

Vibrational Spectroscopy of Pathogens and Concept of Resonance Therapy

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Abstract

The possibility of vibration always exists wherever there is periodic and repeated movement of a particle about a position of equilibrium or balance. This process is also natural for nanosized bioparticles of enveloped, positive-strand RNA viruses which infect amphibians, birds, and mammals and now known as coronaviruses. Coronaviruses are important human and animal pathogens. In late 2019, the new coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in China's Hubei province. It spread quickly, leading to an epidemic across China, followed by an increase in cases in other countries around the world. This study aimed to explore nanobiospectroscopy research and technology in order to provide a theoretical, computer modelling and experimental basis for development of methods and tools of identification of characteristic vibrational frequency of viruses and then their resonance therapy.

Keywords: Pathogens; Vibrational Spectroscopy; Resonance Therapy

Abbreviations: EM: Electromagnetic

Introduction

Bioparticles, like other biological objects, are characterized not only by systemic biological properties, but also purely physical. Physical parameters can be include their mass, speed of movement, mechanical, electrical, magnetic energy, etc. Since the bioobjects like viruses travel much less than the speed of light, are small in size and mass, vibrate with a certain frequency relative to a fixed coordinate system, and then it is possible to use as a model a Schrödinger equation.

$$i\hbar \frac{\partial \psi}{\partial t} = -\frac{\hbar^2}{2m} \Delta \psi + V(x,y,z)\psi ,$$

Where

$$\Delta = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}$$

is Laplace operator in xyz coordinates, t – time, m – mass, $\psi(x,y,z)$ psi function. P probability = $\alpha|\psi|^2$ the probability of finding a virus at a point with coordinates (xyz) at time t.

This model makes it possible to assert that a nano size object is located not only inside a living

cell, but at any distance from it. Moreover, the nano bio-object, particularly virus itself, as a physical object, simultaneously possesses both corpuscular and wave properties [1,2].

Using the wave properties of the virus, we can consider the models of information transfer, scattering and diffraction on other physical objects, including the elements of a living cell. Using the elements of quantum mechanics, We can determine some of the wave characteristics of the viruses.

Following the simple estimations of de Broglie wavelength fits into the linear size of the virus. Evaluation of other viruses using this calculation method gives similar results, which makes it possible to assume that the wave properties of viruses are closely related to their geometry.

Thus, apparently, it is possible to use purely wave terms and diffraction methods of calculation for a more complete study of the vital processes of viruses both inside a living cell and outside it.

We assume that by integrating into the genetic apparatus, causing the formation of genetic defects, viruses change the process of formation and functional activity of cells, which results in the development of various diseases in living organisms.

In comparison with cellular molecules (nano-ensembles) the size of viruses varies from 20 to 300 nanometers. Practically all viruses by the sizes are smaller, than bacteria. However, the largest viruses, for example a virus of cow smallpox, have the same sizes, as well as the smallest bacteria (hlamidiya and rikketsiya) who too are obligate parasites and breed only in living cells [3]. Therefore, as distinctive features of viruses in comparison with other microscopic causative agents of infections the sizes or obligatory parasitism, and features of a structure and unique mechanisms of replication (reproduction

themselves) serve not. Viruses are masterpieces of nanoengineering with a basic common architecture that consists of the capsid – a protein shell made up of repeating protein subunits- which packs within it the viral genome Nano-sized biological agents and pathogens such as viruses are known to be responsible for a wide variety of diseases such as flu, AIDS and herpes, and have been used as bioreagents.

Coronaviruses belong to the subfamily Coronavirinae in the family of Coronaviridae and the genome of CoVs is a single-stranded positive-sense RNA which is larger than any other RNA viruses [4]. The nucleocapsid protein (N) formed the capsid outside the genome and the genome is further packed by an envelope which is associated with three structural proteins: membrane protein, spike protein and envelope protein. As a member of coronavirus family, the genome size of SARS-CoV-2 which was sequenced recently is approximately 29.9 kb [5]. SARS-CoV-2 contains four structural proteins (S, E, M, and N) and sixteen non-structural proteins (nsp1–16) [6]. By studying the physical characteristics of the SARS-CoV-2 virus, which are still poorly understood, it was found that it may be vulnerable to ultrasonic vibrations at frequencies that are used in medical diagnostics [7]. The virus envelope quickly degrades at frequencies of 25 and 50 MHz, both in water and air.

