2025/02/21

Sakura-Science

Symposium on collaborations with Medical Sciences, Veterinary Sciences and Engineering to fight infectious diseases

at I-site Namba

Development of engineering countermeasures against infectious diseases - Compact droplet remover and ultraviolet irradiation -

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http://bigbird.eng.omu.ac.jp/AntiCovid19/

（In Japanese）

Why Infection Control Research?

Specialist for radiation safety control

Preventing the spread of contamination when handling unsealed radioisotopes (RI) and infection control have a great deal in common.

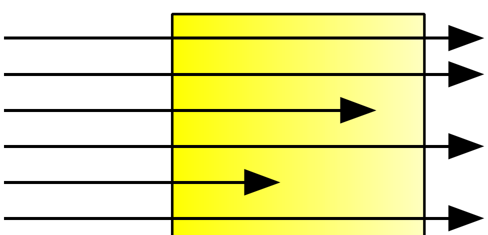
Tyvek suits used as protective clothing are the same for RI and biological use.

In the safety management of Crookes tubes, the dosimetry of low-energy X-rays with halfway-range penetrating power is studied.

Accurate UV dosimetry

highly penetrating radiation

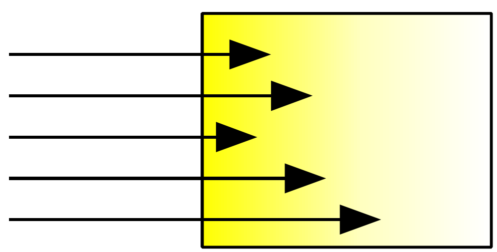
Hp(0.07) ≦ 10 Hp(10)



整列拡張場

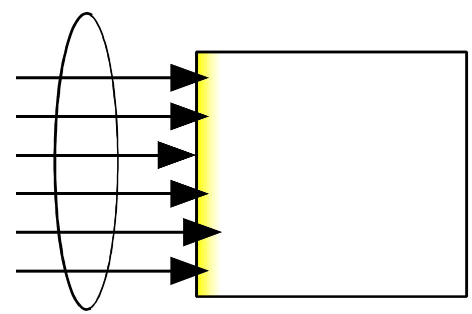
High energy gamma rays pass through almost completely, giving off energy almost uniformly, and the energy received by the material is used for evaluation, not the incident energy fluence.

Low energy X-ray



20 keV X-rays attenuate by half at 1 cm, and the energy transfer in the body is not uniform, making it difficult to evaluate the effective dose.

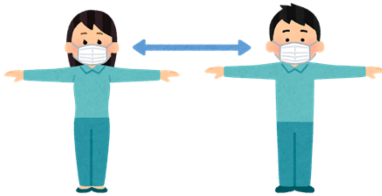
Ultra violet ray



Evaluated in terms of incident energy per unit area (J/m^2), since it is completely absorbed in the range of several 10 µm and it is difficult to evaluate the energy imparted to a small volume in that range.

What are the causes of the spread of infection diseases and 3 Cs?

Social distance

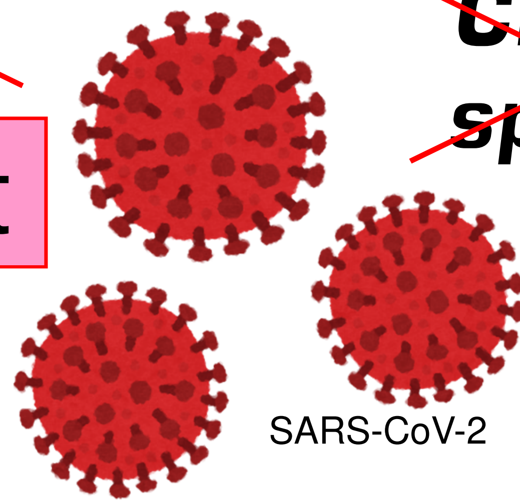


Stay home

~~Crowded places~~

Droplet

Droplet is a drop released from the oral cavity in diameter larger than 5 μm,
It can only reach a range of about 2 m.



SARS-CoV-2

Aerosol

~~Closed spaces~~

Ventilation

Particles smaller than 5 μm in diameter can remain in the air for several minutes, and can diffuse over a wide area.

~~Close-contact setting~~

Wash hands

Disinfection by ethanol

You never know where germs might be lurking. The traps kept infectious for several days.

Contact infection from object surfaces

Study of engineering countermeasures to infection diseases (1)

~~Closed spaces~~

Aerosol

One indicator of ventilation status is the carbon dioxide concentration.

Ventilation

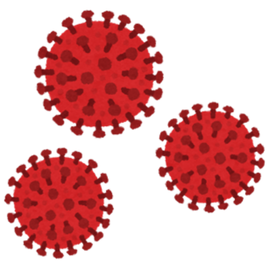
Some places are inevitably poorly ventilated.

Active "space sterilization" in which chlorine dioxide and ozone are sprayed into a space is difficult to control because the effective concentration is close to the concentration that is harmful to the human body.

Air cleaner

Various types are available, including those using photocatalysts, ultraviolet light, and high-performance filters to collect aerosols and inactivate viruses contained in aerosols.

High temperatures, even fan heaters and stoves can inactivate it. (Not possible with air conditioners).



