Inactivating viruses with femtosecond laser pulses

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A new technique for targeting viral capsids may be applicable to a wide variety of pathogens.

Most antiviral and antibacterial treatments are only partially successful in eliminating target pathogens and may raise problems associated with drug resistance, adverse events, and unwanted side effects. Although UV irradiation represents an alternative, it lacks selectivity, eliminating unwanted microorganisms but also damaging other structures while raising concerns over harmful mutations. New methods to circumvent these limitations are particularly desirable.

One experimental technique involves microwave absorption with a view to destroying microorganisms by exciting their vibrational states. But water, the basic environmental medium for most undesirable microorganisms, readily absorbs microwave energy in the range of 10–300GHz, which also happen to be the typical vibrational frequencies of viral capsids (shells). In general, it is extremely difficult to affect the vibrational energy of microorganisms. Overcoming this drawback will require, in place of microwave excitation, visible sources in which water is transparent.

To this end, we have employed a low-power visible femtosecond laser system. By exciting low-frequency vibrational modes of the viral capsid through impulsive stimulated Raman scattering (ISRS) to a high-energy state, we have succeeded in inactivating virus. We expect this method to be highly selective and applicable to any viral or bacterial system.

Optical excitation of coherent lattice or molecular vibrations through stimulated light scattering can be carried out either by focusing an intense laser into a medium with a Raman-active vibrational mode or by spatially and temporally overlapping two laser outputs that possess a suitable frequency difference. ISRS has been shown to be a viable method for producing large-amplitude vibrational modes, for both molecules in solution and lattice vibrations in solid-state systems. It has been used to excite coherent acoustic phonons in ethanol, malachite green and cresyl violet in ethanol, and coherent optical phonons in α-perylene crystal. In this process, the electric field from a femtosecond laser produces an impulsive force through induced polarization. This mechanical impact coherently excites Raman-active vibrational modes on the capsid. If the pulse width, spectral width, and intensity of the femtosecond laser are appropriately chosen, the vibrational modes can be excited to high-energy states that break the weak links and damage or destroy the capsid, leading to inactivation of the virus.

We have demonstrated this innovative and unconventional method with M13 bacteriophages, viruses that exclusively infect Escherichia coli. By using a very low power visible femtosecond laser with a wavelength of 425nm and a pulse width of 100fs, we showed that M13 phages became inactive when laser power density was greater than or equal to 50MW/cm² (see Figure 1).

Inactivation was determined by plaque counts and depended critically on pulse width as well as power density of the excitation laser. Figure 2 shows the M13 bacteriophages with and without laser irradiation. The M13 bacteriophage is a helix-shaped...
Figure 2(a). Figure 2. Atomic force microscope image of M13 bacteriophage without (left) and with (right) laser irradiation.

virus with a diameter of about 6nm and length of about 850nm. Disappearance of the wormlike images in indicates capsid disintegration.

Our findings thus suggest a new method for manipulating, controlling, and inactivating undesirable microorganisms while leaving sensitive mammalian cells unharmed. It also demonstrates how basic principles of impulsive coherent acoustic excitation using an ultrafast laser optical system can selectively alter viral function or inactivate viruses and, potentially, other microorganisms. Because acoustic capsid vibrations are usually of long wavelength, they are relatively insensitive to minor local changes, such as those due to mutations. Therefore, our approach may also be applicable to drug-resistant strains of microorganisms. Testing is under way. Finally, work in progress includes efforts to inactivate the human immunodeficiency virus (HIV) and disinfect the blood supply.

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K. T. Tsen’s research interests focus on the interaction of light in solid-state and biological systems, in particular, on the use of ultrafast laser sources to elucidate novel electron transport phenomena, dynamical properties of lattice vibrations in nanostructure semiconductors, and microscopic mechanisms in biological systems such as viruses, bacteria, and cells. He has more than 160 refereed publications and has edited four books in the area of ultrafast phenomena.

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