A team of researchers from Massachusetts Institute of Technology conducted computer simulations of the new coronavirus and its mechanical responses to vibration based on solid state physics and limited information gathered about the structure of the virus [7]. Since its exact characteristics are not known, the scientists first modelled the behaviour of the sample with different elastic parameters for the shell and for the spikes (Figure 1).

Natural fluctuations in the virus were almost imperceptible. But after a fraction of a millisecond, external vibrations, resonating with the frequency of the natural vibrations of the virus, led to the formation of a dent in the shell, like when a ball hits the ground.

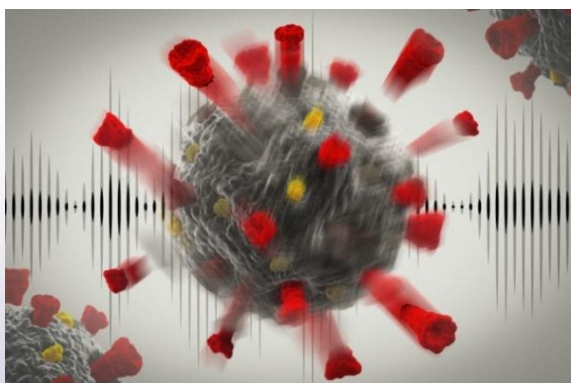


Figure 1: Ultrasound has potential to damage coronaviruses.

Credits: Image MIT News, with images from iStockphoto

When the vibration amplitude increased, the coronavirus cracked. At lower frequencies of 25 or 50 MHz, this happened even faster, both in water and air. These frequencies and intensity of vibrations are within the capabilities of medical diagnostic devices [8].

Results of Theoretical and Experimental Investigations

Study of physical properties of viruses, their scattering and absorption characteristics, estimation of electromagnetic (EM) spectrum and resonance wave length ranges are important for determination of biostructures unique spectral signatures, so essential in bio-agents detecting and identification systems. Investigation of EM field distribution makes possible to have insight vision of the nanoparticles. Behavior of nano sized pathogenic microorganisms

such as viruses, is selectively sensitive toward the electromagnetic (EM) field excitation. Elaboration of physical models of bioparticles, as well as computer simulation study of near and far EM field distribution in the areas of particles and surrounded medium is a correct way for investigation of physical properties of bio-particles of different morphology.

Method of estimation of spectral response on EM field & particle interaction is based on solutions of electrodynamics two (2D) or three (3D) dimensional boundary tasks [9]. Obtained analytical expressions of EM fields are derived from rigorous solutions of Maxwell's and Helmholtz's equations and defined through the dimensionless parameters, diameters (d) over excitation wave-length (λ). Proposed method was used for investigation of viral particle's physical properties. EM near and far fields distribution, EM spectrum are proposed for viruses, having rod-like, prolate un-enveloped virions (e.g. Tobacco Mosaic Virus (TMV), bacteriophage M13). Virions, the extracellular infective forms of viruses are modelled by the particles of cylindrical shape of different structures, such as homogeneous dielectric particles and inhomogeneous through the radius, also particles of core-shell structure reflecting the properties of ribonucleic acids (DNA or RNA) of viruses and capsid's proteins. Shape, structure and the set of geometrical, magnetic and electrical characteristics are the main parameters defining the particles' EM spectral properties. Advantage of simulation study of complex molecular systems such as virions in contrast of measuring experiments associated with weak signals detection is significant.

Computer simulation (based on MatLabR2013b software) was carried out for TMV particles characterization. Parameters of TMV particle are obtained from scientific publications based on different measuring technics [10]. Two

models are used for simulation study of TMV virion: homogeneous and core-shell structured cylinders. Computer simulation shows that expected resonant spectral response is observable on far-field ($r \gg (2d_2)/\lambda$) characteristics, resonant vibrational frequencies of whole TMV particle may be associated to scattering cross section maximums.

Experimental studies of vibrational parameters of bioobjects were performed by methods of vibrational spectroscopy e.g. Infrared, Ultraviolet, High Resolution Ultrasonic and Raman spectroscopies and Sum Frequency Generation as well [11].

Characteristic group frequencies allow the application of vibrational spectroscopy for structure elucidation. The sensitivity of the vibrational modes for changes in their chemical environment make the different vibrational spectroscopic techniques well suited and widely used analytical techniques.

There are two vibrational spectroscopic techniques (and their variations) to probe the molecular vibrations: IR absorption spectroscopy where the vibrational transitions are directly excited and Raman spectroscopy where the vibrational transitions are probed via an inelastic scattering process.

