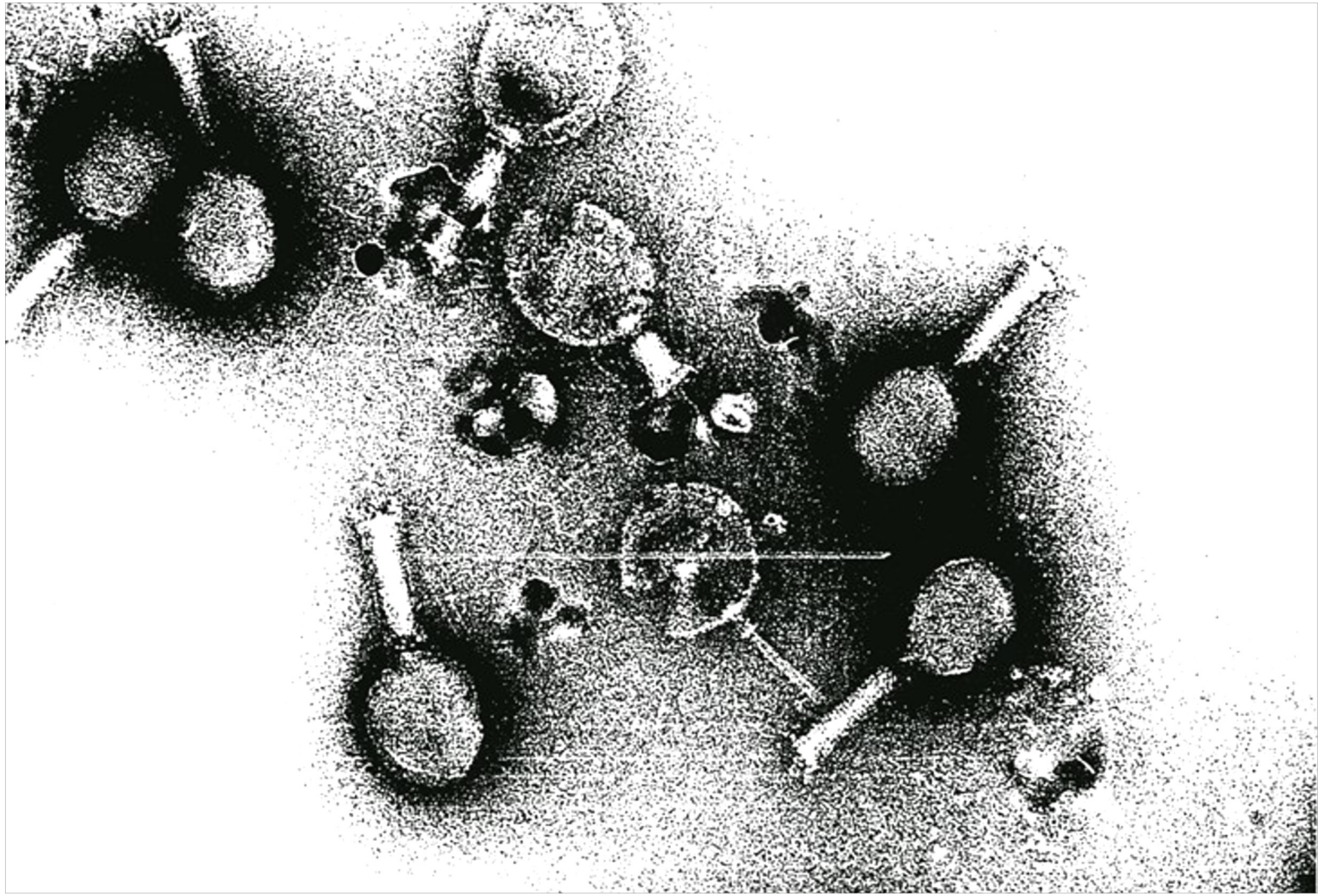
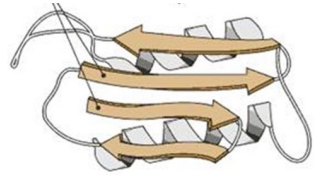
Filtration of Bioparticles: Filters on a test bench

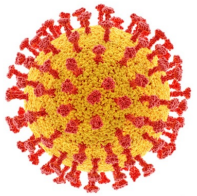


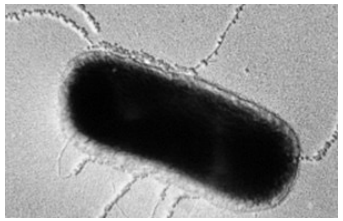
Joachim Frey PhD
Prof. em. Universität Bern

Bio-particles: Classification of pathogenic micro-organisms

Microorganism	Characteristic	Taxonomic affiliation	Particle size	Genetic Material	Main transmission mode	Possible therapeutics
Prion	Infectious **protein** particle Specific structure	Prions	**1-5 nm**	----	**ingestion**	
Virus	Replicating particle depending on live cells	Virus	**20 – 200 nm**	RNA, DNA	**airborne** ingestion contact	Antiviral substances, nucleotide analogues (toxic side effects)
Mycoplasma Bacteria	Independent replicating live beings	Prokaryote (no nucleus)	300 – 1000 nm **1 – 30 µm**	DNA	**airborne ingestion** contact	Antibiotics
Fungi	Independent replicating higher live beings	Eukaryotes (Nucleus, monocellular or multicellular)	**50 – 500 µm**	DNA	**airborne** contact ingestion	Fungicides (mostly only exterior applications)

