S-glycoproteins of some coronaviruses, including SARS-CoV [4] and SARS-CoV-2 viruses, and is thus the point of entry of the virus into the cell [5–7].

Figure 1 shows a fragment of the complementary region of RNA with adenine complementary to uracil and guanine complementary to cytosine. The longer the complementary regions on the RNA, the stronger the structure formed; conversely, the short regions are unstable. This determines the function of a particular RNA and the interaction of the RNA fragments and the virus.

The analysis of the charge characteristics of the studied objects suggests that there is no charge transfer between the RNA and the viral particle, given an insignificant redistribution within the structural components of the system (Table 1). However, the virus distorts RNA, while the entropy, frequency, and total energy of the viral particle–RNA system increase, and the system’s enthalpy is lower than for the RNA fragment (Table 2).

Human susceptibility to the particularly relevant SARS-CoV-2 virus is determined by the ability of the virus itself to resist the host’s immune system, which is affected by both collective and individual factors. Geographic (temperature, humidity, radiation) and ethnogenetic factors and the nature of national vaccine prevention programs, which form the collective immunity of the population in the state, have the most significant effect. On an individual basis, the susceptibility primarily depends on age and the state of

Fig. 1. Structure of (a) a complementary RNA region and (b) fragments of viral envelopes; international amino acid codes: (*I*) isoleucine, (*L*) leucine, (*S*) serine, and (*V*) valine.

the immune system, determined by the number and composition of vaccinations passed, infections, and chronic diseases. These factors include the effect of free radicals (FRs) on the immune system.

We have carried out a quantum-chemical simulation of the effect of free radicals on the RNA fragment of the host cell. We selected a hydroxyl radical as an example, which can be formed by the radiolysis of water in the Haber–Weiss reaction and by the Fenton reaction between the ferrous ion and hydrogen peroxide, that is,

The hydroxyl radical is relatively active and has a destructive effect on RNA. Calculations have shown that the free radical increases vibration frequencies; for example, the asymmetric valence frequency of N–H bond vibrations in the structural component of RNA, alanine, increases by 38.02 cm^{-1} compared to the RNA fragment without free radical and by 62.92 cm^{-1} under additional action of a fragment of the viral envelope. In the RNA–virus–free radical system, the entropy sharply increases (Table 2). The radical

Table 1. Charge at C, H, O, and N atoms in the studied systems

Affiliation of atoms to the system	Atom	System		
		isolated viral particle	isolated RNA fragment	molecular fragment RNA–viral particle
		a.m.u		
Isolated viral particle	H	0.127	—	0.134
	C	−0.057	—	−0.076
	O	−0.396	—	−0.424
	N	−0.504	—	−0.486
Isolated RNA fragment	H	—	0.287	0.286
	C	—	0.394	0.377
	O	—	−0.456	−0.486
	N	—	−0.214	−0.271

Table 2. Energy characteristics and vibration frequency of the studied objects

Parameter	System			
	RNA fragment	viral particle–RNA	RNA fragment and FR	viral particle–RNA and FR
$F, \nu(\text{as}), \text{cm}^{-1}$	3937.02	3959.10	3975.04	3999.97
$S, \text{kJ/mol}$	857.344	993.09	337.360	1110.718
$H, \text{kJ/mol}$	1144.320	1475.143	221.520	1495.22
$\Delta E_a, \text{kJ/mol}$	—	25.814	—	8.365

decreases the energy barrier of the reaction of the addition of the virus to the RNA; this once again emphasizes the discovered resonant principle of the interaction of the virus with the RNA of the organism.

Each virus has an individual set of mechanisms for “overcoming” the host’s immune system. Along with the products of transcription and replication of the viral genome or viral proteins, acting as triggers of pathological reactions in the body, free radicals actively disorganizing the immune system (the body’s regulatory system) can also respond to emerging external and internal stimuli.

The molecular electrostatic potential (MEP) distribution in the RNA fragment and free radical $\text{OH}^\bullet$ are presented in Fig. 2. The free radical attacks sites with the negative MEP in the RNA. The region of positive MEP is localized around the hydrogen atom in $\text{OH}^\bullet$.