Molecular vibrations can be excited with radiation in the infrared (IR). If the incident electromagnetic (IR) radiation matches a vibrational transition which involves a change in the electromagnetic dipole moment of the molecule, the molecule gets excited into a higher vibrational level and photons of the matching electromagnetic frequency get absorbed from the incident radiation (Figure 2).

That means a strong change in the electromagnetic transition dipole causes high IR

absorption intensity. This is e.g. observed for polar groups such as carbonyl, nitrosyl and hydroxyl groups. Non-polar groups, such as homonuclear diatomic molecules are IR inactive. Each vibrational transition is accompanied by a change in the state of rotation of the molecule. Therefore, the IR absorption spectrum represents a rotational-vibration spectrum.

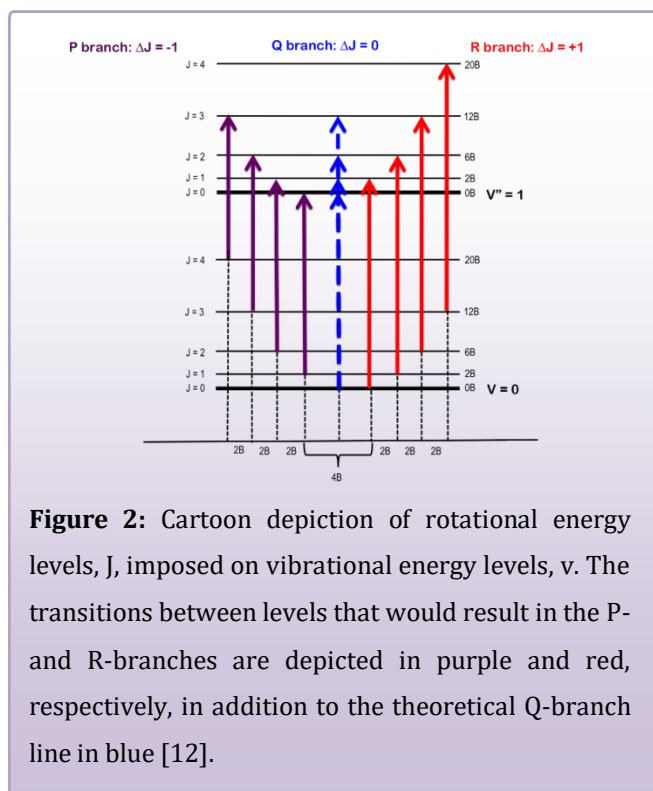
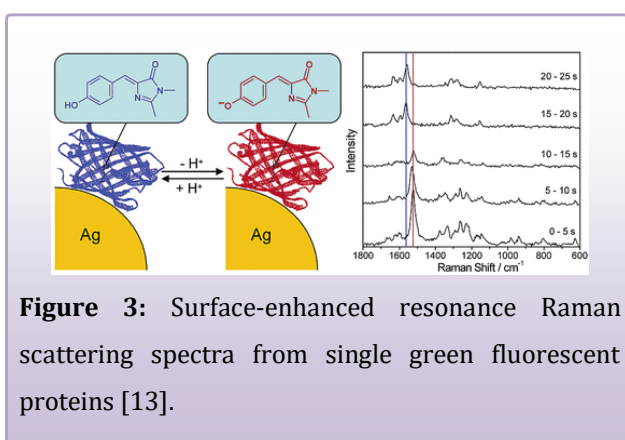


Figure 2: Cartoon depiction of rotational energy levels, J , imposed on vibrational energy levels, v . The transitions between levels that would result in the P- and R-branches are depicted in purple and red, respectively, in addition to the theoretical Q-branch line in blue [12].

Another possibility to obtain high quality Raman spectra bioobjects in solution at low concentration of the substances is resonance Raman spectroscopy. Due to the coupling of the Raman signal to the electronic absorption high selectivity and sensitivity is obtained and it is possible to record Raman spectra at physiological low concentrations with a good signal-to-noise ratio.

Due to the selective enhancement of the vibrations coupled to the electronic transition (in this case the vibrations of the aromatic ring) changes of the relative intensities of several bands are observed in the resonance Raman spectrum [13].

