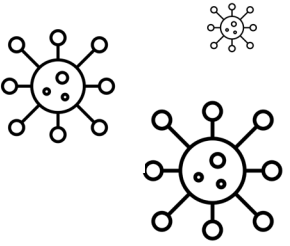


*Modern miasmas; a
biological perspective*

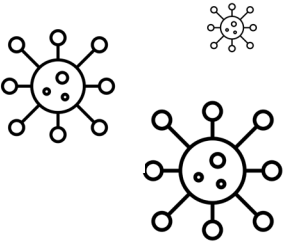
samira.mubareka@sunnybrook.ca

Objectives



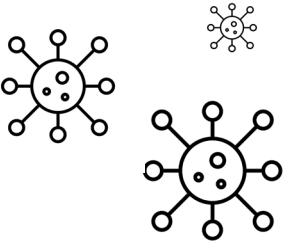
- To outline key ecological and biological factors contributing to the spread of viruses through bioaerosols
- To provide an overview of the current state of knowledge, and recent advances and breakthroughs in infectious bioaerosols research.
- To highlight the major gaps and challenges in our understanding of bioaerosols
- To highlight the inter-disciplinarity of bioaerosol detection and mitigation

Outline

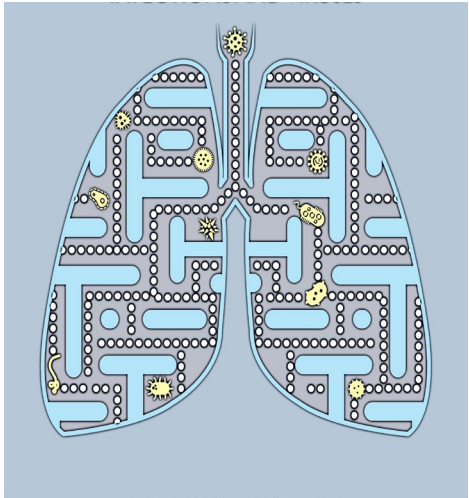
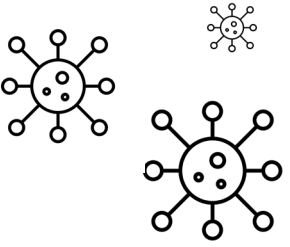


- The big picture
- Tools and instruments for the detection and characterization of bioaerosols
- Scenarios
 - Community, person-to-person
 - Healthcare, person-to-person
 - Human-animal-environment interface
- Challenges and next steps

Glossary of terms



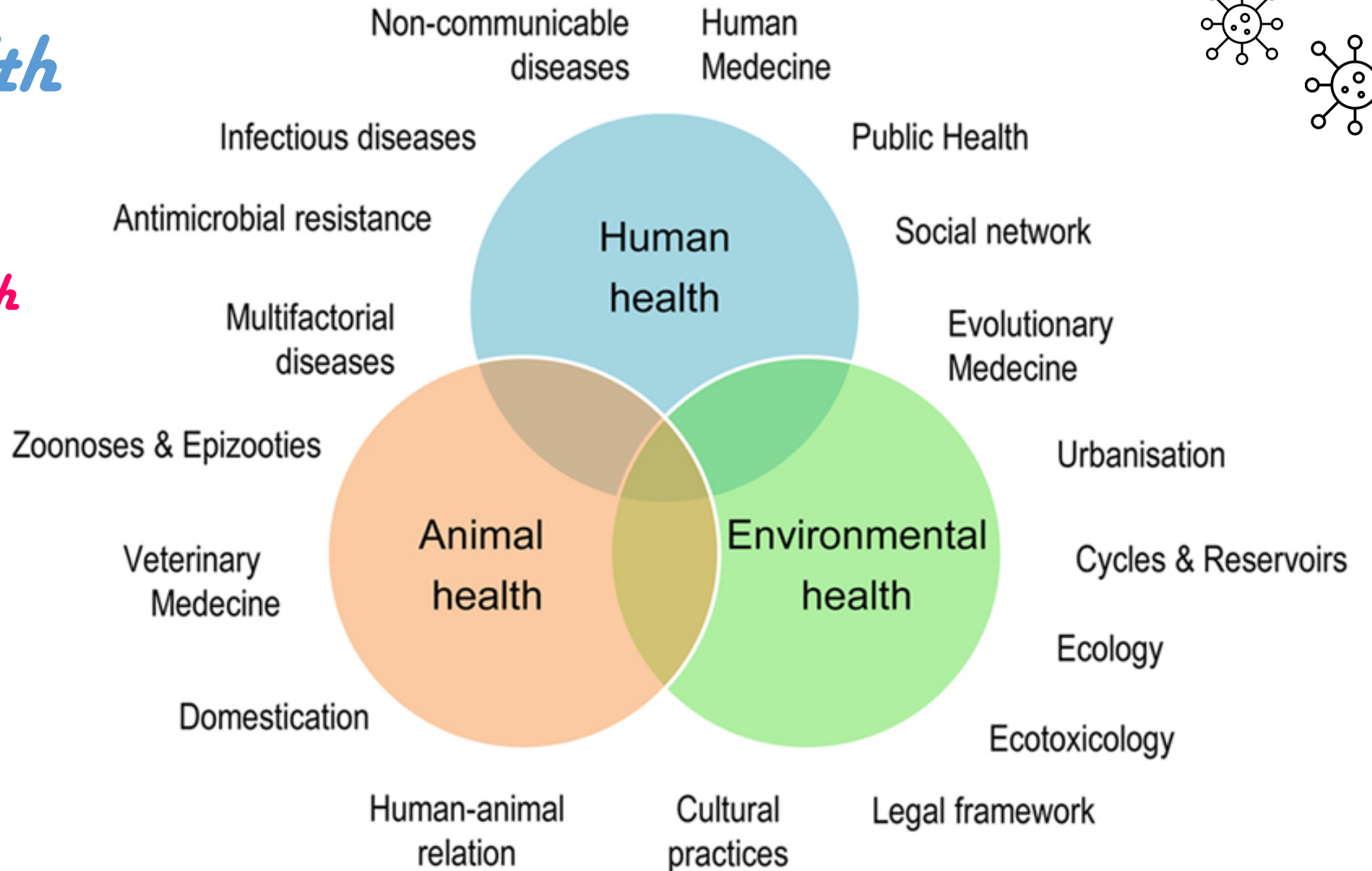
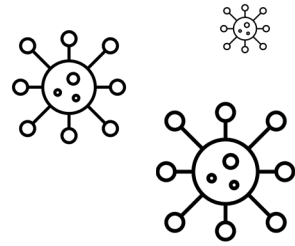
- Airborne
 - Droplet nuclei, $<5-10\mu\text{m}$
 - Negative pressure room, air handling, N95 mask
- Droplet
 - $>10\mu\text{m}$ droplets
 - Negative pressure not required, surgical mask, gown, gloves
- Bioaerosol
 - Particles suspended in air containing or generated from organic material