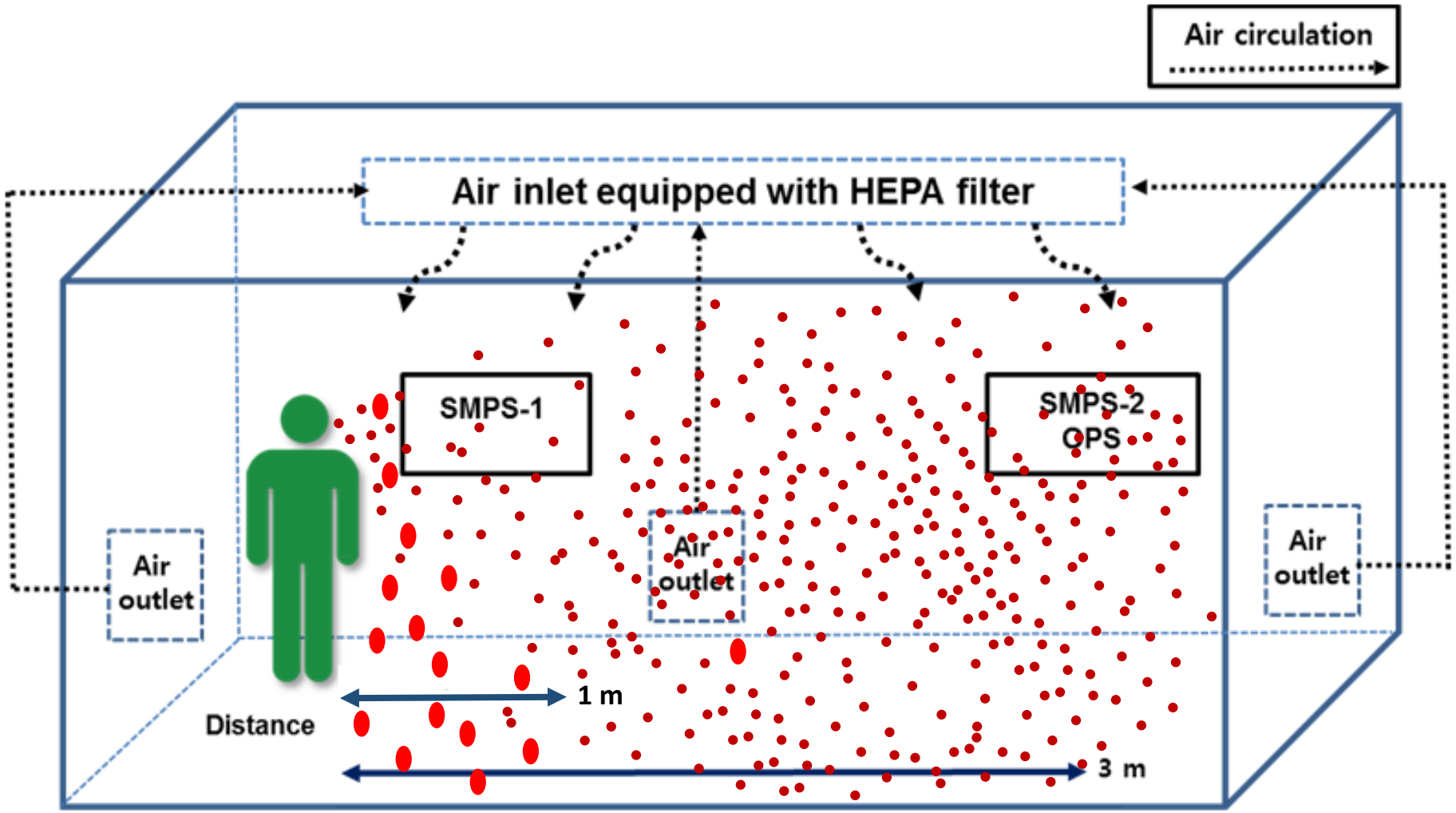






Particles generated by human exhalation

(measured at 3 m distance)



mean temperature: 23.8°C; mean relative humidity: 37.2%

Lee et al., (2019) Aerosol and Air Quality Research 19: 840-853

Particles generated by human exhalation

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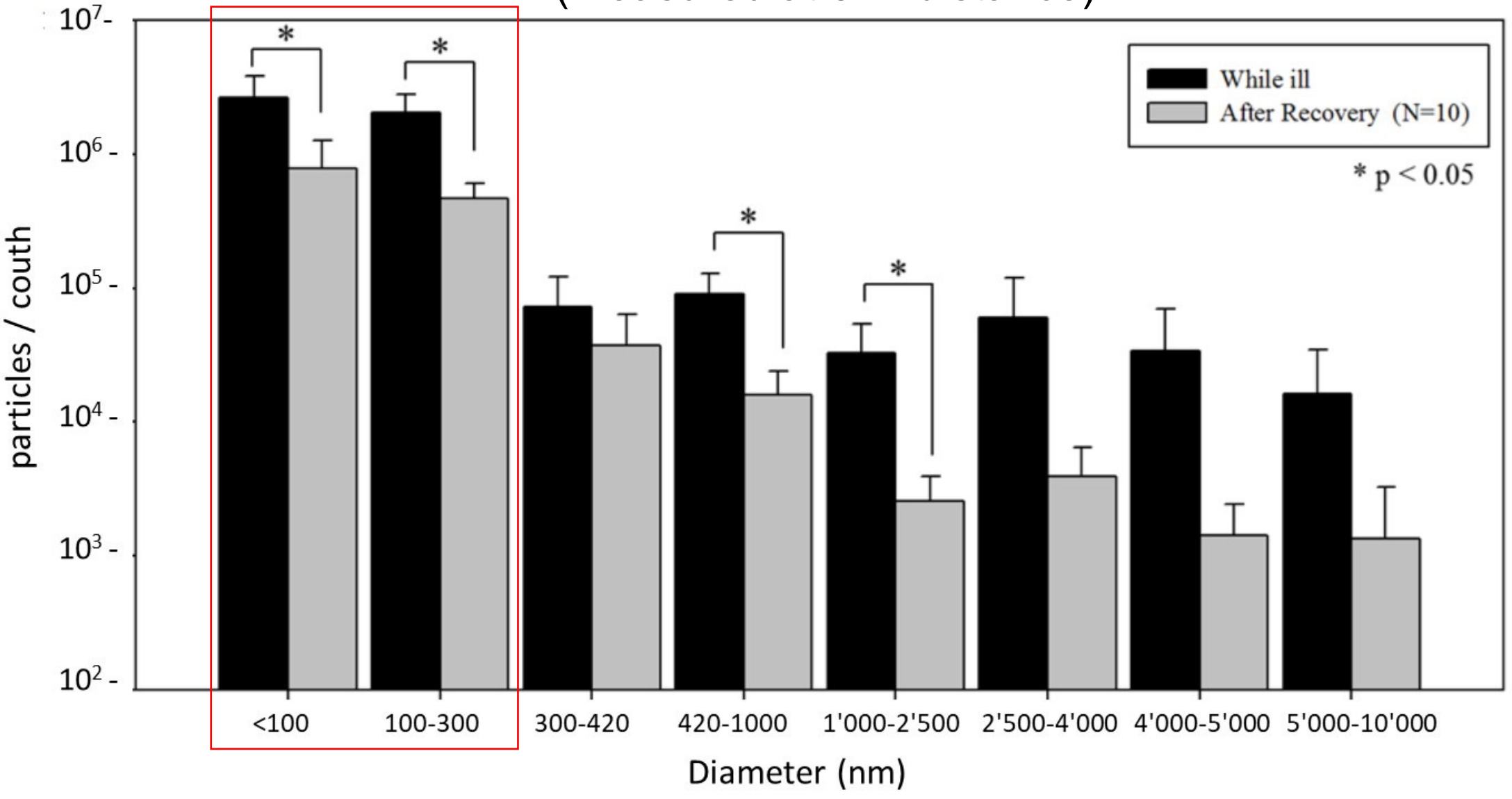