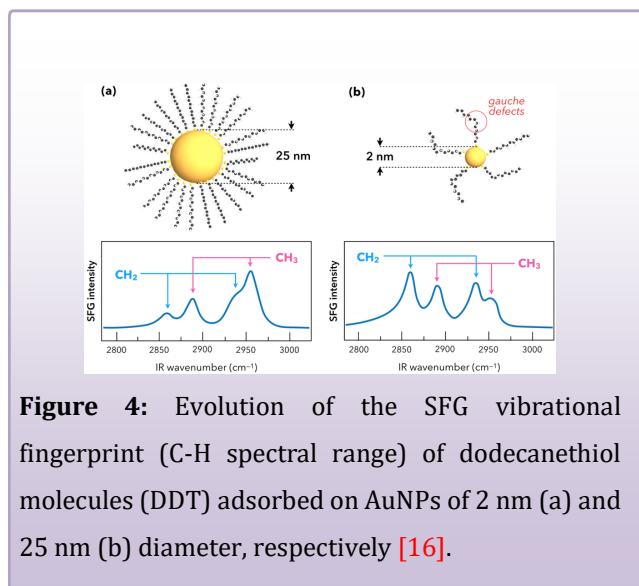
The vibrational mode most enhanced is the C=C stretching vibration and the ring deformation vibration around 1620 cm^{-1} . As the enhancement results from a coupling of the vibrational modes (most of the time totally symmetric vibrational modes) to an electronically excited state it is possible to exclusively select vibrational modes by choosing an appropriate wavelength (Figure 3). The off-resonance Raman spectrum excited at 532 nm shows a very complex vibrational structure, since all Raman active vibrations contribute to this spectrum.



The special attention was paid to nonlinear Two-Color Sum-Frequency Generation Spectroscopy (2C-SFG) that meets the desired spectroscopic requirements [14].

The goal of this approach is to probe membrane models of various forms and in various environments: (i) lipid monolayers and bilayers; (ii) deposited on substrates, floating on water as Langmuir layers and at a liquid-liquid interface; (iii) alone and in interaction with molecules, including peptides and proteins; (iv) submitted to controlled stress (chemical, pH, electrochemical potential). Configuration of SFG experiment in case of thin solid films like a ligand-conjugated CdTe QDs might be described by following main actions: its deposition on a CaF_2 prism and probed by 2C-SFG spectroscopy. The visible, IR and SFG beams belong to the incidence plane (y, z), like their respective

polarizations as their frequency is ω_{vis} , excites NCs by creating confined electron-hole pairs (e^- , h^+) called excitons, while the IR beam, at frequency ω_{IR} , excites vibration modes of their ligands [15]. The SFG beam is generated as a combination of both, and as a signature of the NC/ligand vibroelectronic coupling. Evolution of the SFG vibrational fingerprint is shown on the Figure 4.



We are thinking that biological viruses, have an ability to play at the same time the role of information carriers (information-wave viruses). They should contain encoded information about the object of which they are informational expressions. Each information-wave virus has its own digital code.

Viruses, invading the field envelope of a person, can actively interact with the cells of the body (organs). It is logical to assume that there is a resonant interaction of the wave structure of viruses with those parts of the human genetic apparatus where there are biological chains of viruses.

Our studies aimed to explore nanobiospectroscopy research and technology in the field of virology in order to provide a theoretical, computer modeling and experimental support for

the techniques used, and to suggest the applying tools that have not been used previously [17].

Viruses are assembled in the infected host cells of human, animals, or plants. Because of viral breeding the, host cell dies. There are especially viruses which are breeding in the cell of the bacteria. Viruses spread in many different ways. Just as many viruses are very specific as to which host species or tissue they attack, each species of virus relies on a particular propagation way [18].

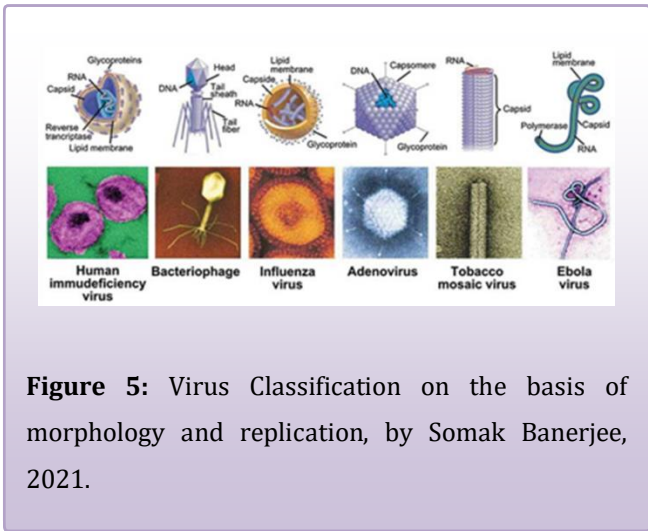


Figure 5: Virus Classification on the basis of morphology and replication, by Somak Banerjee, 2021.