The big picture

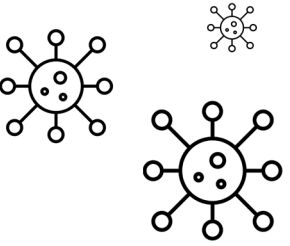
One Health

Ecohealth
Planetary health



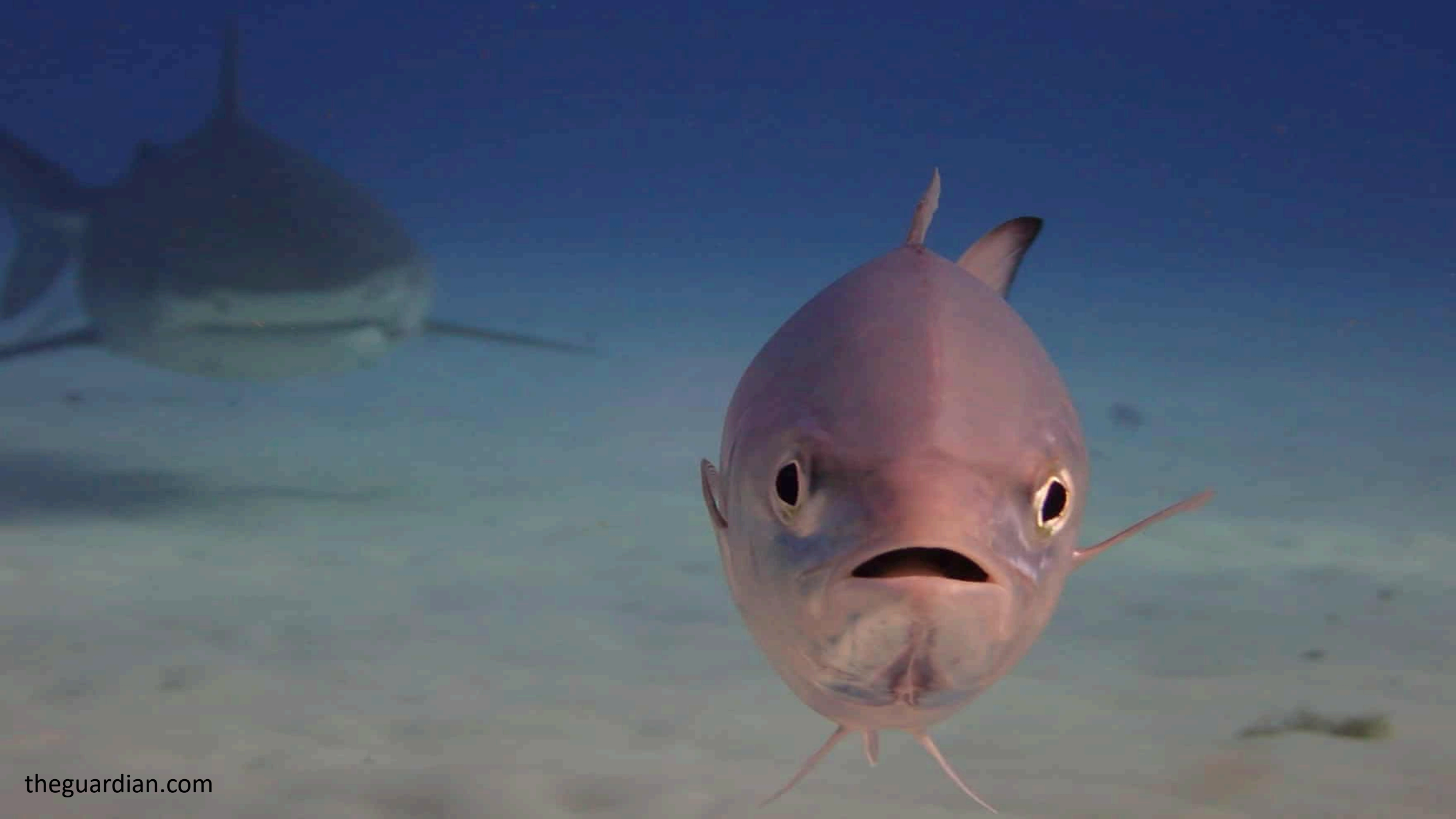




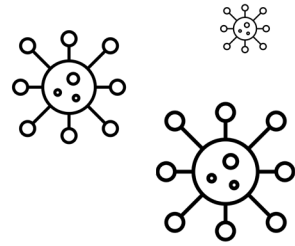


*“SARS taught us that we must
be ready for the unseen.”*

- The Honorable Judge Archie
Campbell, SARS Commission,
Spring of Fear



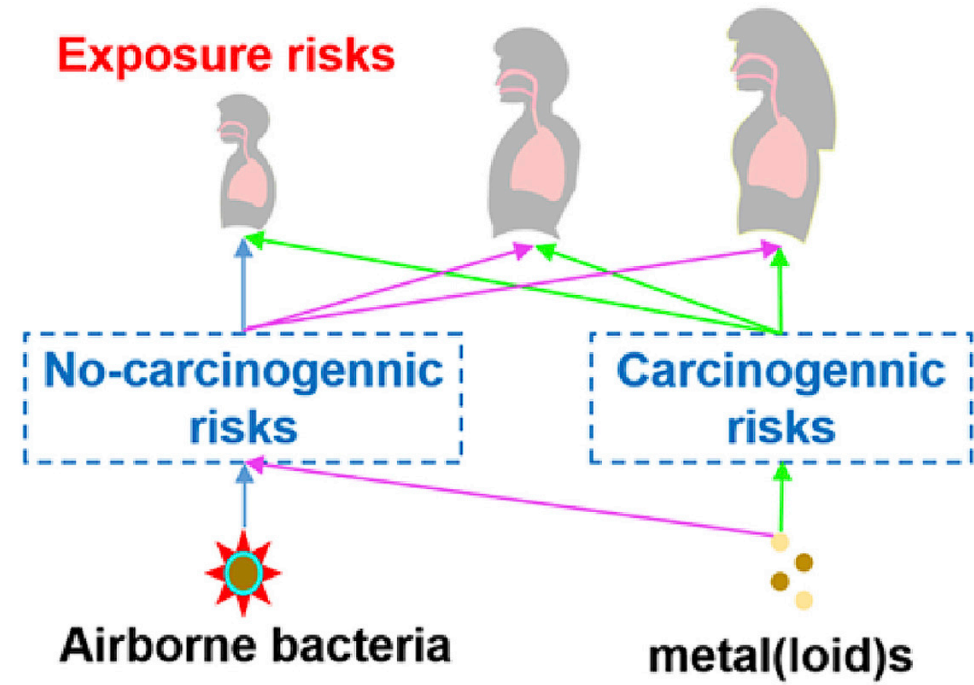
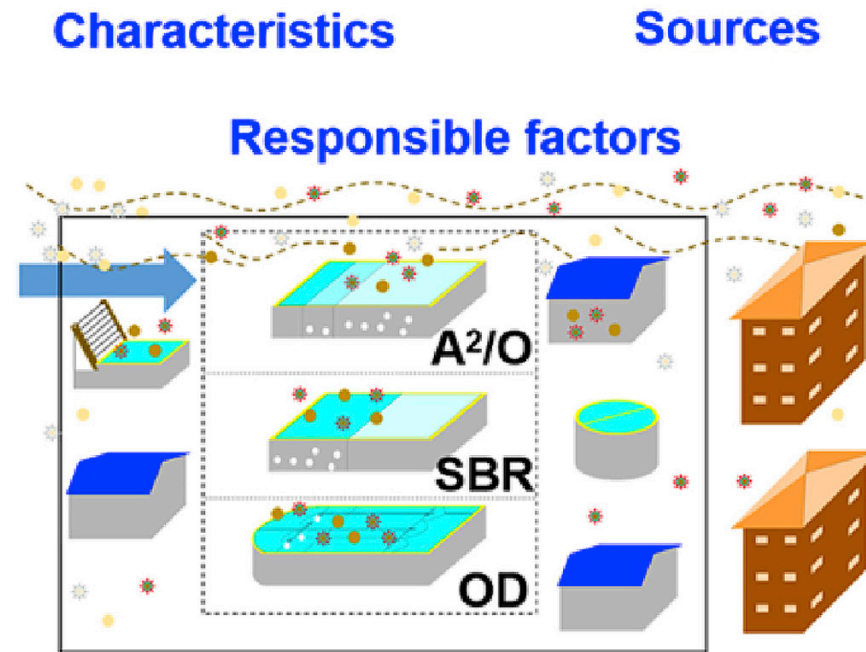
Reservoir



respirable fraction (RF) defined as aerodynamic diameter <math>< 3.30 \mu\text{m}</math>

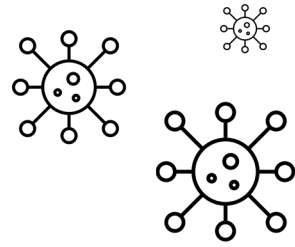


theprivycounsel.blogspot



$$ADD_{inhalation} [CFU / (kg \cdot d)] = \frac{C \times IR \times EF \times ED}{BW \times AT}$$

Workplace bioaerosols



Workplace	Total bacteria (CFU/m ³) ^a	Gram negative bacteria (CFU/m ³)	Thermophilic Actinomycetes (CFU/m ³)	Molds (CFU/m ³)
Outdoors	10 ²	10 ¹	10 ¹	10 ³
Agriculture (normal)	10 ⁷	10 ³	10 ³	10 ³⁻⁴
Agriculture (moldy hay)	10 ⁹	10 ³	10 ⁹	10 ⁹
Bakery				10 ²⁻³
Composting center	10 ⁵	10 ²	10 ⁴	10 ⁴
Wastewater treatment plant	10 ⁴	10 ⁴	10 ⁰	10 ³
Mushrooms (compost)	10 ⁶	- ^b	10 ⁷	10 ⁴
Mushrooms (cultivation)	10 ³	-	10 ²	10 ²
Household waste (collection)	10 ⁴	10 ³	10 ³	10 ⁴
Office building	10 ²	10 ¹	10 ¹	10 ²⁻³
Paper mill effluents	10 ⁴	10 ³	10 ¹	10 ⁴
Cutting fluid	10 ⁶	10 ⁴	-	10 ⁵
Humidifier	10 ³	10 ³	-	10 ²⁻³
Cotton mill	10 ⁵	10 ⁴	10 ⁵	10 ³
Papermill	10 ⁶	10 ²⁻³	-	10 ³
Pig-housing facility	10 ⁶	10 ³⁻⁴	-	10 ⁴
Sawmill	10 ⁴	10 ³⁻⁴	10 ³	10 ⁶
Peat bog	-	-	-	10 ⁸
Sugar processing	10 ⁵	10 ³	10 ²	10 ³
Household waste sorting	10 ⁴	10 ³	10 ⁰	10 ⁴
Tobacco plant	10 ⁵	10 ²	-	10 ⁴

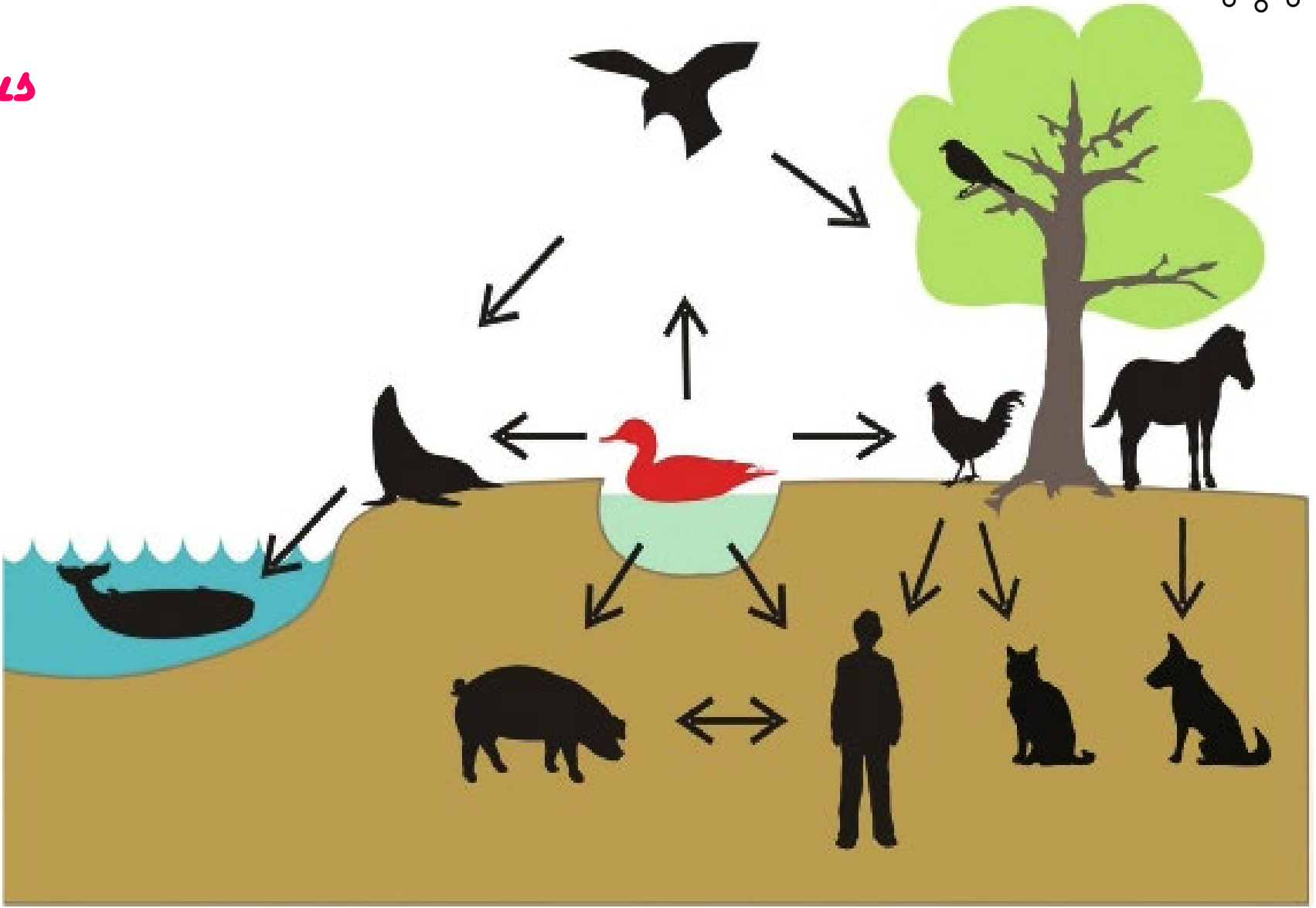
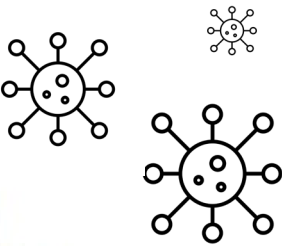
Goyer et al, Bioaerosols in the workplace.
IRSST Nov 2001

^a CFU/m³ = colony forming units per cubic meter of air

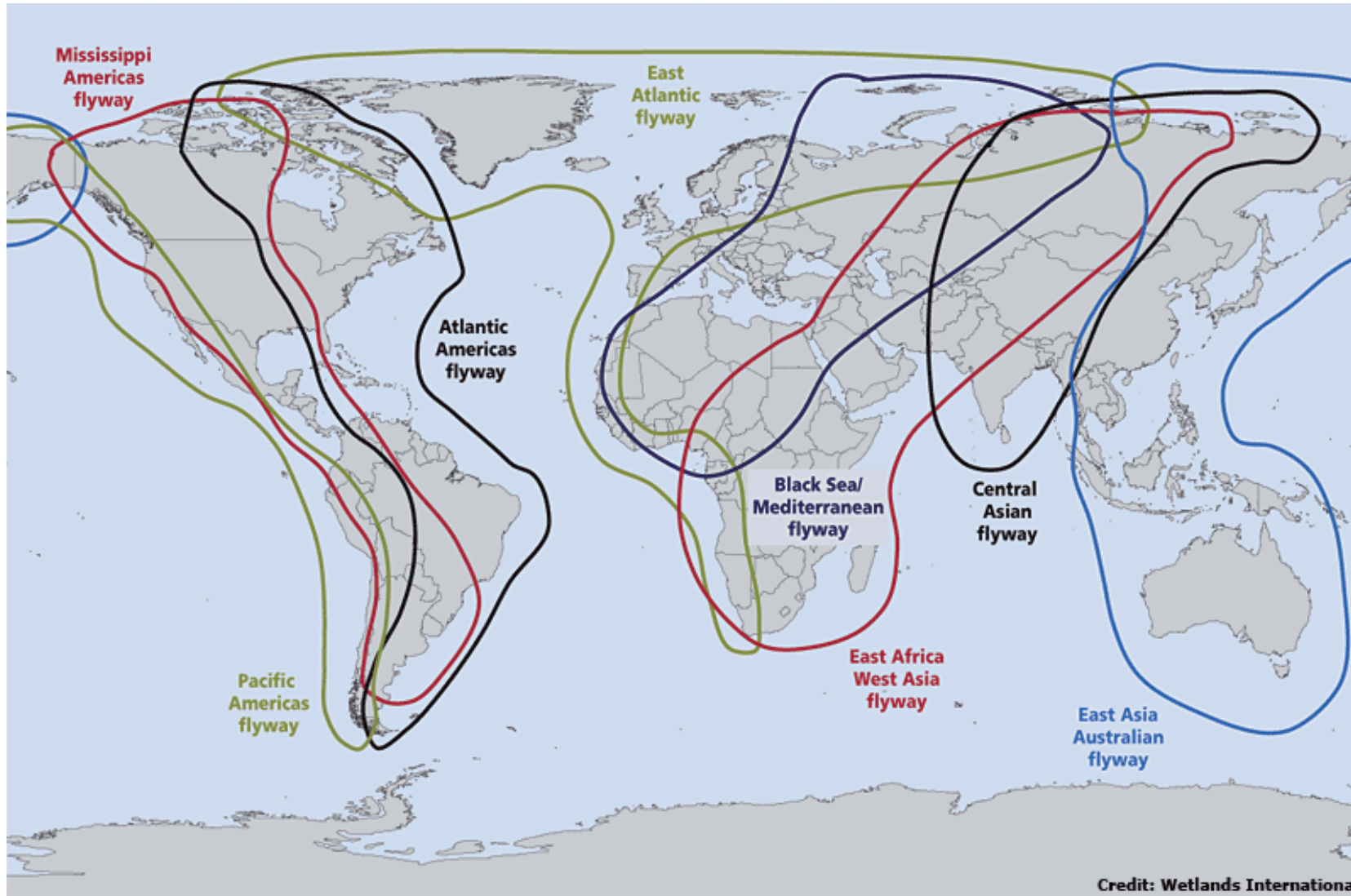
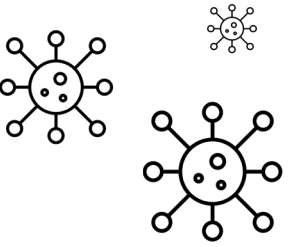
^b - = not documented