Stays in the air for long periods of time and travels far in the wind

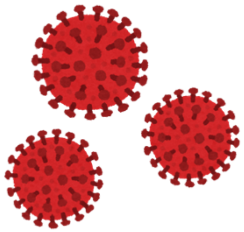
There are two types of particles, droplets that are released directly from the oral cavity and droplet nuclei, which are smaller droplets that have dried. They remain in the air for several minutes and can spread over a wide area.

Even when wearing a mask, nearly half of the aerosol is dispersed between the fibers and gap to the face. Aerosols stay for a long time, so their concentration gradually increases if ventilation is poor.

Ultraviolet irradiation to unoccupied spaces

UV-C, which has high disinfection effect, is harmful to the human body (strong inflammation to skin and cornea of eye), so it has long been used in food factories to inactivate airborne viruses by irradiating UV-C upward so that it does not hit people. The Centers for Disease Control and Prevention (CDC) recommends Upper-room Ultraviolet Germicidal Irradiation (UVGI) on its official website.

Study of engineering countermeasures to infection diseases (2)



~~Close-contact settings~~

Falled droplets cause contact infection

Wash hands

Disinfection by ethanol

Coronaviruses are the type that have an envelope, a lipid membrane, on their surface, so it is important to dissolve the lipid. Just physically washing it away is effective.

Contact infection from object surfaces

Depending on the environment, a virus attached to the surface of an object may retain its infectivity for several days. Dispersed droplets fall in several second, but the virus contained in the droplets remains on the rurface.

UV-C irradiation to PPE

Since the risk of removing personal protective equipment (PPE) is high in medical fields dealing with infectious diseases, UV-C irradiation to PPE at the boundary to the Cold area will reduce the risk of infection.

UV-C irradiation to object surfaces

Various papers have confirmed that it is possible to inactivate SARS-CoV-2 in a short time.
It cannot be used in the presence of people because it is harmful to the human body.
There are some products using 222 nm UV that have very little effect on the human body, but they have not yet been certified as completely safe.
It is necessary to understand various problems before using these products.

Application of photocatalysts and metal particles such as copper and silver to the surface of shared items

The application of photocatalyst to the surface of an object always produces a gradual deactivation effect. Some metal-containing photocatalysts, such as copper, are effective for a certain period of time even after dark. The simplest way is to apply copper foil tape.

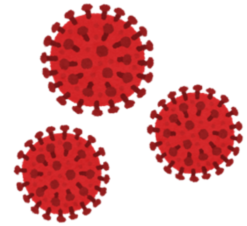
Study of engineering countermeasures to infection diseases (3)

~~Crowded places~~

Social distance

Since the droplets only travel about 2 meters, you can protect yourself from flying droplets by keeping a distance from others.

Droplets



Large droplets with large amounts of virus

Stay home

Wet particles larger than 5 μm emitted from the oral cavity are called **droplets** and actually have a distribution peak at about 150 μm. These large **droplets** can be scattered over a distance of up to 2 meters in a few seconds.

Dive directly into the mouse	Droplet infection
Dries out and becomes a droplet nucleus.	Air-borne infection
Falling and adhering	Contact infection

Wear Mask

To prevent the release of **droplets**, wear mask is effective. Non-woven or cloth masks can stop about 80% of the droplets, but the remaining 20% are dispersed through gaps. Therefore, there is a risk of infection when meeting within the range of droplets. Furthermore, it is difficult to wear a mask during meals and drinking.

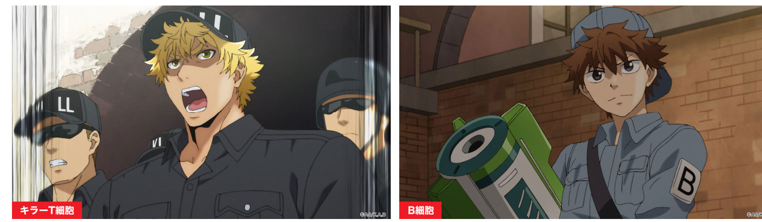
Requirement for Droplets Remover

What is "infection"?

The body is constantly on the offensive against bacteria and viruses through the action of innate and acquired immunity. When the number of pathogens that have invaded the body is too high, and the body's defenses are unable to keep up, they multiply steadily within the body, and the number of pathogens increases to a level where symptoms appear or can be detected by PCR testing, etc., this is called “infection”.

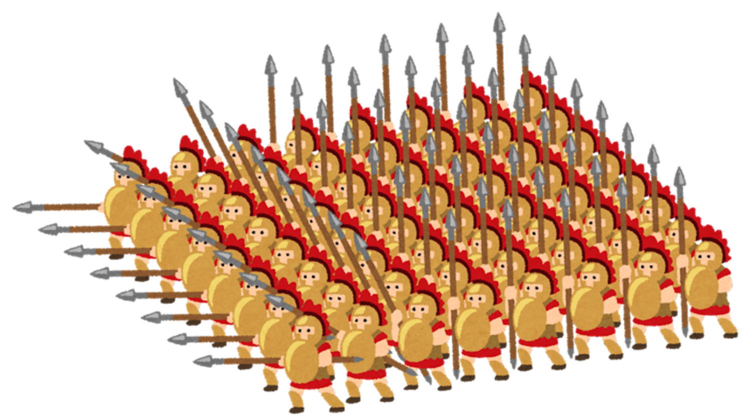
The number of viruses that must be taken in before an infection occurs depends on the pathogen, the individual's immune status, and the physical condition of the individual who took in the virus. On the contrary, even if you have acquired immunity through vaccination, you can become infected if too many viruses enter your body.