The interdisciplinary collaboration (Biomedicine and Biophysics, Physical Research, Information Technologies and Systems) is an engine of strengthen the abilities of researchers in development of new biophysical and biomedical methods and tools. Those works which are based on novel achievements in optical spectrometry, laser and molecular physics as well as information technologies and systems are critically important for study of common properties of nano-scale virus-like particles, and elaboration of basic concepts and new revolutionary method for estimation unique vibration/oscillation properties, determine the unique “fingerprints” of pathogenic micro-organisms, especially viruses Figure 6.

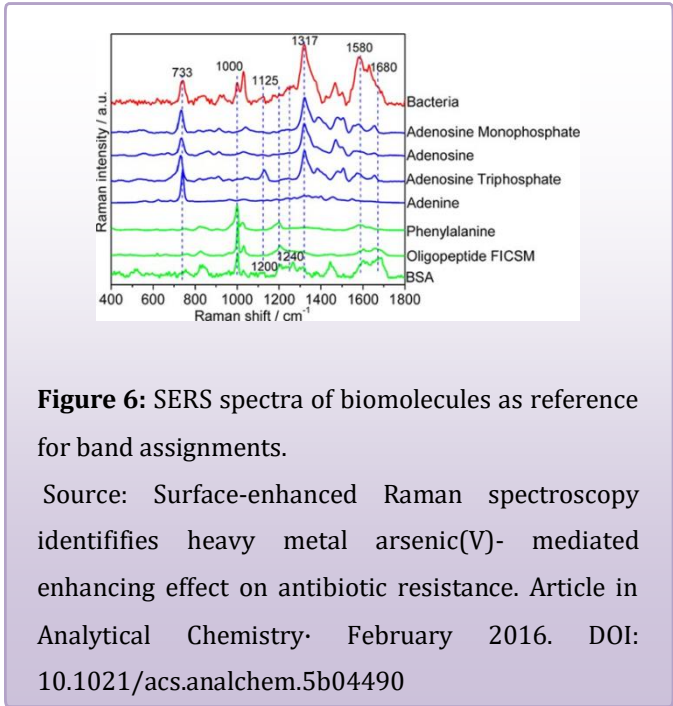


Figure 6: SERS spectra of biomolecules as reference for band assignments.

Source: Surface-enhanced Raman spectroscopy identifies heavy metal arsenic(V)- mediated enhancing effect on antibiotic resistance. Article in Analytical Chemistry· February 2016. DOI: 10.1021/acs.analchem.5b04490

During the past two decades methods of vibrational spectroscopy have become valuable tools for the study of structural properties and dynamical processes of proteins and particularly of chromoproteins (for a review see e.g. Such spectra generally exhibit a rich and complex structure and, in the range above 800 cm⁻¹, contain a wealth of information about local bonding structures in a coded fashion (Figure 7) [19].

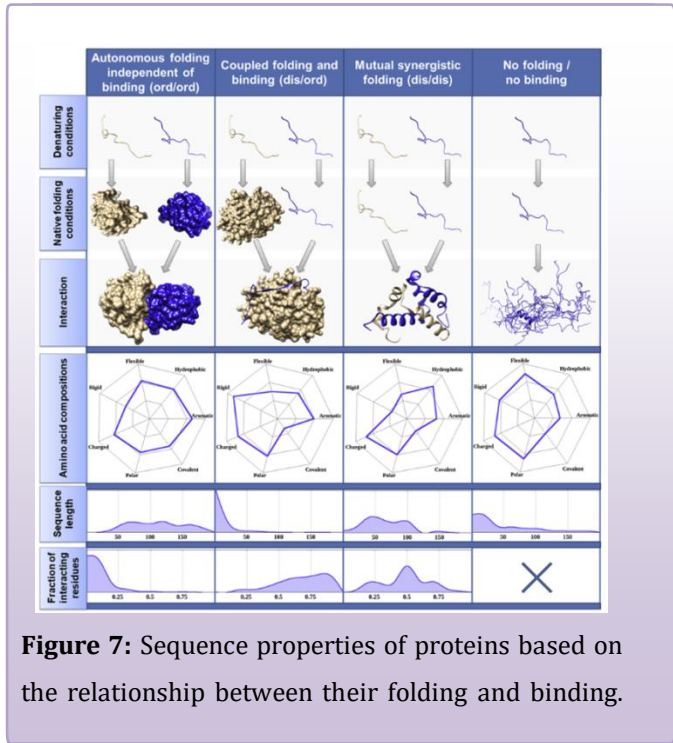


Figure 7: Sequence properties of proteins based on the relationship between their folding and binding.