Reservoir

Influenza virus



Migratory flyways

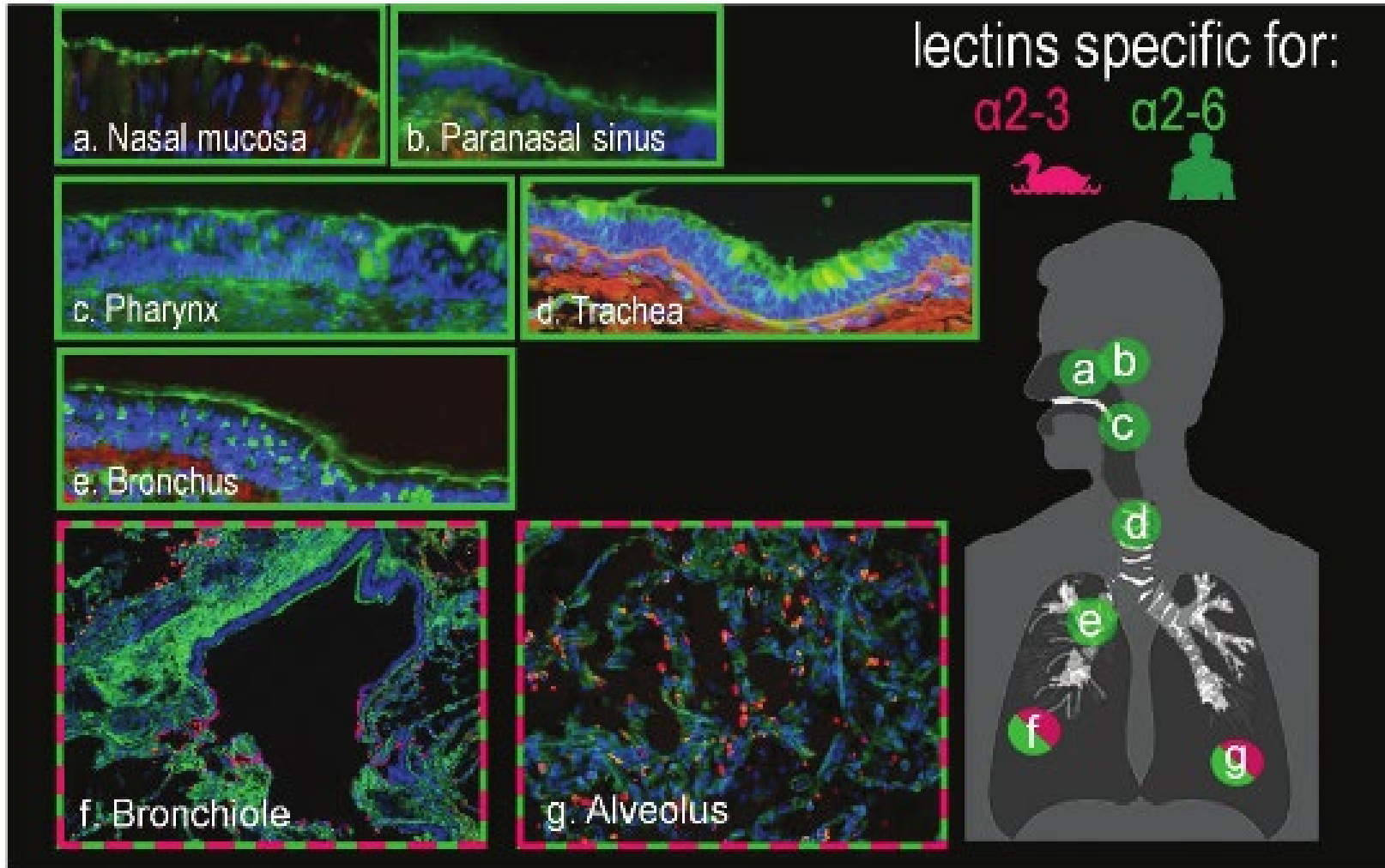
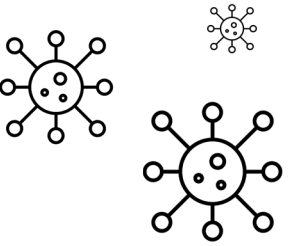


Host

- Susceptibility
- Incubation
- Disease
- Reproductive rate
- Transmissibility

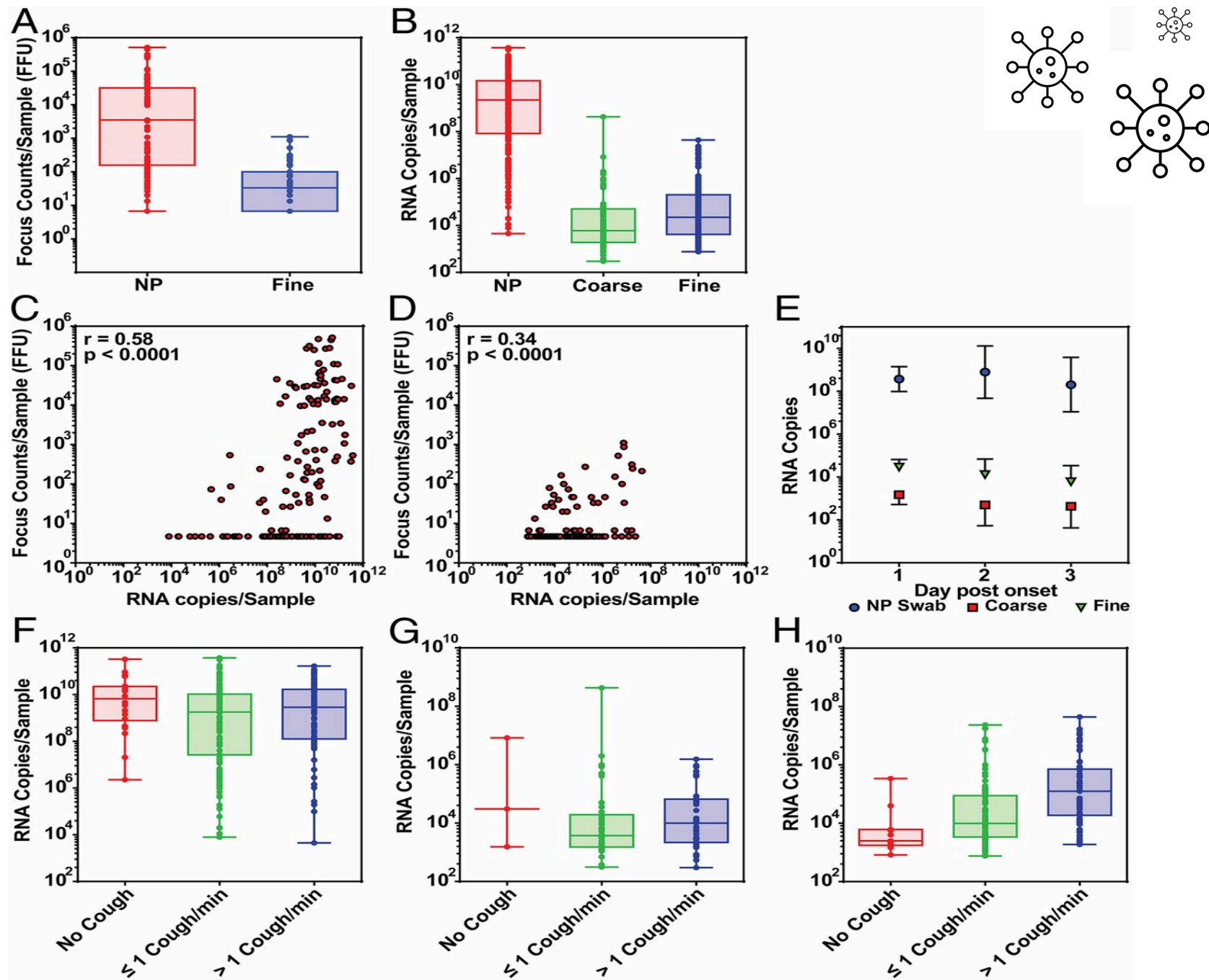


Virus receptor distribution

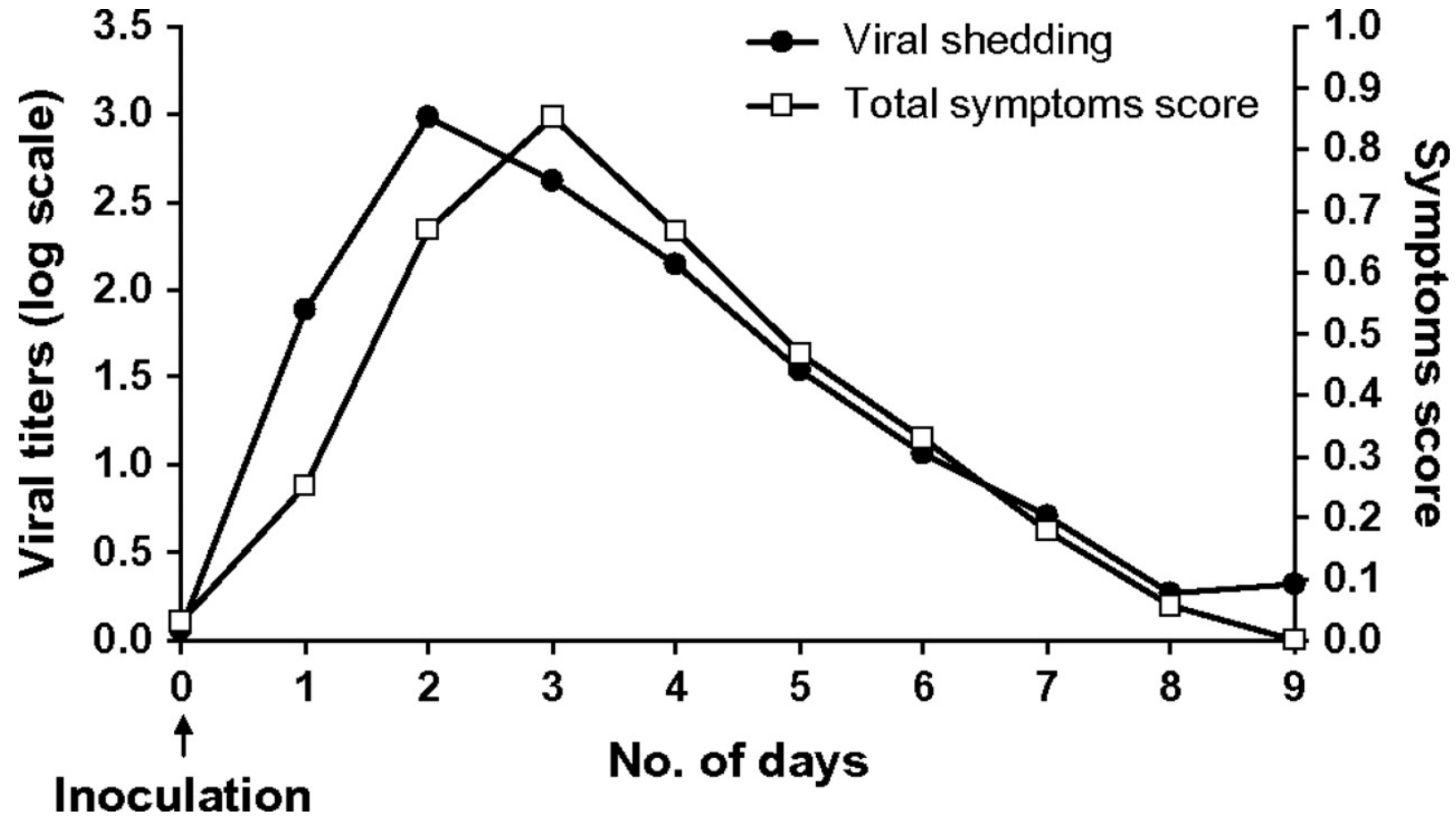
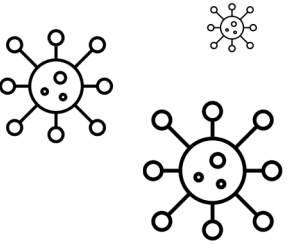