Lee et al., (2019) Aerosol and Air Quality Research 19: 840-853

Filtration of Bio-particles

- Purpose:

- Which bio-particles must be filtered (particle size, virus, bacteria)
- Which conditions of bio-particles must be filtered off (droplets, aerosols, only live or replicating particles)

- Procedure:

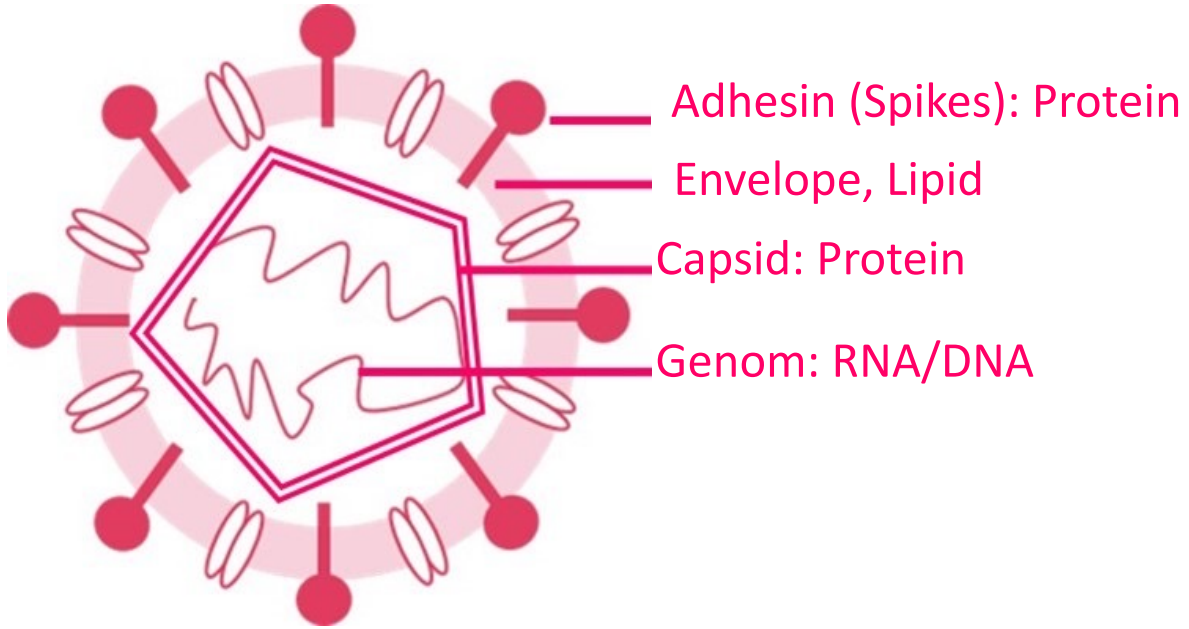
- Which type of filters to be used (many bio-particles are flexible structures)