Columns mark the four basic ways a protein can reach a structured state.

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Farther development of new methods of pathogens treatment is greatly facilitated by an improved understanding of epidemic diseases. There is therefore a need to address the current knowledge gaps in disease aetiology in order to support innovation in evidence-based therapy. In this context, a better understanding of the mechanisms that are common to several diseases, in particular of those leading to co-morbidities, constitutes an important challenge. Performing activities should assess and validate the relevance of these common mechanisms and of their biomarkers (where relevant) on the development of co-morbidities in both males and females. The expected impact should provide: A better understanding of disease pathways and / or mechanisms common to a number of diseases; new directions for clinical research for better disease prevention, health promotion, therapy development, and the management of co-morbidities [20,21].

In this direction the multidisciplinary development of ability to detect rapidly, directly and selectively individual virus particles has the potential to significantly impact healthcare, since it could enable diagnosis at the earliest stages of replication within a host's system. Simultaneous acquisition of the vibrational and electronic fingerprints of molecular systems of biological interest, at the interface between liquid media, or at the air/solid, air/liquid interfaces is difficult to achieve with conventional linear optical spectroscopy due to their rather poor sensitivity to the low number of molecules or their maladjustment

to water environment (infrared absorption). It relies on inelastic scattering of monochromatic light, usually from a laser in the visible, near infrared, or near ultraviolet range. The laser light interacts with molecular vibrations, phonons or other excitations in the system, resulting in the energy of the laser photons being shifted up or down. The shift in energy gives information about the vibrational modes in the system. Infrared spectroscopy yields similar, but complementary, information. Spontaneous scattering is typically very weak, and as a result the main difficulty of this kind of spectroscopy is separating the weak non-elastically scattered light from the intense Rayleigh scattered laser light [22].

With the advancement of technology and consequently advanced spectroscopy, the interest of researchers in spectroscopic techniques in biological studies has grown. This field of science is known as biospectroscopy, and means the use of spectroscopy to analyze biological objects. Several studies have been conducted involving identification of bacteria , viruses, cancer diagnosis, and even in the field of forensic entomotoxicology, demonstrating that spectroscopic techniques are capable of detecting biochemical changes in biological matrices. Viruses are submicroscopic infectious agents and obligate intracellular parasites. They are totally dependent on a host cell because they are not able to generate energy to conduct all biological processes. Virus particles (virions) come in a variety of sizes and shapes.

Conclusion

Spectroscopic methods have the characteristic of providing fast results and reliable information related to the composition of the samples. The studies presented here have shown promising results in a field of science that needs to be better explored. It has been shown that multivariate

analysis techniques are of great importance to analyze spectroscopic data, providing the potential to identify and classify biological samples. We do hope that with advancement in this field of study, spectroscopic methods and tools will be used in bio medicine in the nearest future. Methods of light therapy of different diseases based on estimation of EM field characteristics and resonant wave ranges based on computer simulation of nanobioparticles characterization will be widely implemented, and possibility of determination of resonant (own) frequencies of entire system of molecules including vibrations will be a key point for that. It is a well-known fact that the yogis of ancient times practiced meditational techniques to get rid of diseases and stay healthy. Meditations induce the positive vibrations which are known to kill many of the harmful microorganisms which get into our body. Recent frontiers in technology are exploring the possibility of using external excitations to vibrate a virus to its death. The genetic material of virus is DNA/RNA enclosed within the protective protein shell (Capsid). Every cell in human body has a natural tendency to vibrate at frequency known as the natural frequency, and so the virus. Natural frequency values of these vibrations are very high compared to healthy cells, and depend on the molecular structure and differ from virus to virus [23,24].

In our opinion the concept and relevant methods of resonance therapy will be basis of different viral diseases treatment in the nearest future of practical medicine.

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