natural immunity

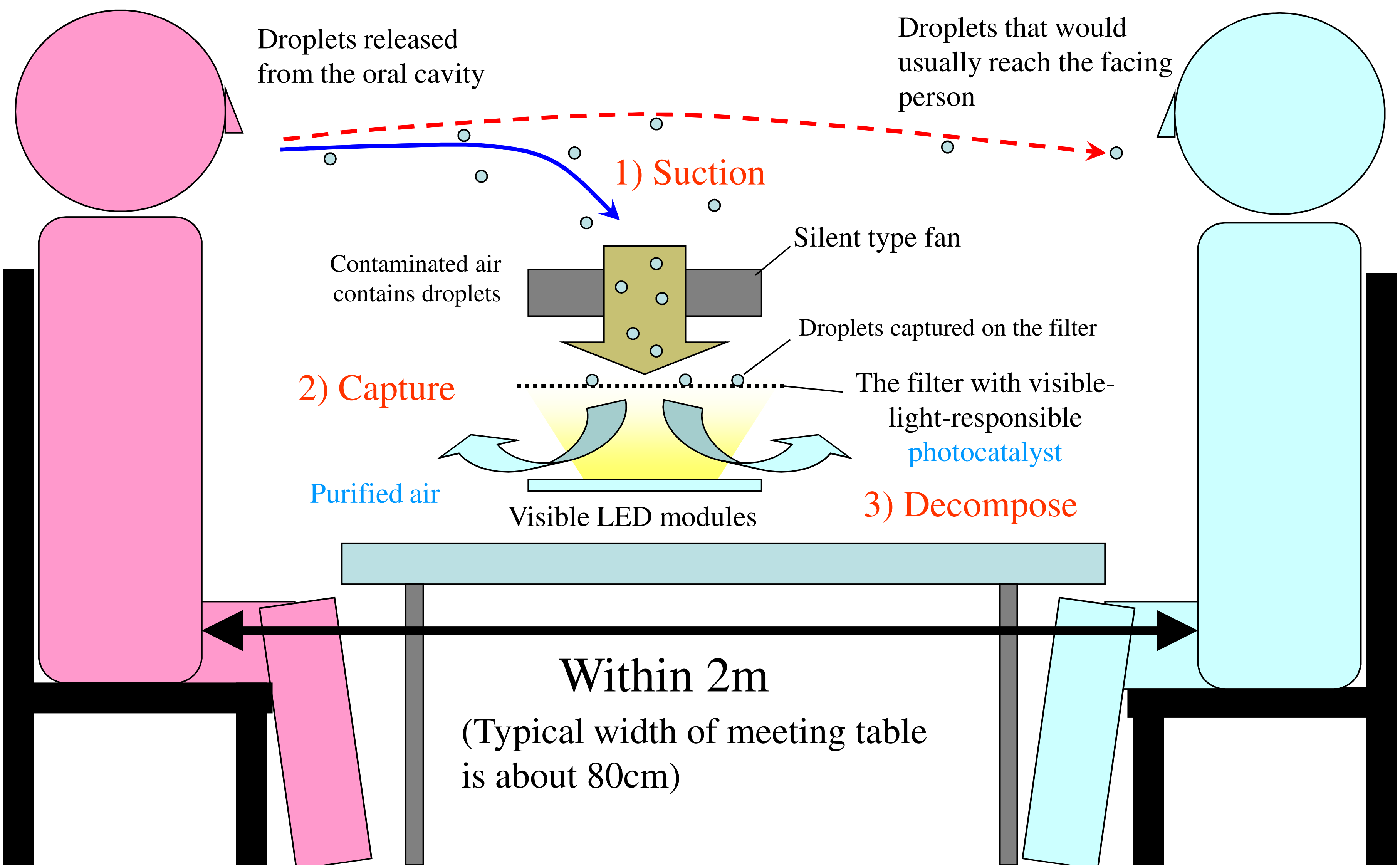


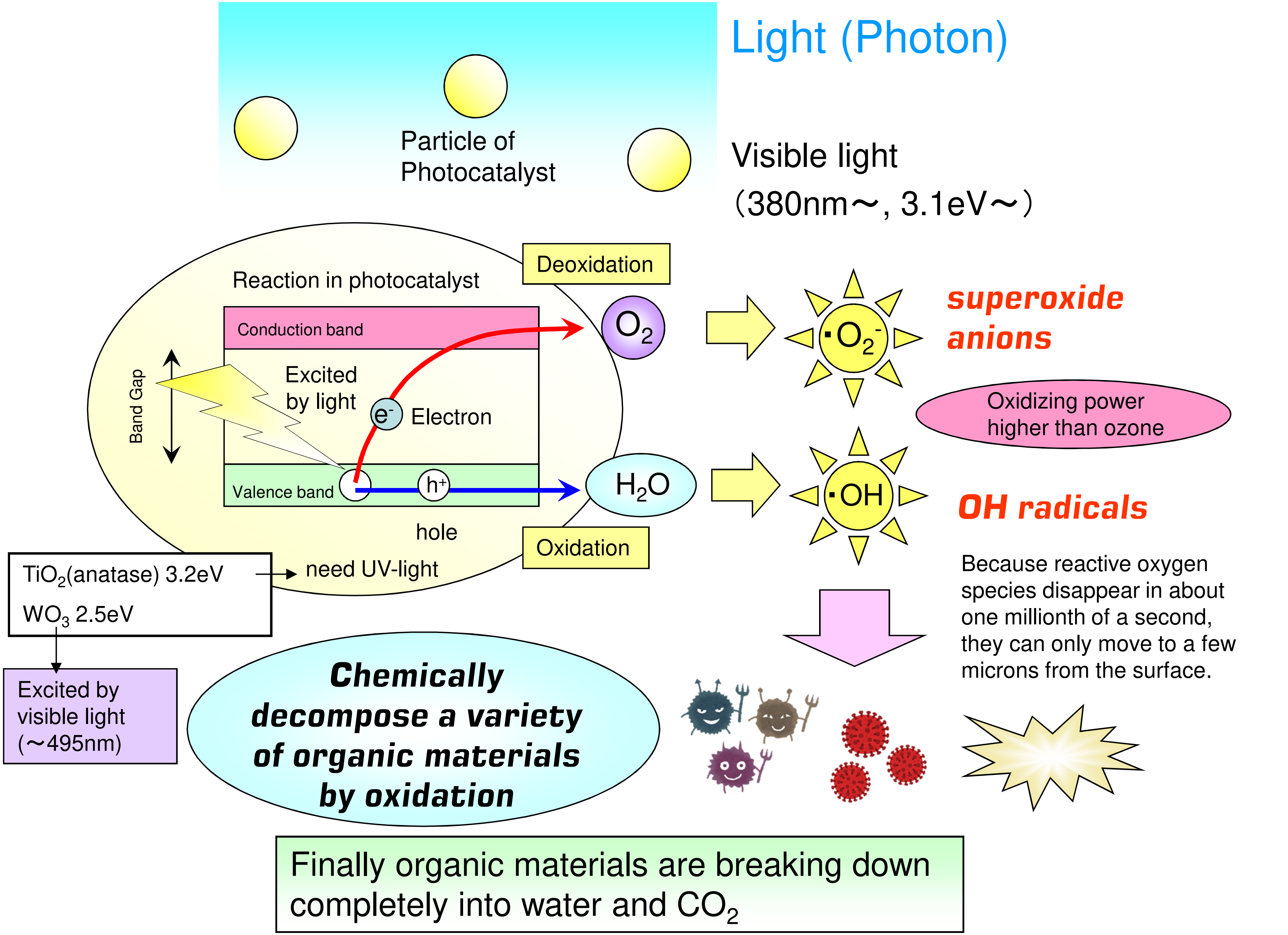
acquired immunity

It is important to reduce the number of germs to be taken in.



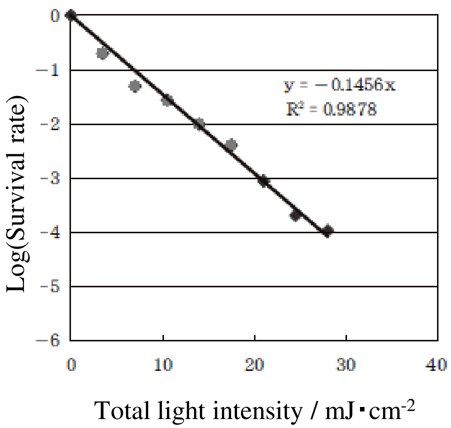
A specialized device that removes droplets flying between facing persons




Light (Photon)
Particle of Photocatalyst
Visible light
(380nm～, 3.1eV～)
Reaction in photocatalyst
Deoxidation
Conduction band
Band Gap
Excited by light
e^-
Electron
O_2
Valence band
h^+
hole
H_2O
Oxidation
$\cdot O_2^-$
superoxide anions
Oxidizing power higher than ozone
$\cdot OH$
OH radicals
TiO_2(anatase) 3.2eV
need UV-light
WO_3 2.5eV
Excited by visible light (～495nm)
Chemically decompose a variety of organic materials by oxidation
Because reactive oxygen species disappear in about one millionth of a second, they can only move to a few microns from the surface.
Finally organic materials are breaking down completely into water and CO_2

Sterilization effect by Ultraviolet radiation

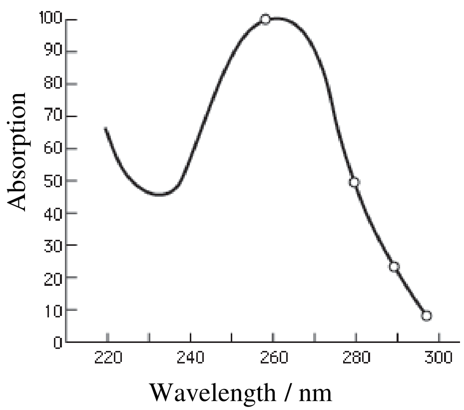
Since ancient times, ultraviolet rays have been a major enemy of living organisms, and until the ozone layer was created, living organisms were unable to ascend to land. Ultraviolet rays are not classified as ionizing radiation (photons and charged particles with energy enough to ionize air are called ionizing radiation under the law), and although they do not have enough energy to break the main strand of DNA, they can excite the bases in the DNA sequence and cause them to join together. In particular, the formation of pyridimine dimers is said to be the main type of UV-induced damage, which is genetic damage that interferes with DNA replication.