- Control tests

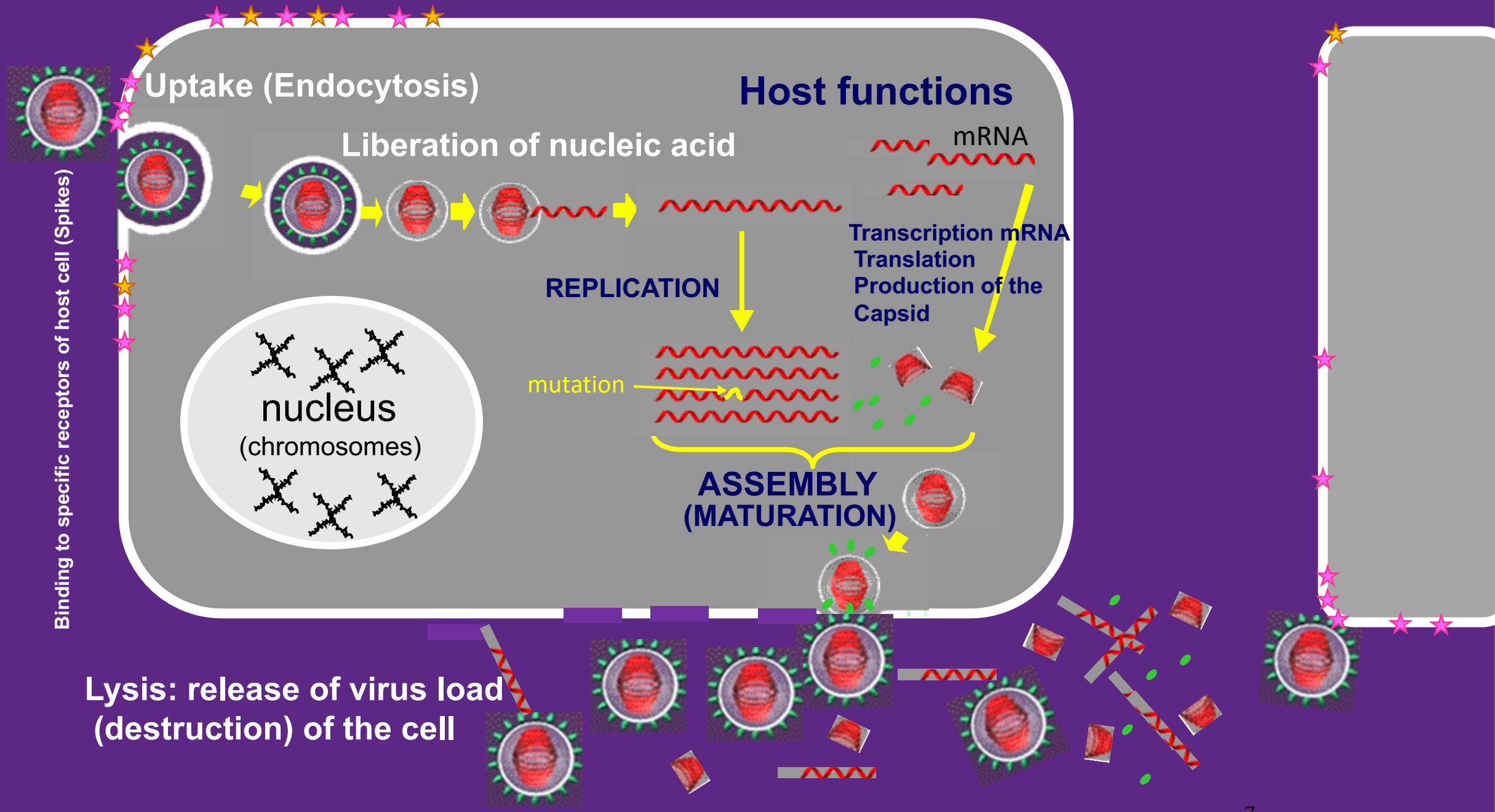
- Which detection system of the bio-particles is suitable to measure efficacy of filtration

Main focus: virus

- Virus are small bio-particles of 20 nm to 250 nm invisible by optical microscope
- Virus do not replicate autonomously ⇒ no live beings
- Virus have a genome (DNA or RNA) coding for their structure
- Virus infect live cells to propagate
- Virus Infection cause damage/death to cells ⇒ disease in human animal plants
- Certain viral genomes integrate into the cell genome ⇒ recurring infections or cancer

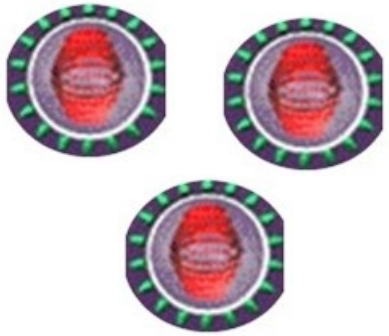


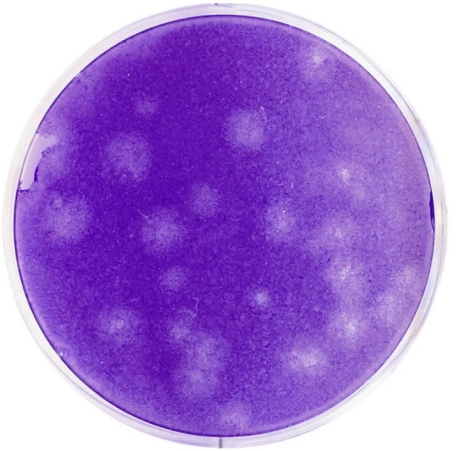
Virus infection and multiplication



Detection methods of viruses

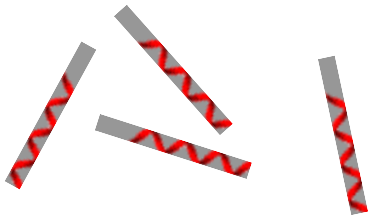
- Plaque assay ⇒ infectious virus





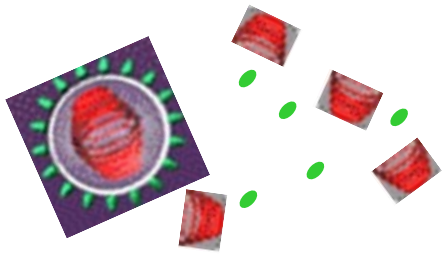
Cell culture

- PCR ⇒ genomic fragments
  DNA or RNA (indirect)