In avian species, influenza virus receptors distributed principally in GI tract

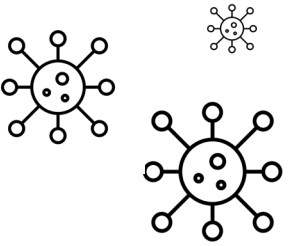
Expulsion events



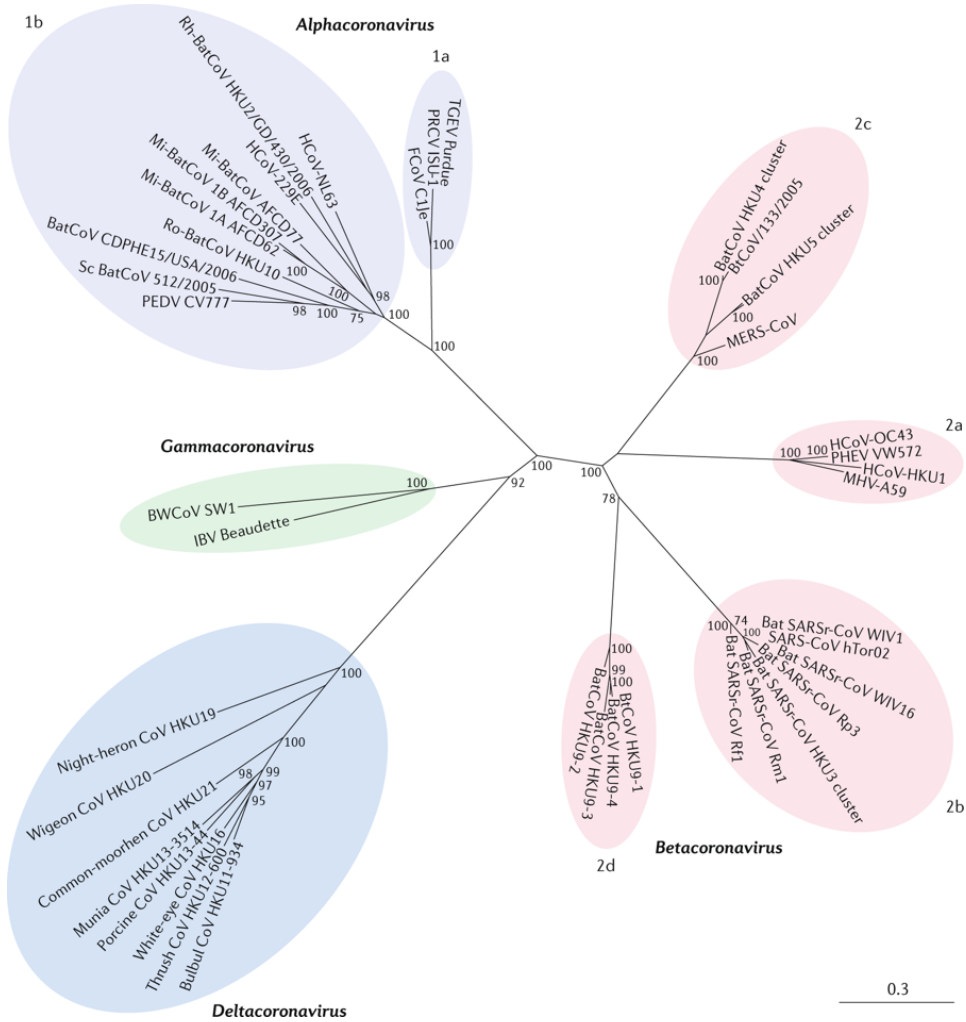
Shedding vs. disease



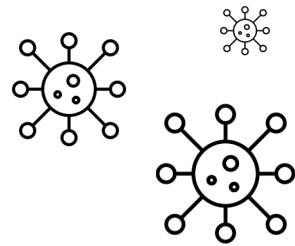
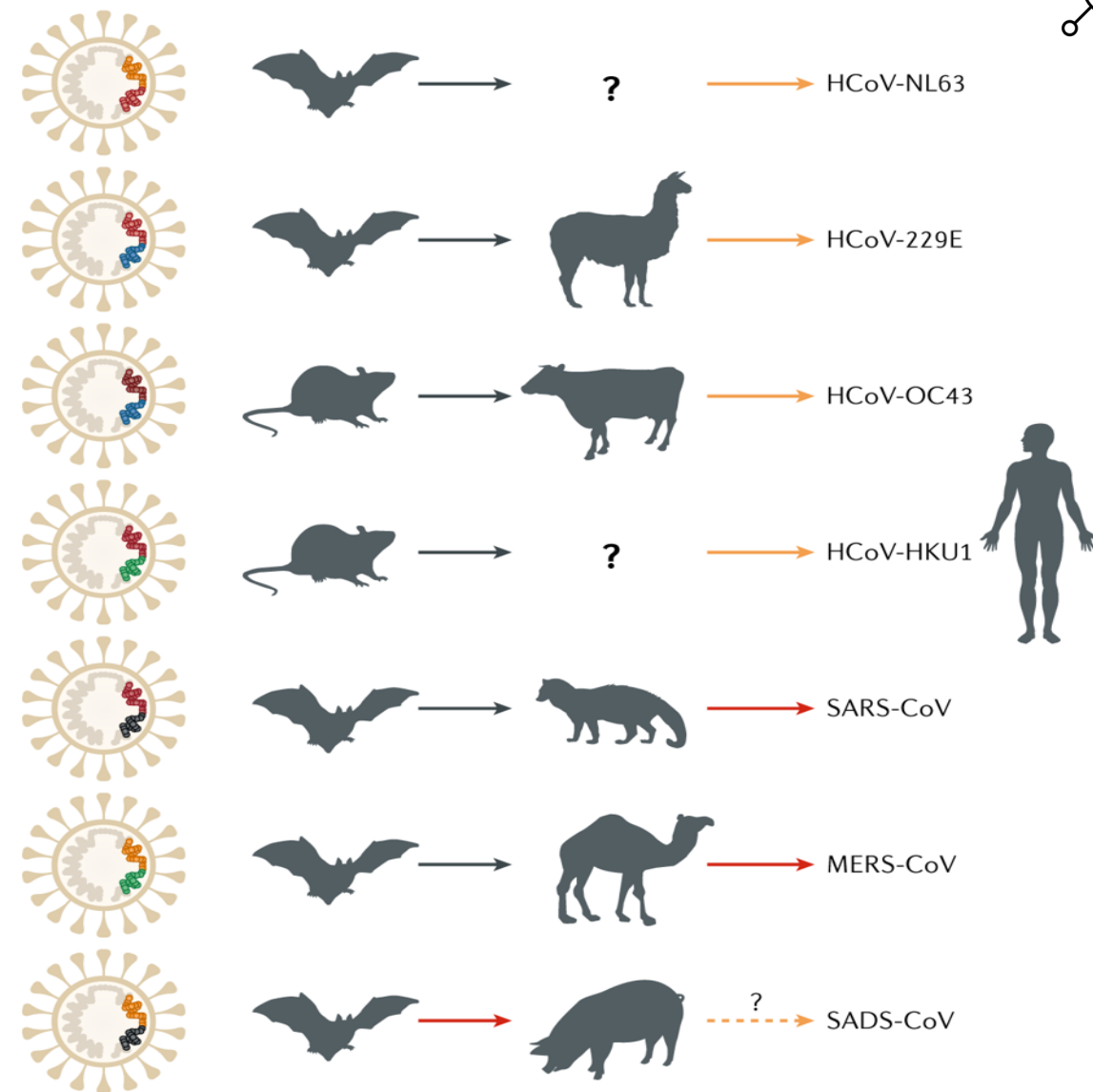
Distribution



Biology meets ecology



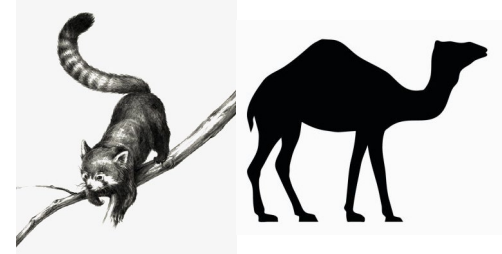
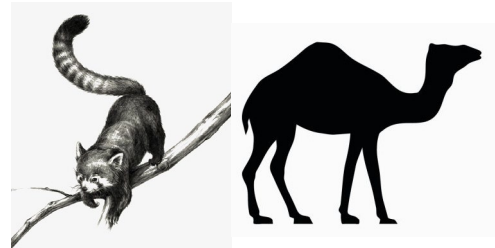
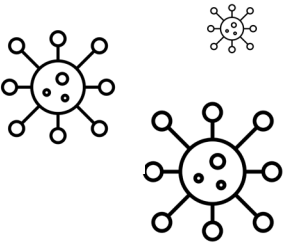
Genetically diverse coronaviruses Natural host Intermediate host Human host



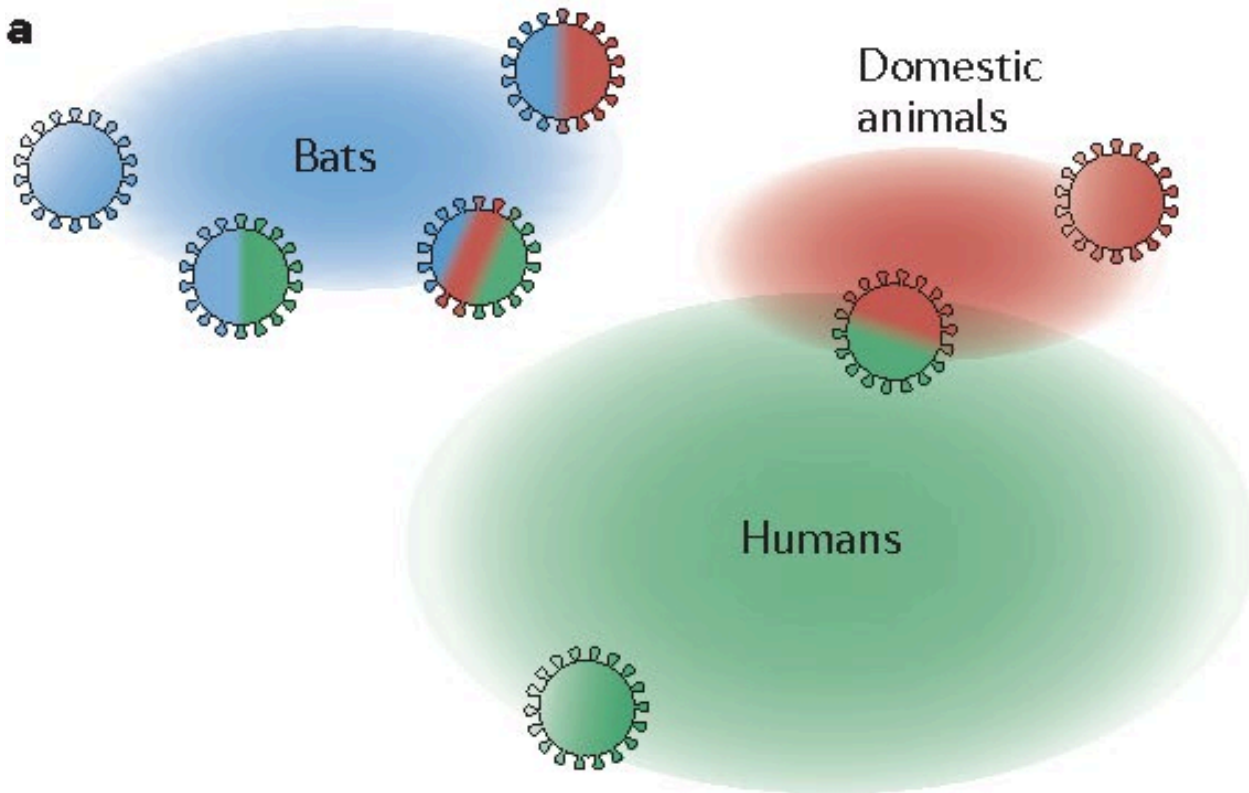
Spillover to intermediate hosts
 Mild infection
 Severe infection

