identical proteins.

In some viruses, a lipoprotein membrane, or envelope, surrounds the capsid. The envelope is derived from host cell membranes and is modified by the virus during its departure from the host cell. The envelope may carry specific virus proteins such as hemagglutinin or neuraminidase that are important for future functions and survival of the virus. The envelope of some viruses is studded with projections, or peplomers, which look like a fringe around the edge. The fringe may also be important for function and survival of the virus.

Classically, the piezoelectric phenomenon is said to exist when the application of a mechanical stress to certain dielectric (electrically nonconducting) crystals produces electric polarization (electric dipole moment per cubic meter) which is proportional to the mechanical stress. Conversely, application of an EM field to a crystal produces mechanical stress and distortion, and hence acoustic energy.

A necessary condition for the piezoelectric phenomenon in a crystal is the absence of a center of symmetry. Twenty of the 32 classically defined crystal classes lack a center of symmetry and are piezoelectric. Viruses are crystalline structures and as such are susceptible to vibrational effects by the use of acoustic and/or acousto-EM energy at resonant frequencies. Icosahedral viruses have 5-fold symmetry and thus do not have a classical center of symmetry in their crystalline structure, the necessary condition for a piezoelectric substance. Helical viruses likewise do not have a classical center of symmetry, as the spiraling capsids are offset from the 90 degree horizontal of the center axis. In addition to the crystalline structure of viruses being susceptible to the vibrational resonant effects of acoustic energy, viruses, as used in the present invention, may also function as piezoelectric, acoustic resonance structures.

The classical 32 groups of naturally occurring crystals defined in non-organic chemistry, do not include a group with 5-fold or offset helical symmetry. It is postulated by the inventors that viruses may represent a 33rd and 34th group of naturally occurring crystals.

The present invention has the potential to significantly reduce the number and severity of viral infections suffered by the world population. The invention has the potential to augment production of vaccines, or viral gene transfer. Also, the present has veterinary

applications, i.e. treating viral infections in livestock and poultry, as well as agricultural applications. Unlike prior art treatments that use non-resonant frequencies in the ultrasound range, the present invention uses specific frequencies that create resonance in specific viruses, but not in the adjacent tissues. The methods of the present invention also use electromagnetic energy equivalent to the acousto-EM signatures produced by viruses in a state of acoustic resonance, and utilize the piezoelectric, intrinsic energy dissipation, acoustoelectric, and/or magnetoacoustic properties of viruses, either alone, in combination with each other or in combination with a resonant acoustic field.

The disruption of viruses is useful to treat multicellular organisms, in particular, animals, including mammals, birds, plants, fruit, insects, arthropods, and the like or portions thereof which are susceptible to infection by viruses. Portions of a multicellular organism which may be treated for disruption of viruses include but are not limited to whole body, limbs, organs such as the kidney, spleen, liver, pancreas, heart, lung, gastrointestinal tract, and the like, tissue such as the cornea, bone, bone marrow, blood, cartilage and the like. Products derived from the multicellular organism such as blood products are included within the scope of the invention.

In one embodiment of the present invention used in disruption of a virus, the body or the portion of the body to be treated may be immersed in a conductive medium and acoustic waves applied through the medium to the body or portion thereof at a resonant frequency to cause resonance and disruption of the virus infecting the body or portion thereof. The duration of the treatment is sufficient to disrupt at least about 25% of the virus present, preferably at least about 50%. In one embodiment the duration of treatment is sufficient to disrupt at least about 50% to about 100% of the virus and at the same time have little or no harmful side effects to the host multicellular organism. The power intensity is dependent upon the tissue or organism and may range from 1×10^{-11} W/m^2 to 1×10^{11} W/m^2 and preferably from about 100 to about 10,000 W/m^2.

In the case where the multicellular organism is infected with more than one genus or species of virus, it is desirable to treat the organism with a resonant frequency specific to disrupt each type of virus infecting the organism. As in the case of a human infected with HIV- 1, opportunistic infections may occur caused by such viruses as cytomegalovirus, adenovirus, Herpes Simplex virus, and the like. In such a case, the unique resonant frequency

may be applied for each organism infecting the human.

The present method is beneficial in organ or tissue transplantation. Treatment of organs or tissues from a donor prior to transplantation prevents or inhibits the transmission of disease-causing viruses to the recipient. Such a method is useful in xenotransplants, allogeneic transplants, syngeneic transplants and the like. Donor organ or tissue to be treated for disruption of virus include but are not limited to cornea, heart, liver, lung, skin, bone, bone marrow cells, blood and blood products, kidney, pancreas, and the like.

Examples of diseases caused by retroviruses which may be inhibited or treated using the disruption methods described herein include but are not limited to AIDS, leukemia, mouse mammary tumor, sarcoma and the like.

Examples of diseases caused by Hepadna viruses include but are not limited to Hepatitis B, Hepatitis C, liver cancer, woodchuck hepatitis, ground squirrel hepatitis, duck hepatitis and the like.

Examples of diseases caused by Herpes viruses which may be prevented, inhibited or treated using the methods described herein include but are not limited to genital and oral herpes, chickenpox, shingles, cytomegalovirus disease (birth defects and pneumonia), mononucleosis, Burkitt's lymphoma, nasopharyngeal cancer, bovine mammillitis, pseudorabies, and the like.