Thermocycler

- Antigen Test ⇒ full virus and/or
  fragments of virus



Immuno detection

Use of a proxy-virus

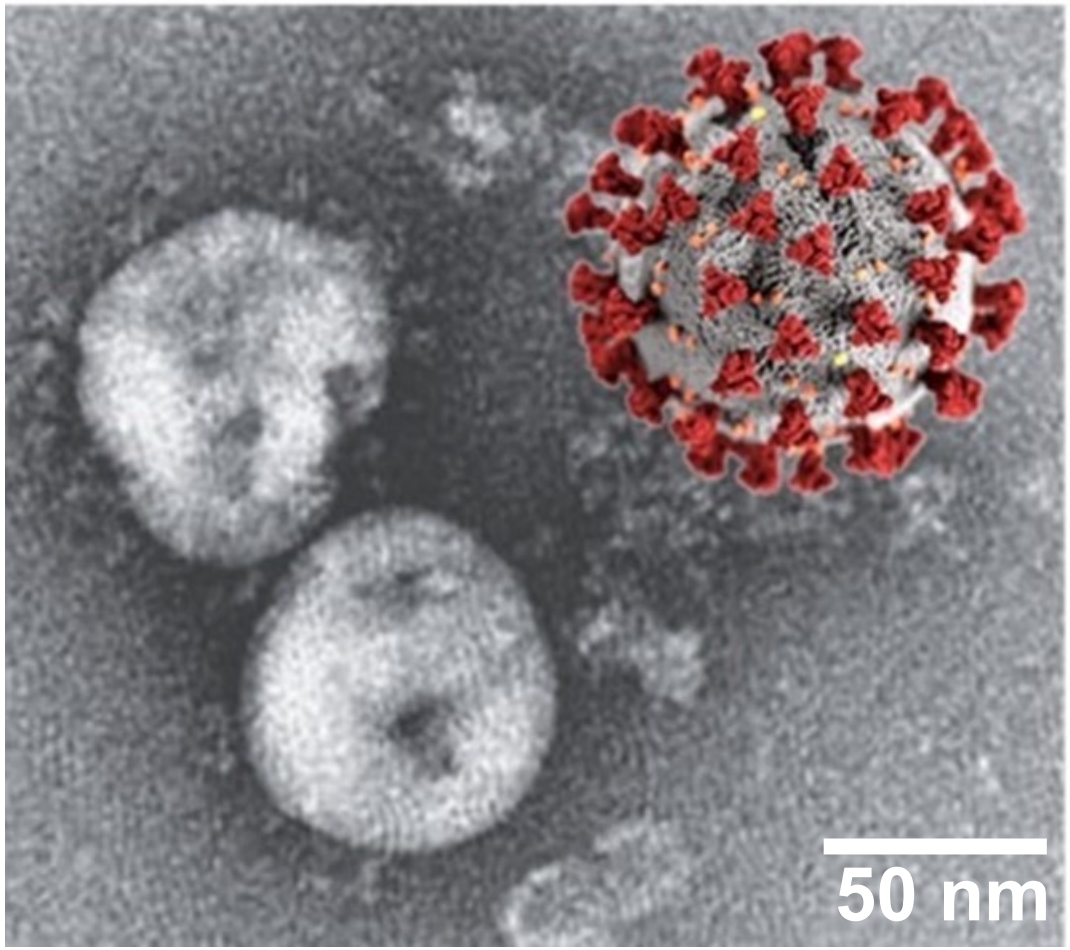
Experimentation with SARS-CoV-2 virus is dangerous and inefficient

- Requirement of a high safety BSL-4 or BSL-3 Laboratory (high running and personnel costs)
- Detection systems for live virus have low sensitivity
- Inactive virus fragments passing the filter and would be measured by PCR or antigen test.

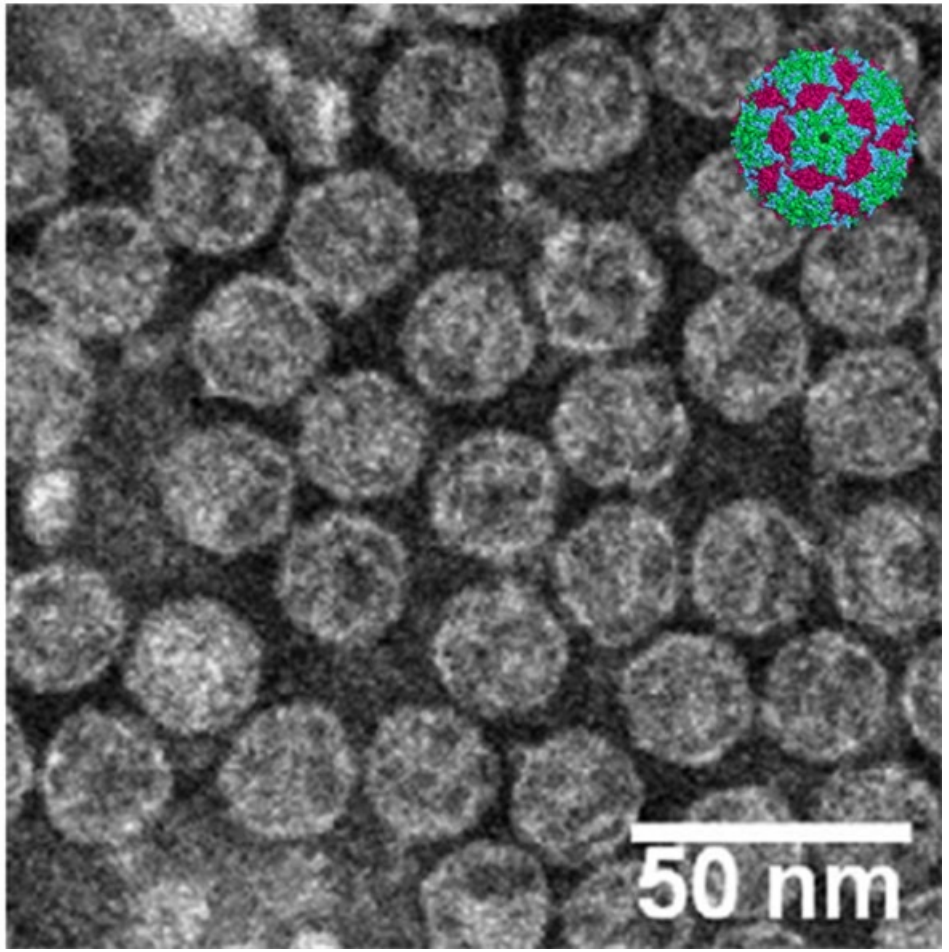
Use of a bacteria-virus (bacteriophage) MS2 as a proxy-virus

- Inoffensive for human, animals and plants
- High specificity to a given bacterial laboratory safety strain e.g. *Escherichia coli* F^+ C300 (ATCC 15597)
- Similar spherical shape like SARS-CoV-2 but smaller (MS2: 30 nm; SARS-CoV-2: 60-140 nm)
- Genome: positive-strand RNA like SARS-CoV-2
- **Highly sensitive test for infectious bacteriophage**