Ecology

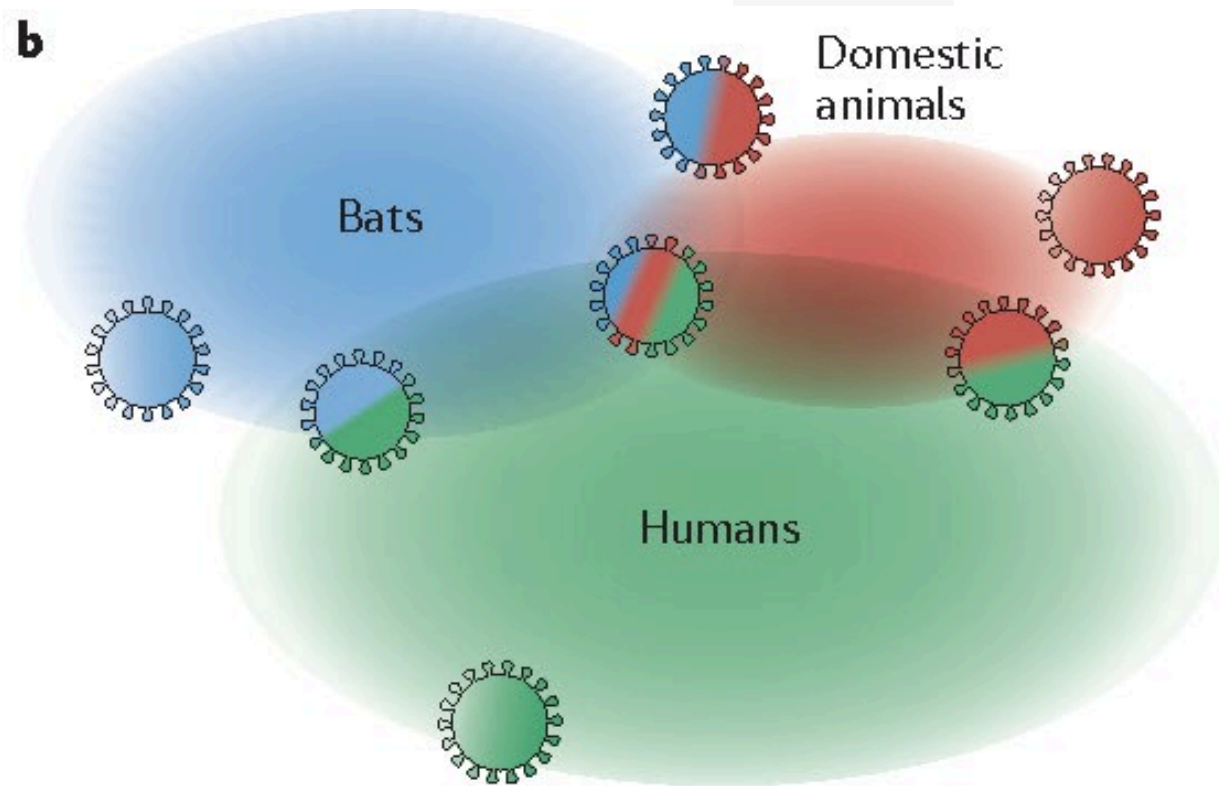
High consequence coronaviruses



a

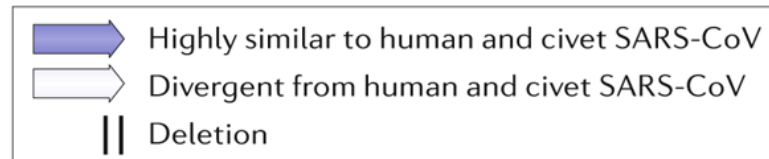
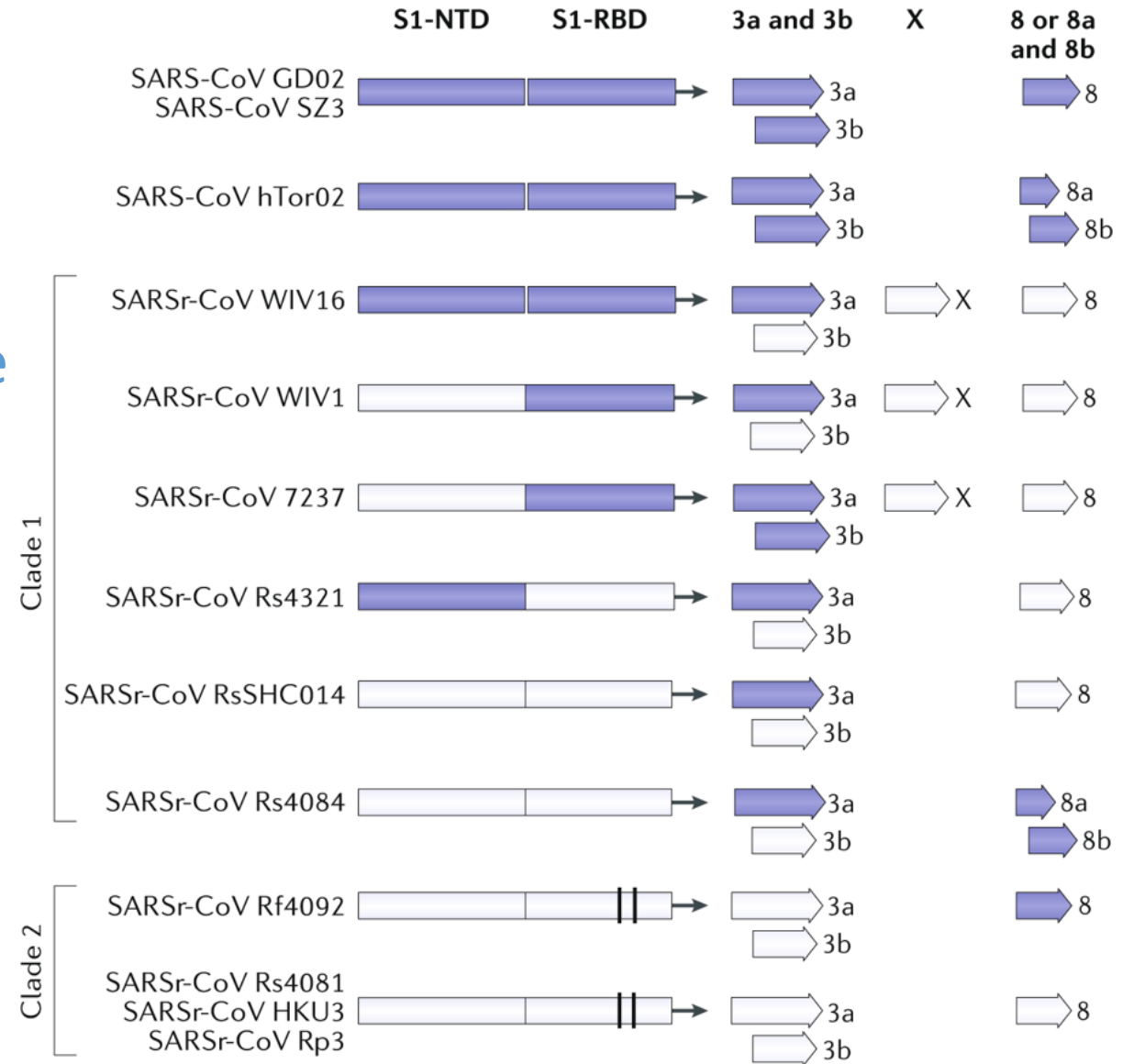


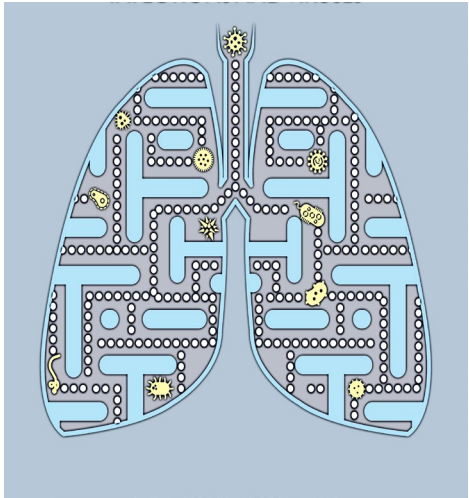
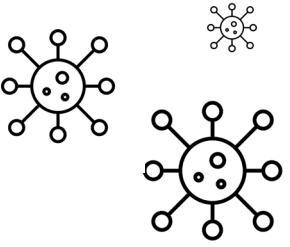
b



Ecology *Meets biology...*

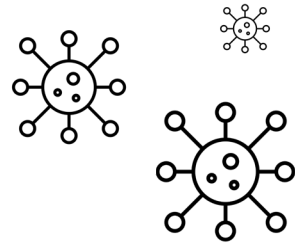
- Variability and thus species adaptation important in emergence of acute respiratory syndrome coronavirus (SARS-CoV)
- Spike protein (S)
 - S1 amino-terminal domain (S1-NTD)
 - S1 receptor-binding domain (S1-RBD) show variability



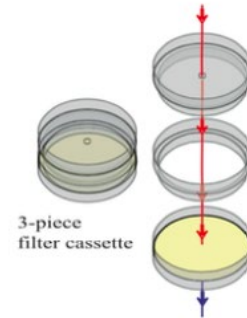


Tools and instruments

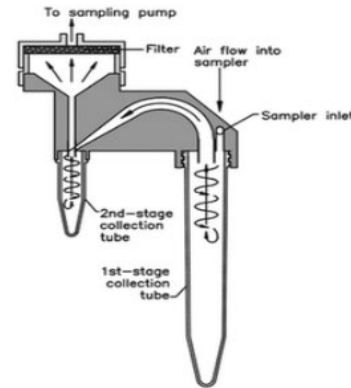
Air Samplers



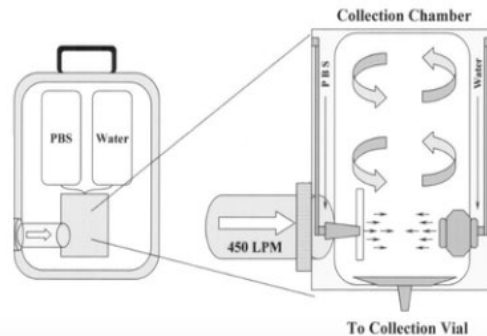
Teflon filter



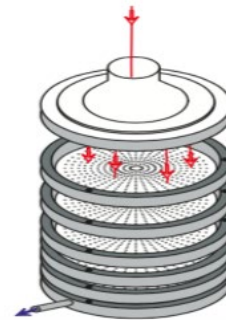
NIOSH cyclone



Spincon® instrument



Andersen impactor



Verreault et al., Microbiology and Molecular Biology Reviews, 2008
Cao et al., Journal of Environmental Monitoring, 2011
Brasel, T.L., et al., Applied and Environmental Microbiology, 2005
bertin-instruments.com

Influenza virus	Relative humidity condition ^a	Viral RNA (copies/L air ^b ± SEM ^c)		Infectious virus (PFU/L air ^d ± SEM ^c)		Viral RNA to infectious virus ratio (copies/PFU) ^e	
		PTFE filter	NIOSH cyclone sampler	PTFE filter	NIOSH cyclone sampler	PTFE filter	NIOSH cyclone sampler
H1N1	Low	2.4 x 10 ⁵ ± 5.7 x 10 ⁴	2.4 x 10 ⁵ ± 6.4 x 10 ⁴	1.2 x 10 ² ± 6.1 x 10 ¹	1.3 x 10 ² ± 7.4 x 10 ¹	2.1 x 10 ³	1.9 x 10 ³
	Medium	3.0 x 10 ⁵ ± 9.1 x 10 ⁴	2.9 x 10 ⁵ ± 9.9 x 10 ⁴	1.7 x 10 ¹ ± 1.6 x 10 ¹	3.1 x 10 ¹ ± 2.3 x 10 ¹	1.8 x 10 ⁴	9.5 x 10 ³
	High	1.8 x 10 ⁵ ± 3.0 x 10 ⁴	1.9 x 10 ⁵ ± 6.4 x 10 ⁴	3.4 x 10 ¹ ± 1.1 x 10 ¹	5.4 x 10 ¹ ± 2.6 x 10 ¹	5.1 x 10 ³	3.4 x 10 ³
H3N2	Low	3.4 x 10 ⁶ ± 5.7 x 10 ⁵	3.5 x 10 ⁶ ± 3.3 x 10 ⁵	2.9 x 10 ² ± 1.6 x 10 ²	3.3 x 10 ² ± 1.9 x 10 ²	1.2 x 10 ⁴	1.1 x 10 ⁴
	Medium	1.9 x 10 ⁶ ± 6.2 x 10 ⁵	1.7 x 10 ⁶ ± 5.5 x 10 ^{5*}	1.3 x 10 ² ± 2.7 x 10 ¹	1.5 x 10 ² ± 2.8 x 10 ¹	1.4 x 10 ⁴	1.1 x 10 ⁴
	High	1.8 x 10 ⁶ ± 2.5 x 10 ⁵	1.8 x 10 ⁶ ± 2.9 x 10 ⁵	1.8 x 10 ² ± 2.8 x 10 ¹	2.1 x 10 ² ± 1.3 x 10 ¹	1.0 x 10 ⁴	8.6 x 10 ³

^aLow is <25% relative humidity, medium is 47-53% relative humidity, and high is 78-83% relative humidity.