Examples of diseases caused by Pox viruses which may be prevented, inhibited or treated using the methods described herein include but are not limited to smallpox, cowpox, pseudocowpox, molluscum contagiosum, contagious pustular dermatitis, buffalopox, camelpox, monkeypox, rabbitpox, mousepox, bovine papular otomatitis, fowlpox, turkeypox, sheeppox, goatpox, harepox, squirrelpox, swinepox and the like.

Examples of diseases caused by Papova viruses which may be prevented, inhibited or treated using the method of disrupting viruses include but are not limited to human wart virus, genital warts, cervical cancer, progressive multifocal leukoencephalopathy, warts and tumors in mice, monkeys and rabbits.

Examples of diseases caused by Adenovirus which may be prevented, inhibited or treated using the method of disrupting viruses include but are not limited to upper respiratory tract infections, gastroenteritis, conjunctivitis and tumors.

Examples of diseases caused by Parvo viruses amenable to prevention, inhibition or

treatment using the methods described herein include but are not limited to Fifth disease, bone marrow failure, Rheumatoid arthritis, fetal death and low birth weight, feline leukemia and the like.

Examples of Picorna virus related diseases which may be prevented, inhibited or treated using the methods described herein include but are not limited to polio, Hepatitis A, common cold, foot and mouth disease, encephalitis, myocarditis, enteritis, swine vesicular disease, contagious vesicular disease and the like.

Examples of diseases caused by Reo viruses amenable to prevention, inhibition or treatment using resonant acoustic energy include, but are not limited to, upper respiratory tract infections, Colorado tick fever, gastroenteritis and the like.

Examples of Orthomyxo virus related diseases which may be prevented, inhibited or treated using the methods described herein include but are not limited to influenza of man, pigs, horses, seals, birds and the like.

Other examples of diseases caused by viruses which may be prevented, inhibited or treated using resonant acoustic energy of the present invention include but are not limited to viral diarrhea, infantile gastroenteritis, vesicular exanthema of swine, sea lion disease encephalomyelitis, Dengue fever, yellow fever, rubella, equine encephalomyelitis, hog cholera, Bwamba fever, Oriboca fever, Rift Valley fever, Congo hemorrhagic fever, Nairobi sheep disease, African swine fever and the like.

The present method of disrupting a virus may also be utilized in agricultural settings. For example, plants, fruits, vegetables, and the like, suspected of containing disease causing viruses may be treated using resonant acoustic and/or acousto-EM energy for disruption of the viruses. Portions of plants which may be treated for disruption of a virus include but are not limited to seeds, seedling, pulp, leaves, vegetables, fruits, and the like.

The methods of the present invention comprise delivering acoustic energy at resonant frequencies to viruses. For example, the qualitative and quantitative resonant frequencies can be determined *in vitro* as shown by the apparatus in Figure 12. A drop of fluid (whole blood, serum, culture fluid, or host cells, etc.) with known resonant acoustic characteristics, and which also contains a known virus as determined by standard virology methods, is placed on a thin disc of absorptive media with known resonant acoustic characteristics (paper, cellulose, cotton, polymer, etc.). A thin slice of viral-laden tissue or

material (embedded or sliced material such as provided commercially by Polysciences, Inc. JB-4 Embedding, Paraffin, Immuno-Bed Kit, LR Gold, Osteo-Bed Bone Kit, Polyfreeze, PEG 4000 Resin, PolyFin Paraffin, etc.) can be used. The virus disc is placed between two broadband low GHz or high MHz transducers such as disclosed above and clamped into place.

The target range of frequencies to be examined for qualitative viral resonance signatures are derived using the speed of sound in biologic tissues 1,500 m/s divided by desired wavelength, based on viral dimensions. If the viral dimensions are unknown, they may be determined by electron microscopy using techniques known in the art.

One transducer generates the acoustic signal and may sweep through a wide band of target frequencies, and the other transducer detects the transmitted acoustic signal. The acoustic signal transmitted from the virus test disc/slice is fed into the positive lead of a signal analyzer. The known acoustic signals from the test fluid and disc, or test embedding material serve as a control and are fed into the negative lead of the signal analyzer. The control signatures are canceled out and the remaining resonant acoustic signature displayed is from the virus in the sample, yielding a qualitative result.

By varying the range of frequencies analyzed and comparing the amplitudes at each frequency, one can identify the primary resonant frequencies, and the associated harmonic resonant frequencies. The primary resonant frequencies will have the highest amplitude. Each virus will have multiple primary frequencies depending on viral dimensions including, but limited to, the diameter, length (if cylindrical or helical), apical distance, and unit distance. See Table 2 for calculated ranges of primary resonant frequencies for individual viruses, using acoustic velocity as 1,500 m/s, and viral dimensions as currently determined by standard virology methods. Results may vary in practice depending on specific viral factors such as bulk modulus, dispersion, acoustic velocity in viral materials, *in vivo* vs. *in vitro* dimensions, etc. and thus the frequencies are in no way limited to the calculated frequencies in Table 2.