Electron micrographs of SARS-CoV-2 and MS2



SARS-CoV-2 virus (covid-19) 60 – 140 nm

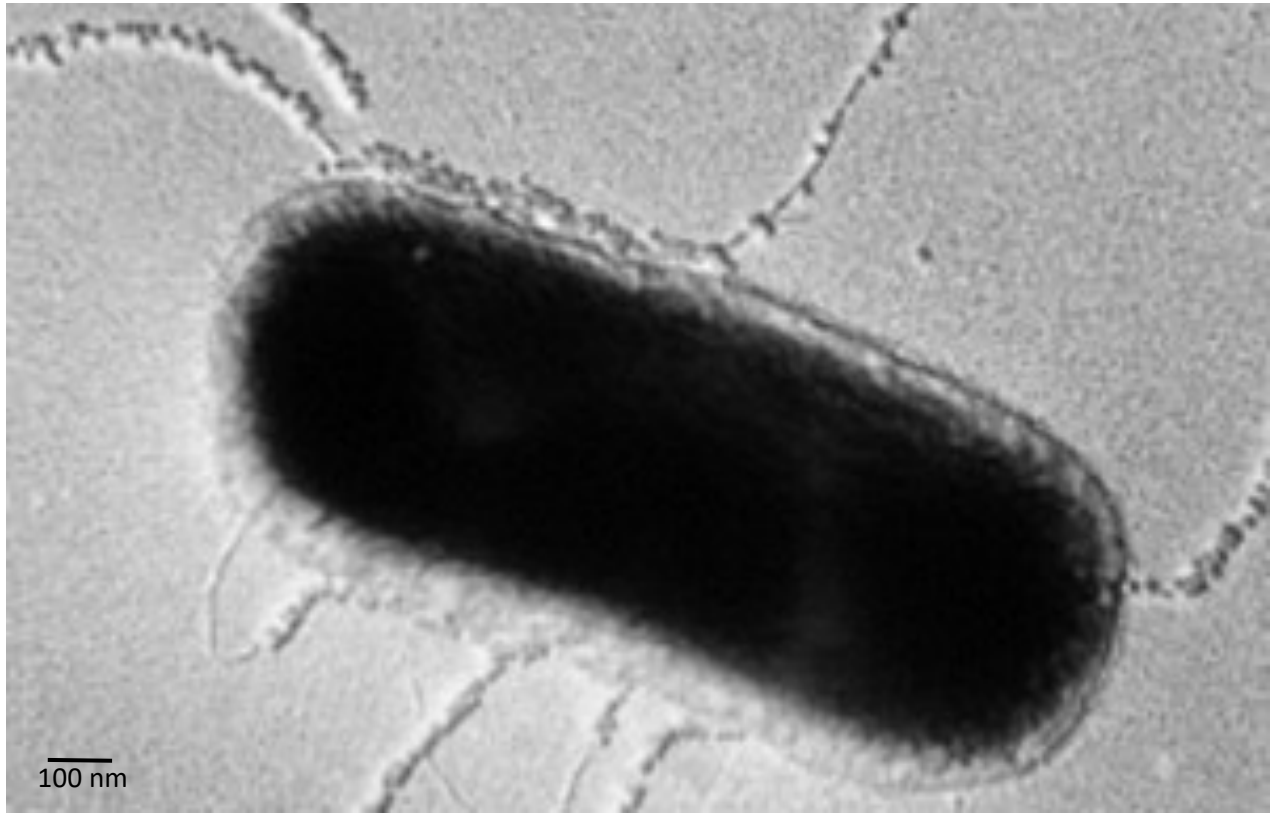


MS2 bacteriophage 30 nm

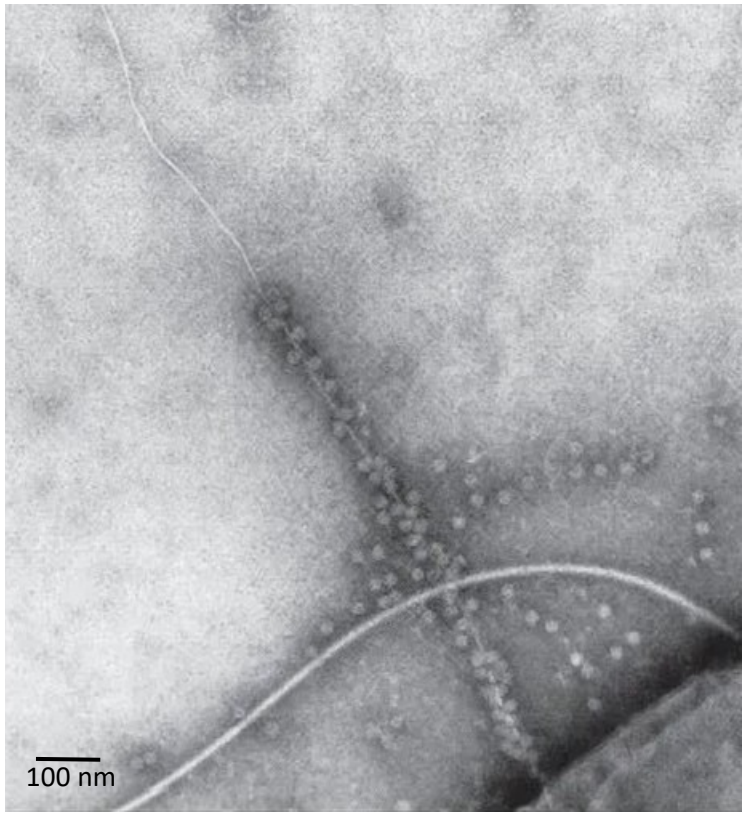
(https://www.pharmaceutical-business-review.com/news/gsk-cepi-coronavirus/; Zhu et al., 2020); (https://de.wikipedia.org/wiki/Enterobakteriophage_MS2; Nguyen et al., 2011)

MS2 bacteriophage infects specifically *Escherichia coli* F$^+$ safety strain C300