^bViral RNA was determined by RT-qPCR and presented as copies of RNA per litre air sampled.

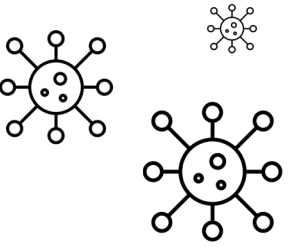
^cSEM = standard error of the mean (n=3 per relative humidity condition).

^dInfectious virus was determined by plaque assay and presented as PFU per litre air sampled.

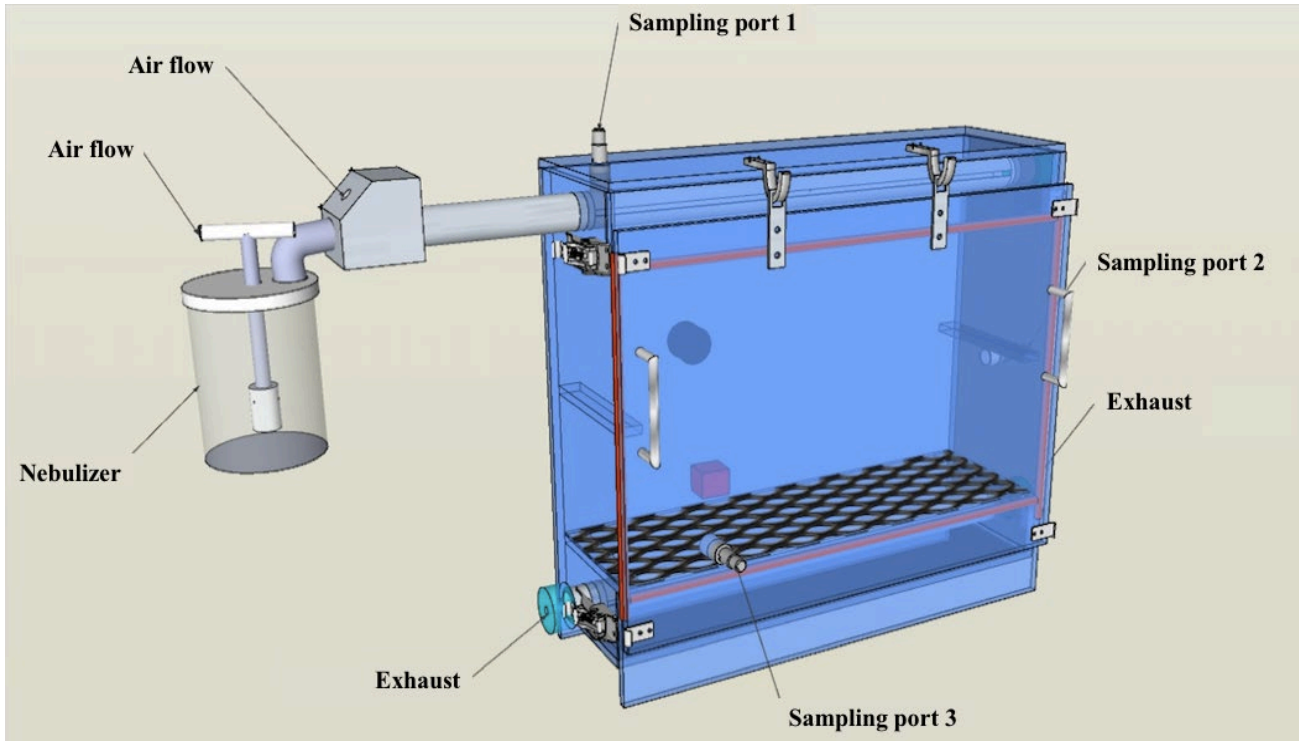
^eViral RNA to infectious virus ratio was determined by dividing viral RNA copies per litre air sampled by PFU per litre air sampled.

*Significantly less than H3N2 RNA recovered by the NIOSH cyclone sampler at low relative humidity ($p < 0.05$).

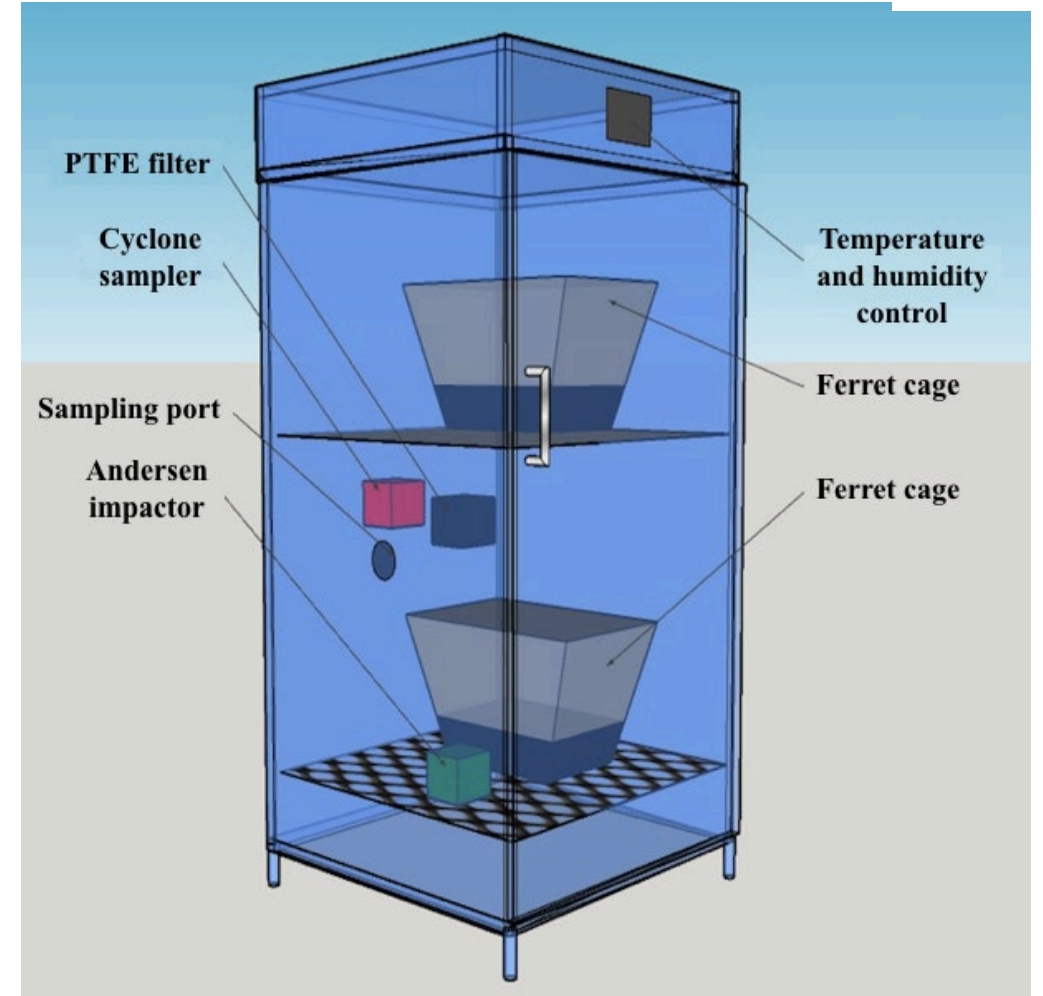
Aerosol chambers



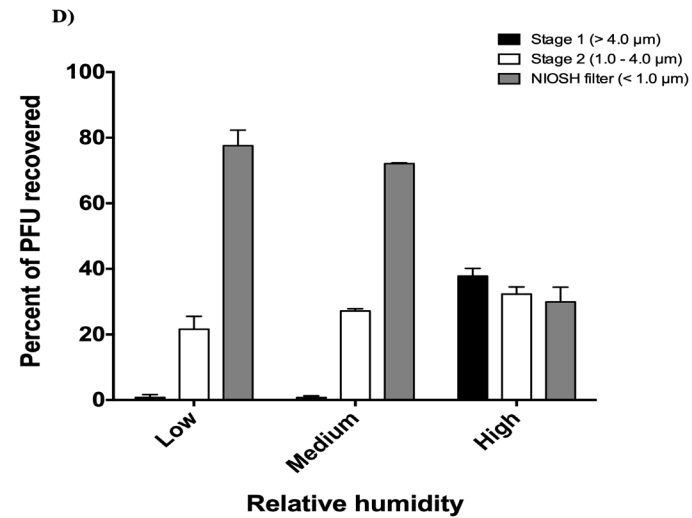
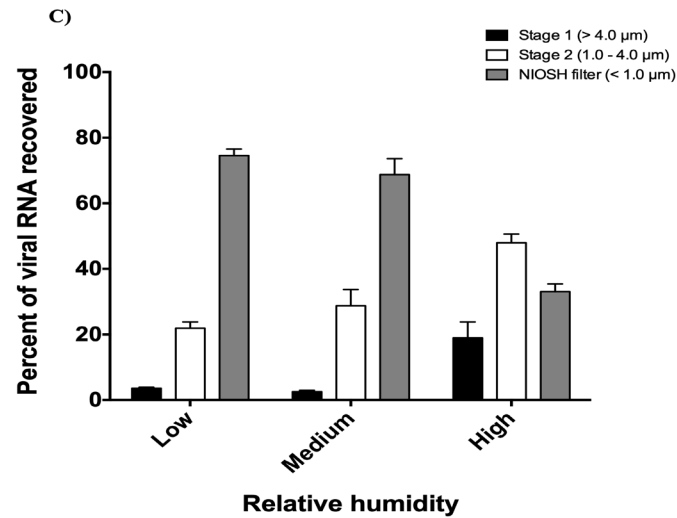
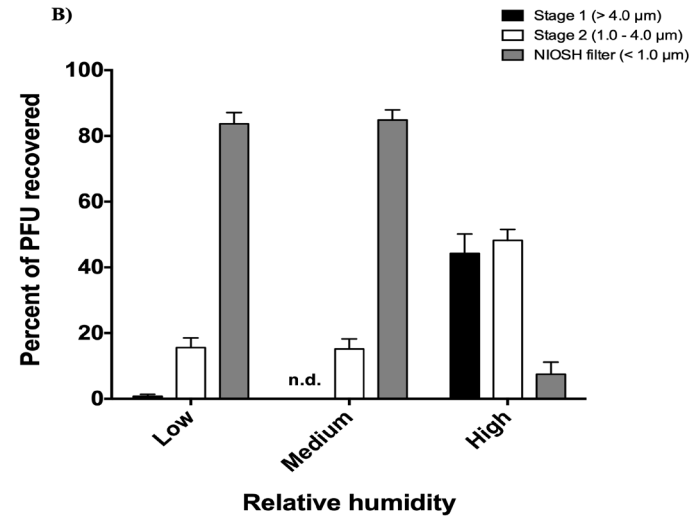
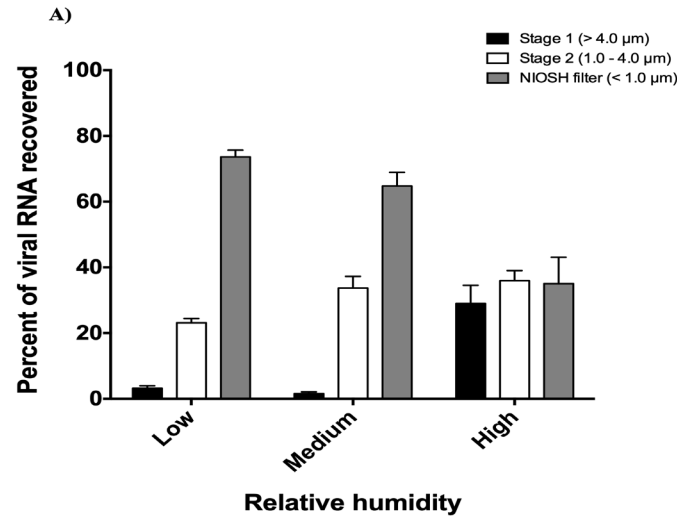
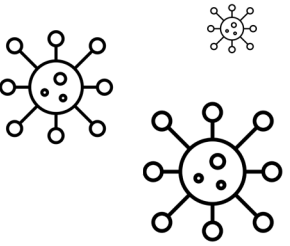
A)