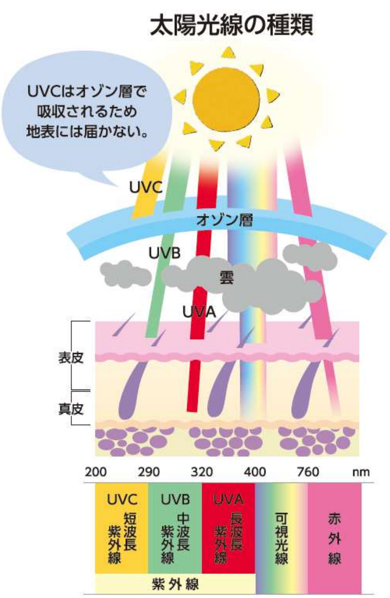
Iwasaki Electric Co.
UV sensitivity of spore-forming bacteria (Part 2)
- Bacillus subtilis spores –
https://www.iwasaki.co.jp/tech-rep/technical/81/

It has been reported in various papers that SARS-CoV-2 is also inactivated by ultraviolet light.

Wavelength dependence of UV absorption to DNA

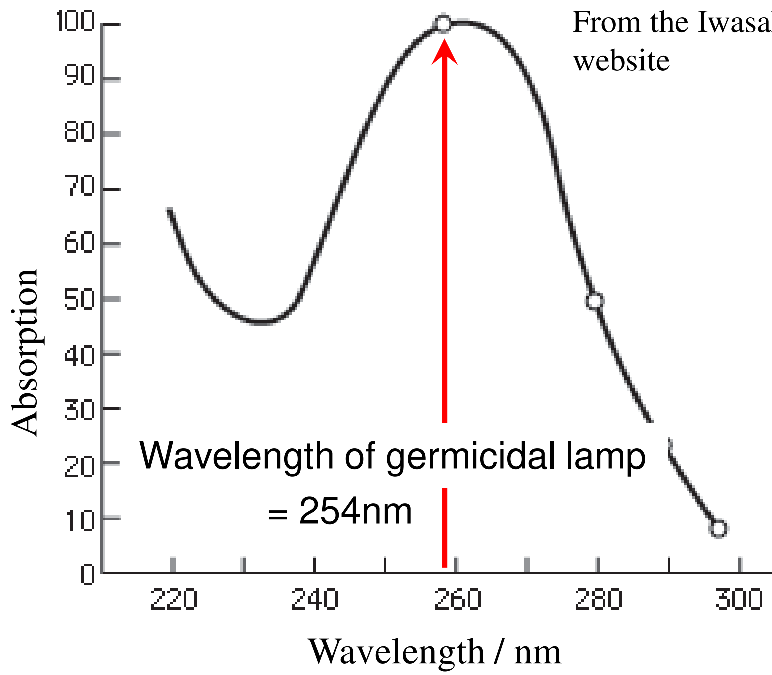


Ultraviolet rays are classified into UV-A (400-315nm), UV-B (315-280nm), and UV-C (<280nm) according to wavelength. The sterilizing effect peaks at about 260 nm, and becomes almost not effective at about 310 nm. Same as in the case of radiation sterilization, the survival curve shows an exponential decrease in the number of pathogens surviving as the irradiation dose increases.

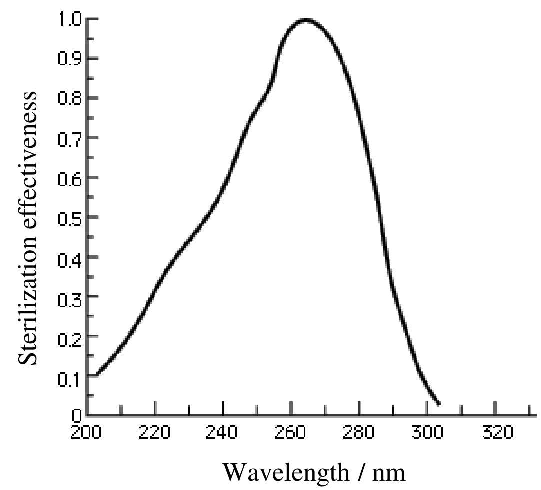


Sterilization using Ultraviolet radiation

Wavelength dependence of UV absorption for DNA



Wavelength dependence of sterilization effectiveness



UV-C	UV-B	UV-A
200-290nm	290-320nm	320-400nm

Almost all of the research on sterilization to ultraviolet rays has been performed on germicidal lamps with a wavelength of 254 nm. Cross-sectional data exist for a variety of bacteria and viruses.

Although the sterilization effect of UV-B in sunlight has long been known, quantitative studies are extremely limited.

Far-ultraviolet light at 222 nm has extremely low penetrating power and does not reach to living cells and stopped at the stratum corneum, which is about 20 μm thick on the very surface of the skin. Therefore, it does not cause inflammation or skin cancer. On the other hand, it can reach viruses with a diameter of about 0.1 μm attached to the surface of an object, damaging their genes and inactivating them. In the case of bacteria larger than viruses (about 1 μm in diameter), the amount of irradiation dose reaches to DNA in the cytoplasm is reduced, so the effect is smaller.

Inactivation of virus by UV-A / UV-B

One of the most reliable data on virus inactivation by UV-A/UV-B is a paper by Dr. Takahashi of the Univ. Tokushima on influenza viruses.
Based on the data in this paper, how long it would take for the virus to be inactivated by sunlight is calculated with several solar lighting data.

UV-A only (365nm LED)

UV-A requires total light intensity of 50J/cm^2 to reduce influenza viruses to 1/100.
The UV-A intensity in solar ray at its strongest is approximately 2.5 mW/cm^2 , so
50 / 2.5x10^{-3} = 20,000 sec (5.5 hours).