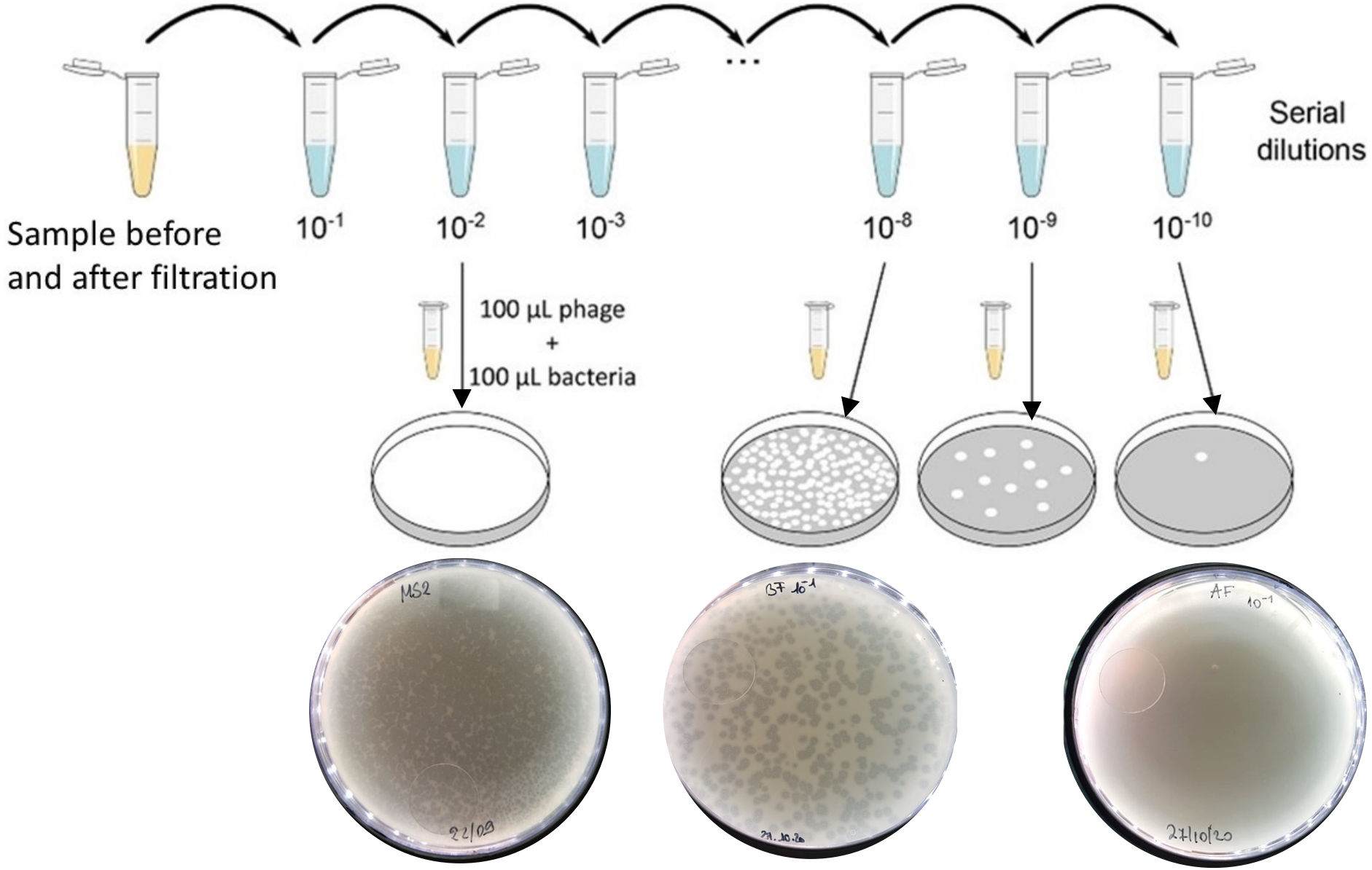
Escherichia coli F$^+$ bacterium ≈ 2 µm



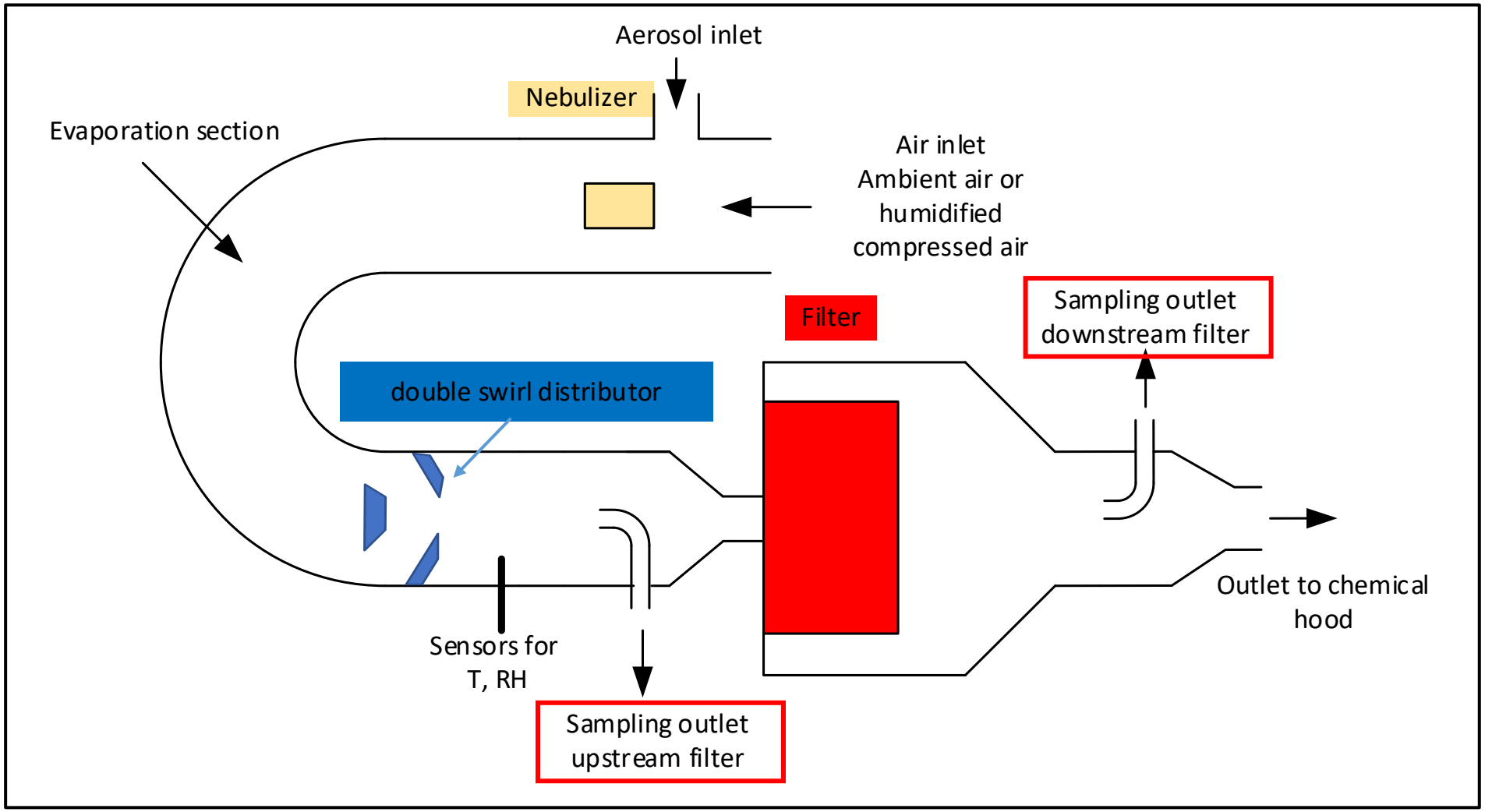
MS2 bacteriophage ≈ 30 nm



Titration of bacteriophages



Filter test device



T= 21°C; RH = 40–50%; flow rate ≈ 20 m^3 h^{-1} main flow and 5 L min^{-1} sample flow

Experimental set-up

Test installation at AMI Uni Fribourg for bacteriophage filtration test under a chemical hood

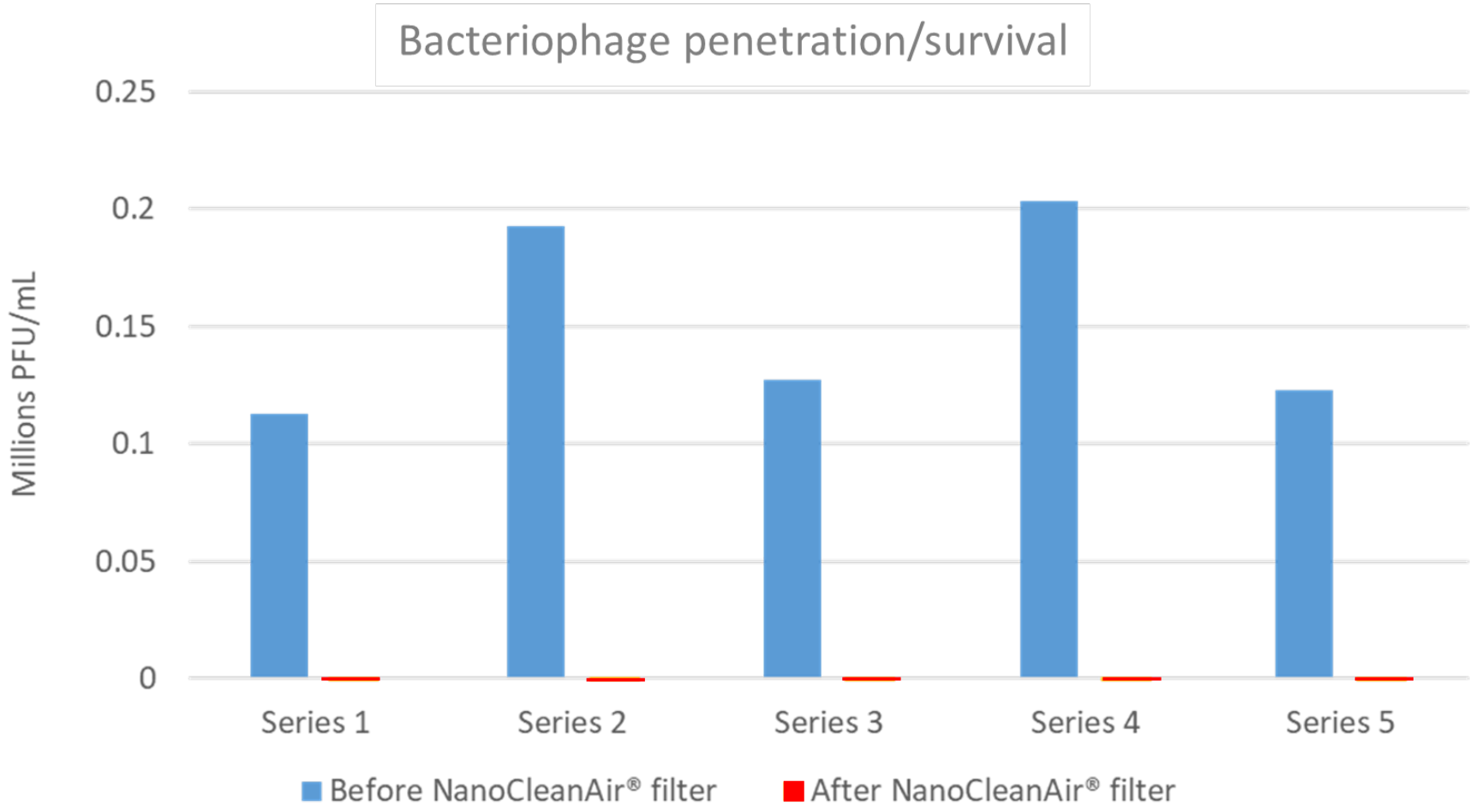
2) Collection of virus on gelatine filter before the nanocleanair filter

1) Aerosolisation of virus (bacteriophage)

NanoCleanAir® filter

3) Collection of virus on gelatine filter after the nanocleanair filter

Results



The efficiency of virus (bacteriophage) elimination by NanoCleanAir® filter is > 99% (n=5)

Conclusions

- Bacteriophage MS2 is a safe **proxy** for determination of filter efficacy for pathogenic virus
- Requirement: a suitable wind channel allowing **production of virus aerosols**
- Gelatine filters represent a good system to capture virus from aerosols
- NanoCleanAir® filter showed a high efficacy (> 99%) to eliminate virus from aerosols
- NanoCleanAir® 215 mm Ø allowed filtration of aerosols of approximately 10^9 Φ m^{-3}

Acknowledgments

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Hochschule für Technik

NanoCleanAir

Schweizerische Eidgenossenschaft
Confédération suisse
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