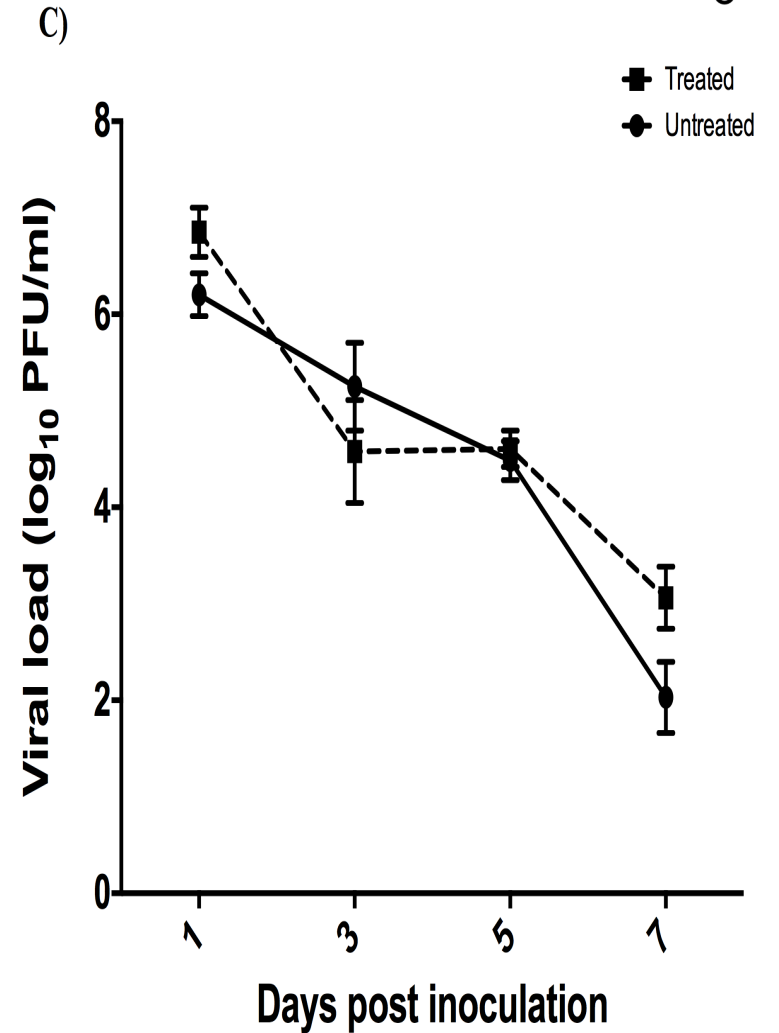
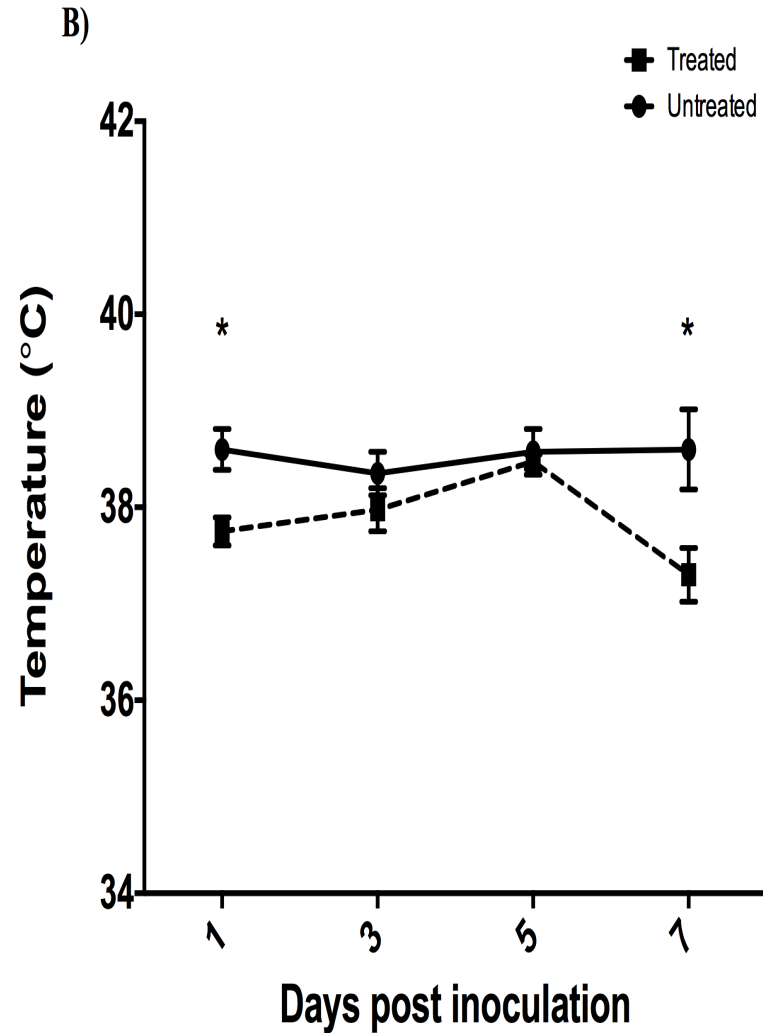
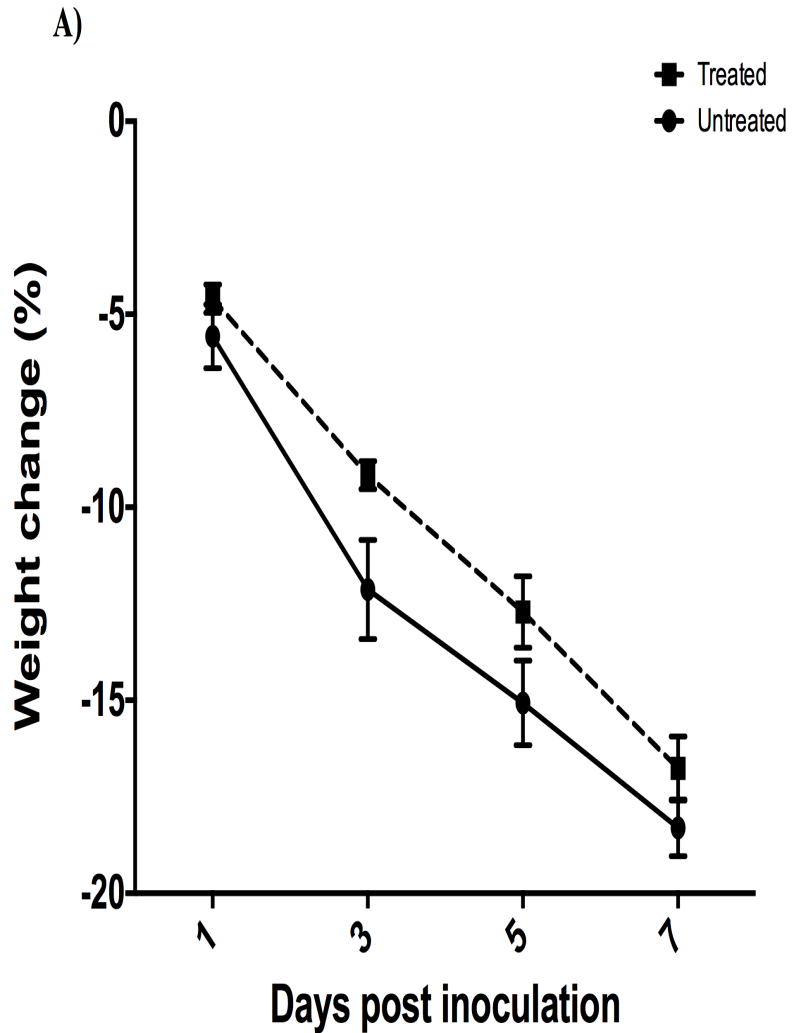
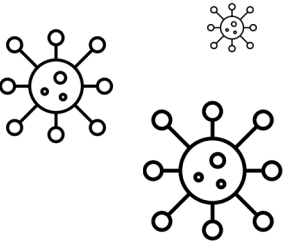
B)



Relative humidity and *in vitro* bioaerosols

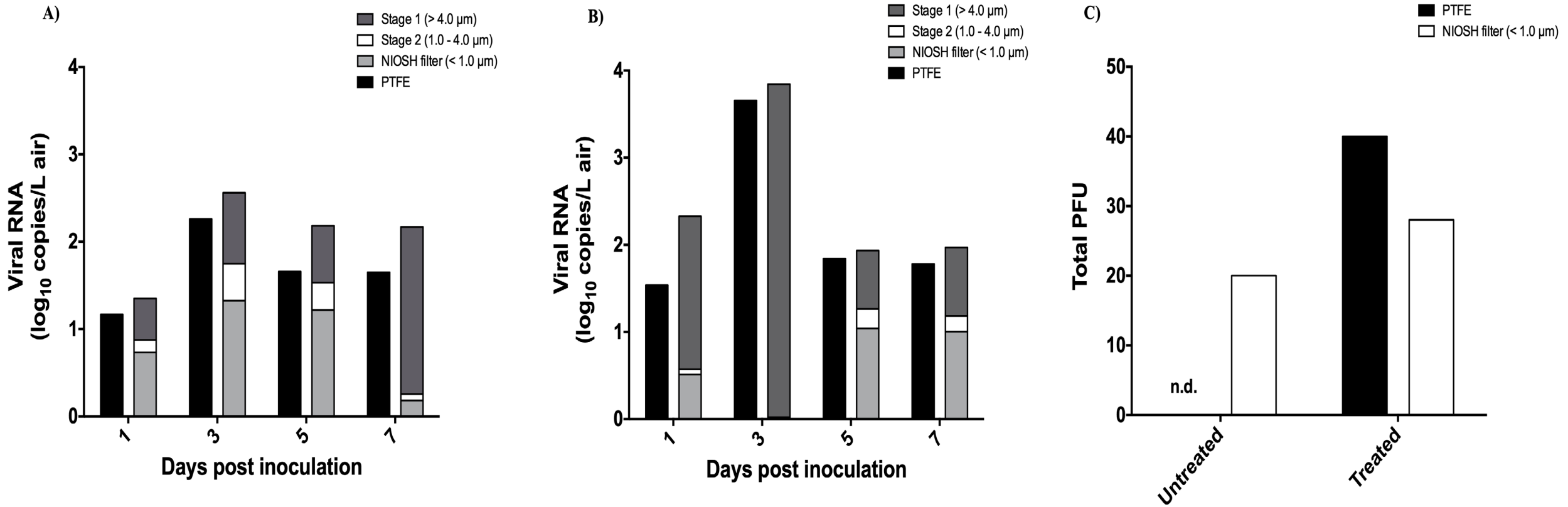
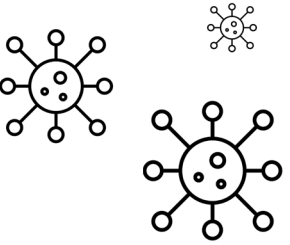