UV-B only (310nm LED)

UV-B requires total light intensity of 0.45 J/cm^2 to reduce influenza viruses to 1/100.
In July and August, the UV-B intensity in solar ray is 25 kJ/m^2 /day, so only 1.6 hours during peak hours is required. However, UV-B is absorbed more easily than UV-A, and in winter, the UV-B dose drops to 1/5 of the UV-A dose, which means that almost a whole day is required.

Inactivation of viruse by UV-C

Based on the data for influenza viruses, inactivation is achieved at total light intensity of 4.4 mJ/cm^2 to 1/100 (1/100 the dose of UV-B) and 6.6 mJ/cm^2 to 99.9% = 1/1,000.

Using germicidal low pressure mercury lamp, the total UV output from an 8 W lamp is about 2.5 W, which gives illuminance approximately 0.9 mW/cm^2 at a distance of 15 cm. At this UV intensity, it is possible to inactivate influenza viruses to 1/10,000 in only 10 seconds. Peer-reviewed papers have already been published on SARS-CoV-2 inactivation, which showed it was more easily inactivated than influenza viruses.

We propose to use 10 mJ/cm^2 as a provisional guide-line for sterilization using UV-C based on the safe side.

Quantitative evaluation of the effect of inactivation by 254 nm UV-C germicidal lamps using the SARS-CoV-2 has already been completed by the BSL3 laboratory at the veterinary department of our Univ. collaborated with Prof. Yamasaki and Yasugi, and it has become clear that inactivation occurs at lower accumulated illuminance than in the previously reported paper.

Inactivation of SARS-CoV-2 by UV-C

Inactivation studies for SARS-CoV-2 by UV-C are already performed around the world.

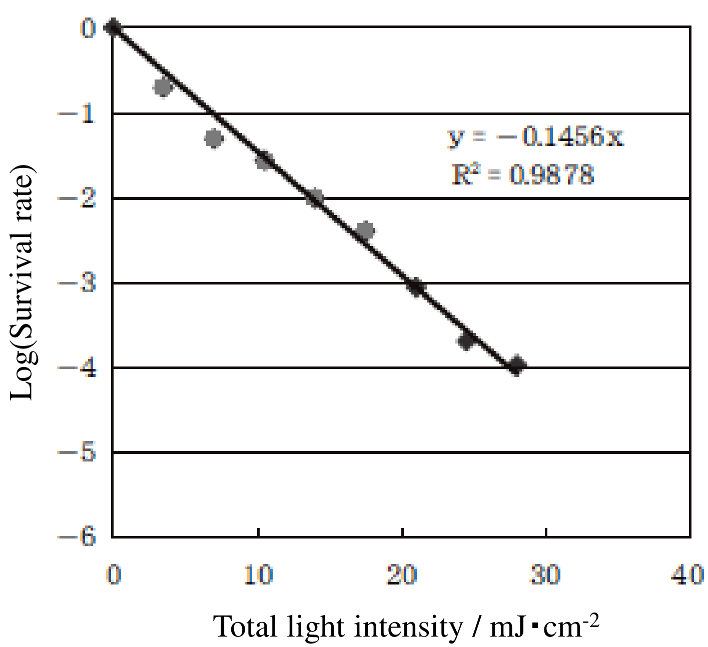
No	1)	2)	3)	4)	5)
group (usu. of people)	Milan University Biasin et al.	Boston University Storm et al.	Stanley Electric	University of Miyazaki Inagaki et al.	Hiroshima University Kitagawa et al.
light source	254nm germicidal lamp	254nm germicidal lamp	265nm LED	280nm LED	222nm Excimer Lamp
Dose required for inactivation up to 99.9 (mJ/cm)^2	3.7	Wet: 5.3 Dry: 4.1	5.1	37.5	3.6
peer review	peer-reviewed	peer-reviewed	non-refereed	peer-reviewed	peer-reviewed

These data showed required dose to inactivate SARS-CoV-2 is lower than the dose for influenza viruses up to 99.9% at 6.6 mJ/cm^2 in 254 nm germicidal lamps.

Even for 280 nm LEDs, Dr. Takahashi ‘s experiment on influenza required 75 mJ/cm^2 (60 mJ/cm^2 in the latest paper) for up to 99.9% inactivation and it is higher than the dose for SARS-CoV-2.

Total light intensity of UV and survival curve

In the case of ultraviolet irradiation, the energy given to a unit area per unit time is called illuminance (W/m^2 in the SI unit system, mW/cm^2 is conventionally used), and the total energy integrated over the irradiation time is called total light intensity (J/m^2 , mJ/cm^2). The number of alive bacteria or viruses keep infectious decrease exponentially as the total light intensity increases. This relation is called the survival curve. The effect depends on the dose, not on whether it is effective or not.



Iwasaki Electric UV sensitivity of spore-forming bacteria (Part 2)
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Example of a survival curve. A plot of total light intensity of 254 nm UV ray (mJ/cm^2) on the horizontal axis and the logarithm of survival rate (-3 at 10^{-3} = 0.1%, which means up to 99.9% sterlized) on the vertical axis. It is not necessarily linear, and often does not go down easily at first, or has a shoulder. Also, the slope of this curve varies depending on the target microorganism, and required total light intensity is different with each microorganism.