The transmission of the virus by airborne droplets and its preservation in the environment are impossible without resistance to such factors as humidity, temperature, and radiation. The stability of the virus, in turn, is determined mainly by the characteristics of the structural proteins of virions, for example, by the peculiarities of their amino acid composition. Therefore, the study of the role of the isotopic effects of hydrogen and oxygen in the resistance and contagiousness of the virus is of current interest. As expected, the replacement of one protium in a fragment of the viral envelope with deuterium leads to a sharp decrease in the vibration frequencies of the virus, and further replacement of deuterium with tritium leads to a less dramatic effect of a decrease in the vibration frequencies (Fig. 3). For example, the asymmetric stretching frequency of N–H vibrations decreased from 3847.2 to 3775.01 cm^{-1} with partial substitution of H for D and to 3744.07 with a subsequent substitution of D for T; with the partial replacement of ^{16}O with ^{17}O , the asymmetric stretching frequency of N–H vibrations decreased from 3847.2 to 3805.01 cm^{-1} , and with the replacement of ^{17}O with ^{18}O , it dropped to 3794.07 cm^{-1} .

Thus, the results of this work are a logical continuation of the previous study [2] and focus on frequency resonance as a tool to control some physicochemical processes. Considering the results, we put forward

Fig. 2. Distribution of electrostatic potential in the complementary region of RNA and FR.

Fig. 3. Stretching asymmetric frequency of vibrations of the N–H bond in the virus fragment; isotopes of (1) hydrogen and (2) oxygen.

the following hypothesis. Back in 1872, Eduard Friedrich Wilhelm Pflüger, the famous German physiologist, wrote: “The main secret of the regulation of the amount of oxygen consumed by the body is that this amount is determined only by the cell itself. The oxygen concentration in arterial blood, pressure in the aorta, blood flow rate, and the type of respiration are all secondary and subordinate to one goal: maintenance of cells.”

Far ahead of his time, the scientist formulated the main task of blood circulation: the delivery of oxygen in an amount corresponding to the needs of the final recipients, cells. Under normal conditions, oxygen delivery consistently exceeds oxygen consumption. However, under certain conditions, for example, the destabilizing effect of the virus on the body, oxygen delivery is not balanced and does not correspond to the real needs of internal respiration. Oxygen consumption can be impaired since cells cannot extract oxygen from the blood even with adequate microcirculation. Under critical conditions, the need for O₂ can exceed its consumption, which is accompanied by tissue hypoxia. Upon intensive care, efforts are always aimed at optimizing the delivery of oxygen to organs and tissues. Until now, scientists have not paid attention to the frequency factor of this process. In our opinion, based on the result of the possible replacement of ¹⁶O by ¹⁷O in water, virus, and cell (especially that obtained in [2]), the conditions for the balance of consumption and tissue demand for oxygen may change. This issue is not a matter of one day, and the estimation of the frequencies of intermolecular oscillations of oxygen in its isotopic diversity with cell fragments and the study of the resonance conditions between the delivery and demand for O₂ reveal the presence of a balance or imbalance between oxygen and the cell.

CONCLUSIONS

Thus, isotopologues of the virus with an increase in molecular weight (that is, the number of neutrons) demonstrate a decrease in vibration frequencies and a symmetrical decrease in the N–H binding energy from 0.453 to 0.447 kJ/mol when replacing H for D and to 0.453 kJ/mol when replacing ¹⁶O for ¹⁸O. Hence, the virus can lower its resistance and contagiousness when conditions are created for changing the isotopic composition of the virus, at least within the framework of our calculations.

Calculations suggest that the structure of the viral envelope that has entered the body is associated with the characteristics of the host cell RNA by a resonance mechanism.

Indeed, we are far from predicting the cessation of the coronavirus pandemic and ways to accelerate this process. Although it is still too early to summarize since this work is only the beginning of the study, we can assume (provided that the sum of the obtained microeffects is greater than the sum of the macroeffects of the virus on the body) that the virus can enter the host cell, if the frequency resonance of the viral capsid and the components of the body cell is fulfilled, and the presence of free radicals in the body can serve as a catalyst for this process. Changes in its isotopic composition can regulate the resistance and contagiousness of the virus.

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