The effect is the same whether irradiated at high illuminance for a short time or at low illuminance for a long time, as long as the total light intensity is the same (except in the case of extremely high illuminance as laser).

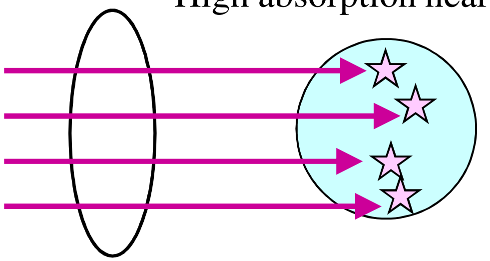
Consider the Energy absorbed by the object

$$\text{Absorbed dose (Gy)} = \frac{\text{Energy of absorbed radiation (J)}}{\text{Mass of the system under consideration (kg)}}$$

Until now, the irradiation amount of ultraviolet light has been evaluated only by the total light intensity, which is the energy fluence per unit area (J/m^2). However, since the transmittance differs depending on the composition of the object and the wavelength of the irradiated UV ray, the energy absorbed by the object differs even at the same total light intensity.

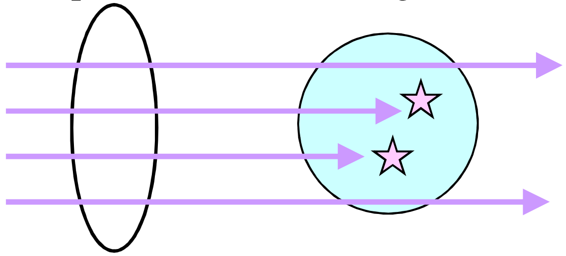
For this reason, the concept of absorbed dose in ionizing radiation is introduced to the field of UV. The absorbed dose (J/kg) is the amount of energy of ionizing radiation absorbed in a certain system divided by the mass of the system. Note that in the case of non-uniform irradiation, the value may vary depending on the system (denominator size). Absorbed dose (Gy) is defined for ionizing radiation, and since no corresponding unit is defined for ultraviolet radiation, the term mass absorbed light energy (J/kg) is provisionally proposed.

High absorption near 260 nm



Energy absorbed by “the system" is different even at the same total light intensity

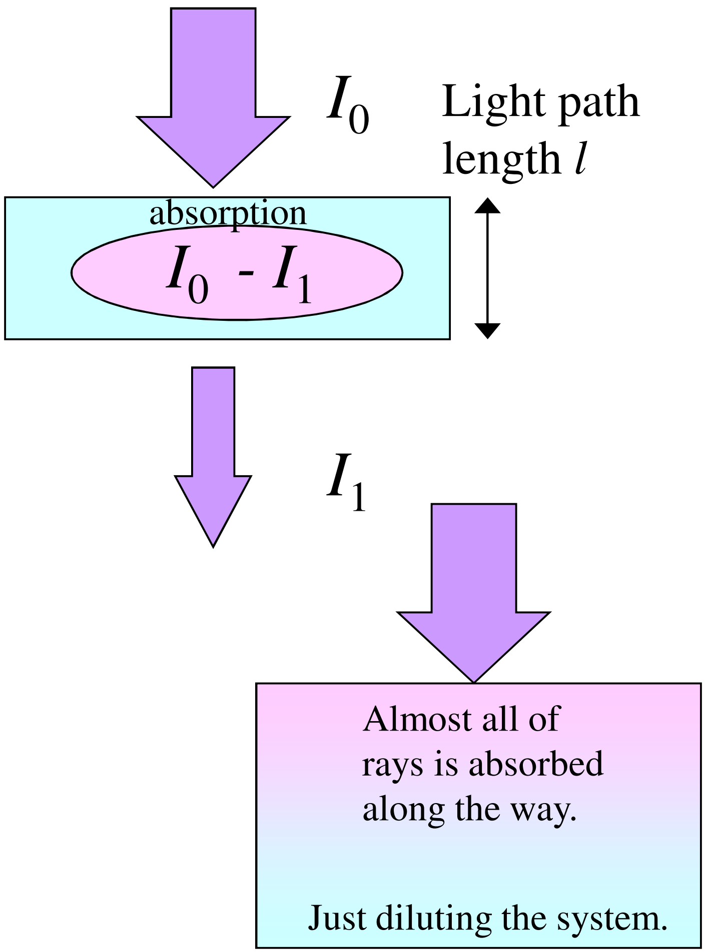
Absorption is smaller at longer wavelengths



The total light intensity includes the energy of photons passing through the system

Mass absorbed light energy determined from absorbance

$$\text{Mass absorbed light energy (J/kg)} = \frac{\text{Absorbed UV energy (J)}}{\text{Mass of the system under consideration (kg)}}$$



Lambert-Baer law

Absorbance A = $-\log_{10}(I_1 / I_0) = \varepsilon c\, l$
(ε: Absorption coefficient, c: Medium concentration, l: Light path length)

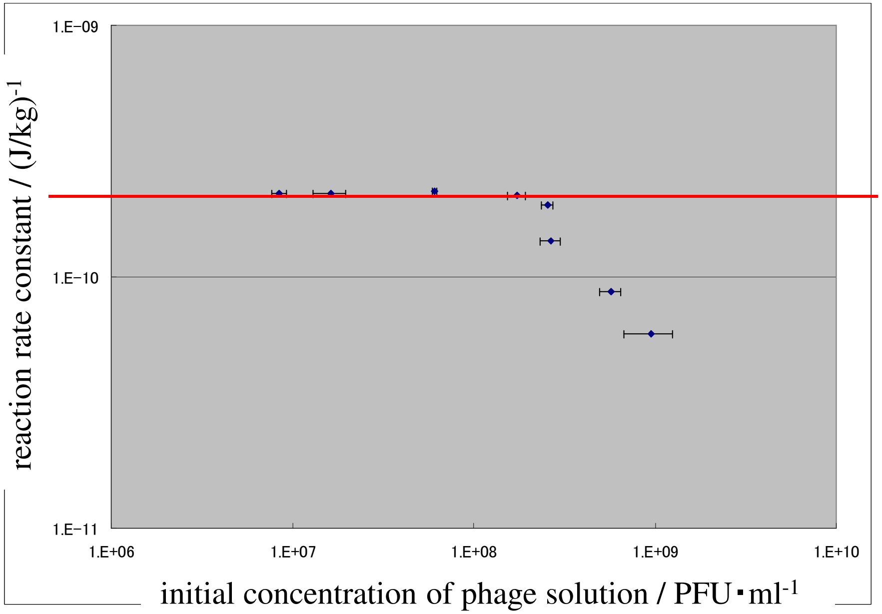
The energy $I_0 - I_1$ absorbed by the system from $I_0\,(1-10^{-\varepsilon c l})$. An absorbance of 1 means 90% absorption and an absorbance of 2 means 99% absorption. The thicker the system and the higher the concentration of the medium, the more energy is absorbed.

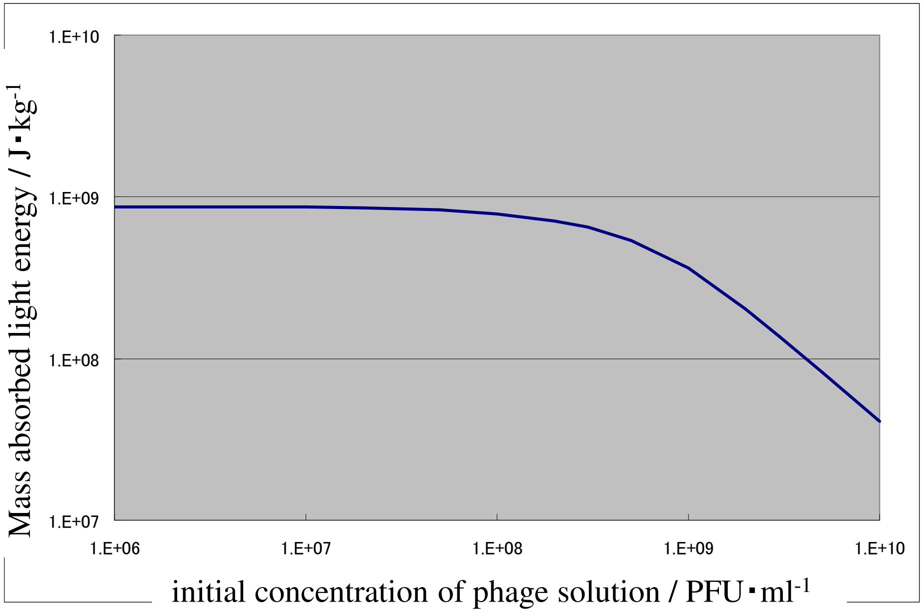
However, if the light path length is too long or the concentration of the medium is too high, almost all of the ultraviolet rays are absorbed along the way and the energy absorbed does not increase any further, and the energy absorbed per unit mass of medium becomes smaller as the amount of medium increases.

Validation of survival curves based on Mass absorbed light energy

An experiment was conducted to obtain survival curves by irradiating 5 ml of bacteriophage Qβ solution of different concentrations in a 60 mm dia. petri dish with 254 nm UV-C irradiation. The thickness (light path length) of the phage solution was 1.77 mm. The irradiation dose was given as the mass absorbed light energy based on the total light intensity and the absorbance at the initial concentration of each phage solution. The left figure shows the dependence of the slope of the survival curve on the initial concentration of phage solution.

It can be predicted from the calculation of the amount of mass absorbed light energy for each phage concentration shown on the right figure that at too high concentrations, all of the incident light is absorbed in the middle of the optical path, making it impossible to irradiate the entire system.





Points to note on using ultraviolet sterilization

Illuminance falls as the distance

Illuminance falls inversely proportional to the square of the distance. If the light source is placed farther away to illuminate a larger area, the illuminance becomes very weak and the required time to achieve enough dose becomes longer.

Very low permeability to most substances

With the exception of a few objects such as quartz glass and water, it can penetrate only a few 10 μm. A rubber glove or a sheet of paper will stop it completely. Effective irradiation is limited to objects adhering to the surface, and is ineffective for areas in shadow from the light source. Also, unlike ionizing radiation with high penetrating power, the illuminance decreases according to the cosine law when the radiation is incident at an oblique angle.

Causes severe skin and eye irritation and harmful to the human

UV-C, with its short wavelength and high energy, causes severe irritation of the skin and the cornea of the eye without being noticed immediately during the irradiation. It also may cause skin cancer or blindness later. For this reason, it basically cannot be used in places where people are present; according to JIS Z8812, the allowable limit value standard for UV-C is 6 mJ/cm^2 . Organic materials such as plastics, fibers, and paints are also gradually degraded by large amounts of irradiation.