Recovery of influenza virus from inoculated ferrets



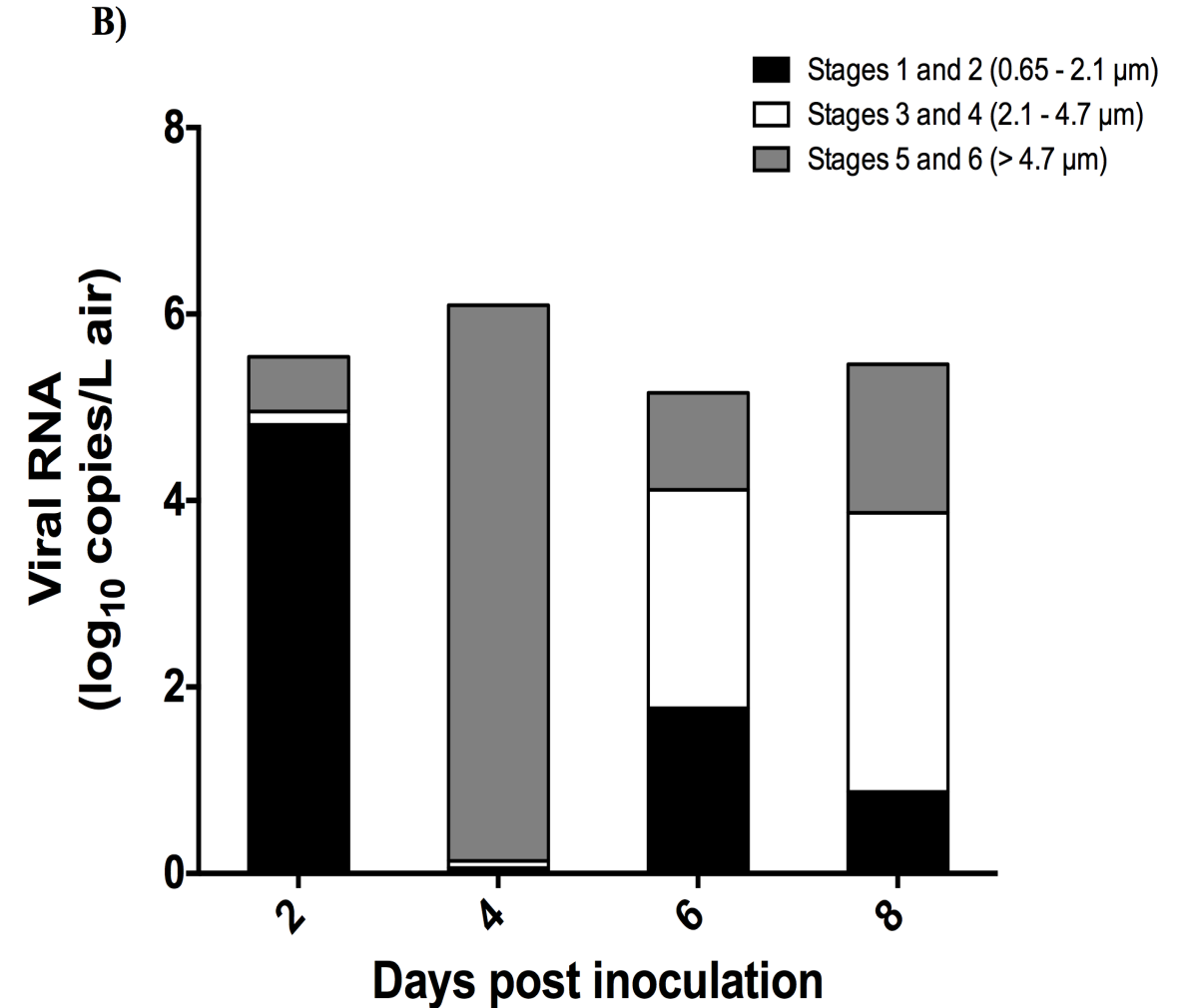
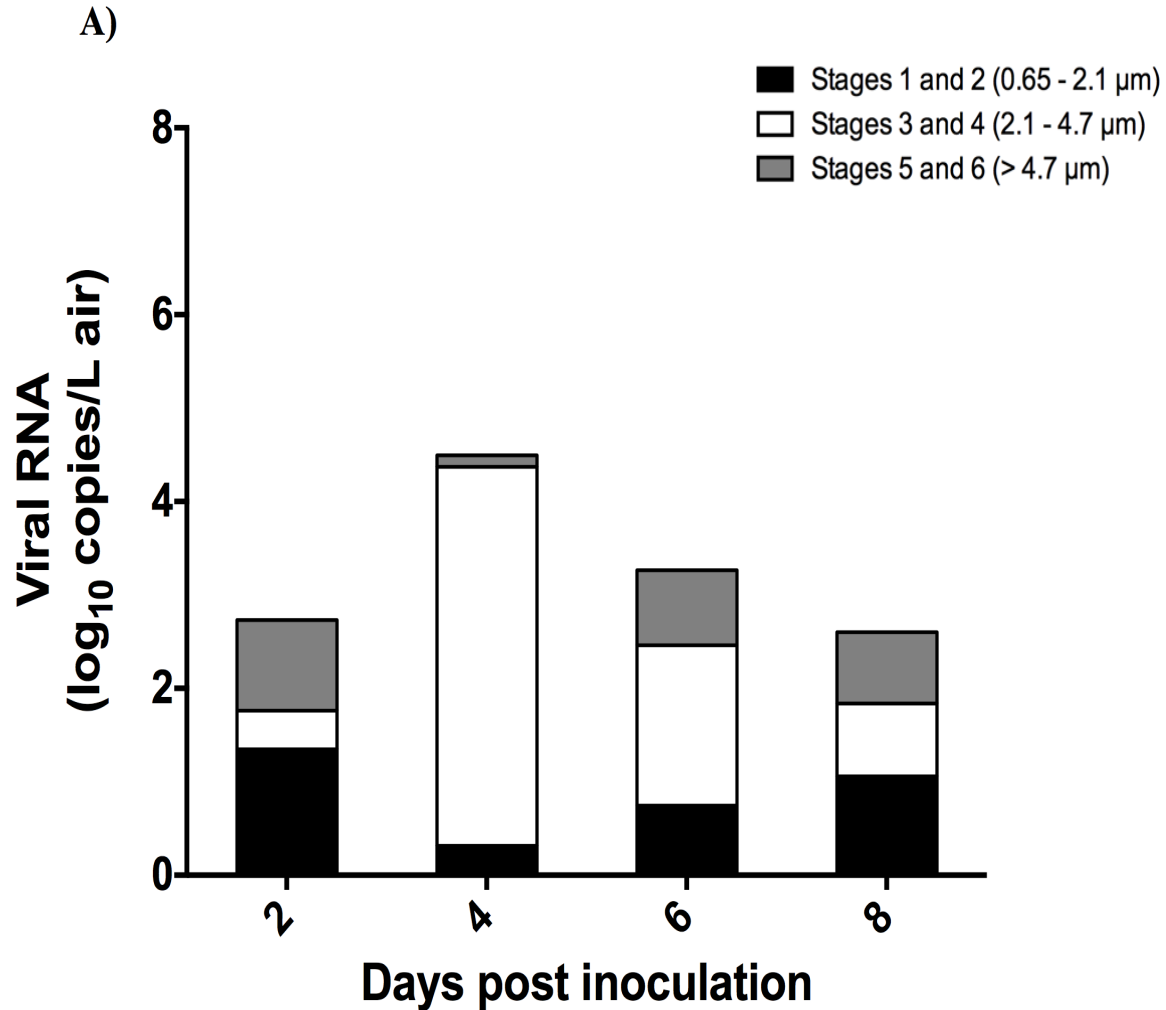
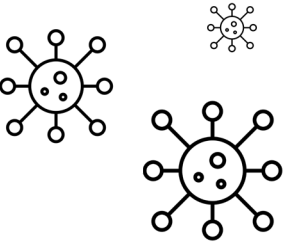
Recovery of influenza virus from bioaerosols produced in vivo

PTFE and NIOSH samplers



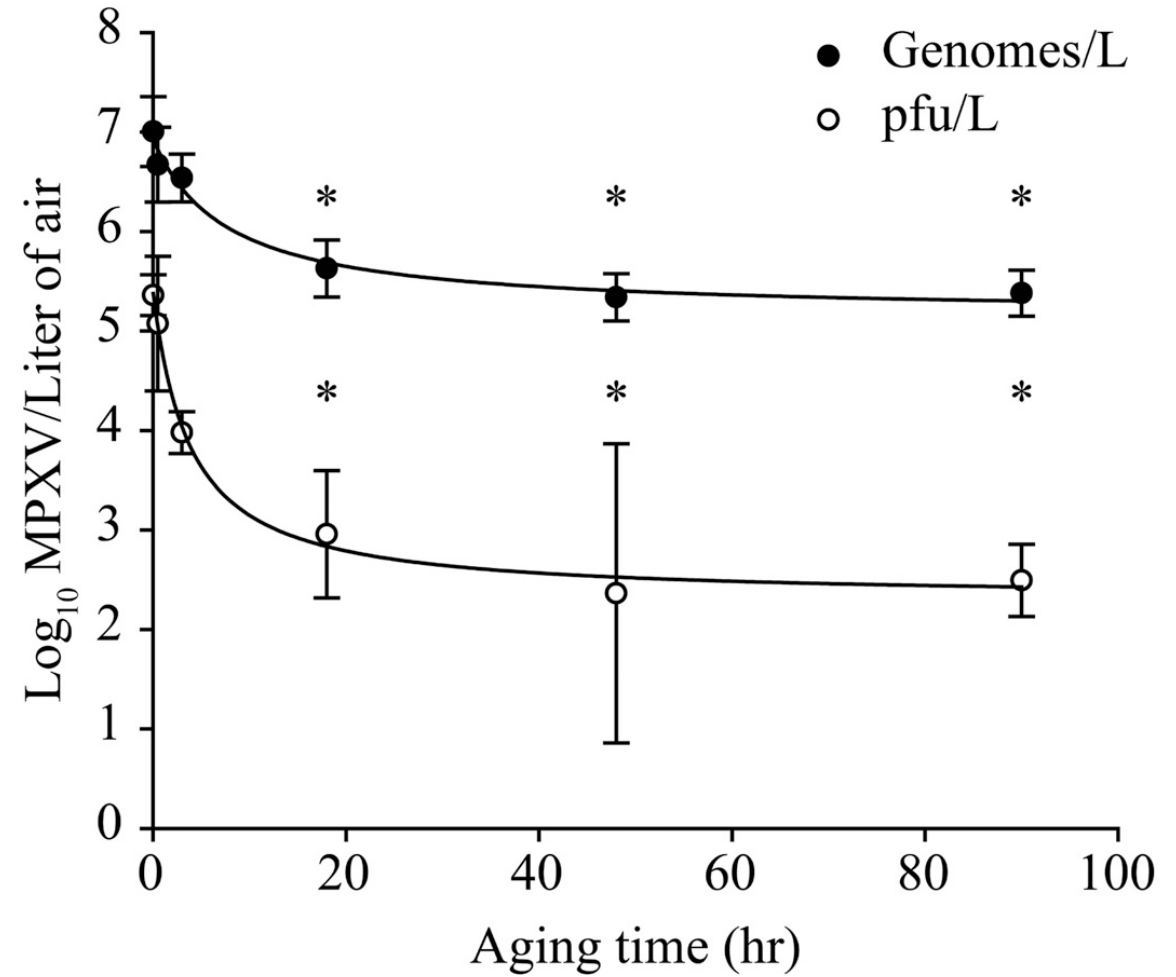
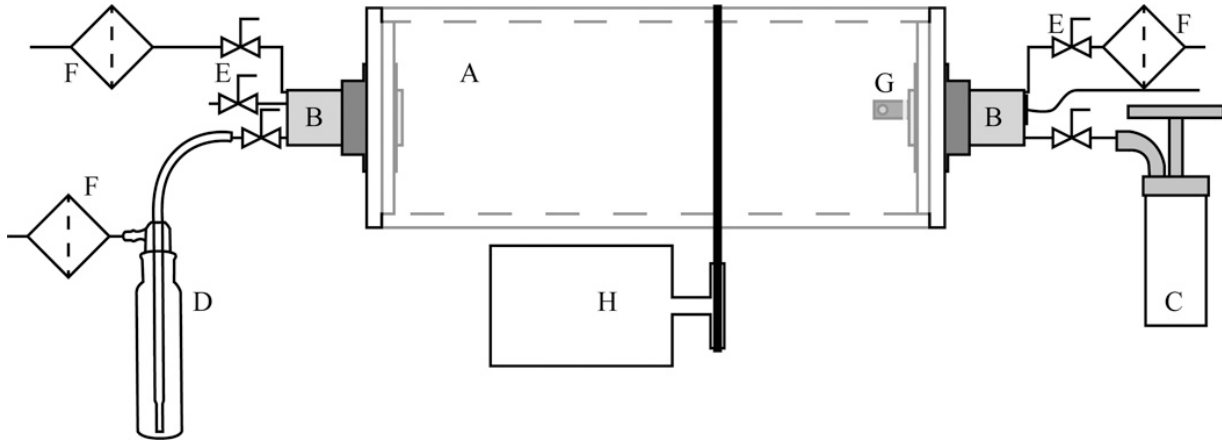
Recovery of influenza virus from bioaerosols produced in vivo

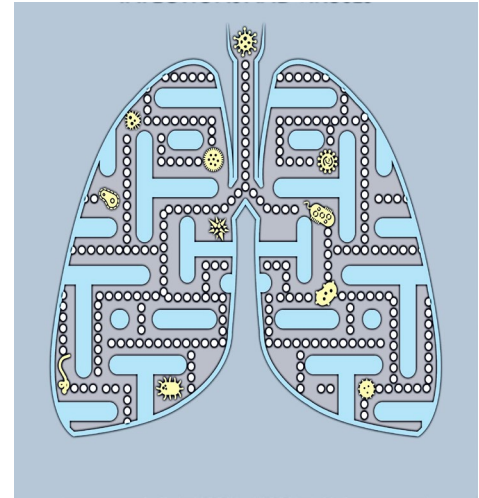
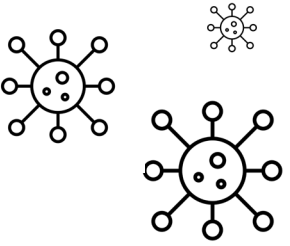
Andersen impactor



Aerosol survival

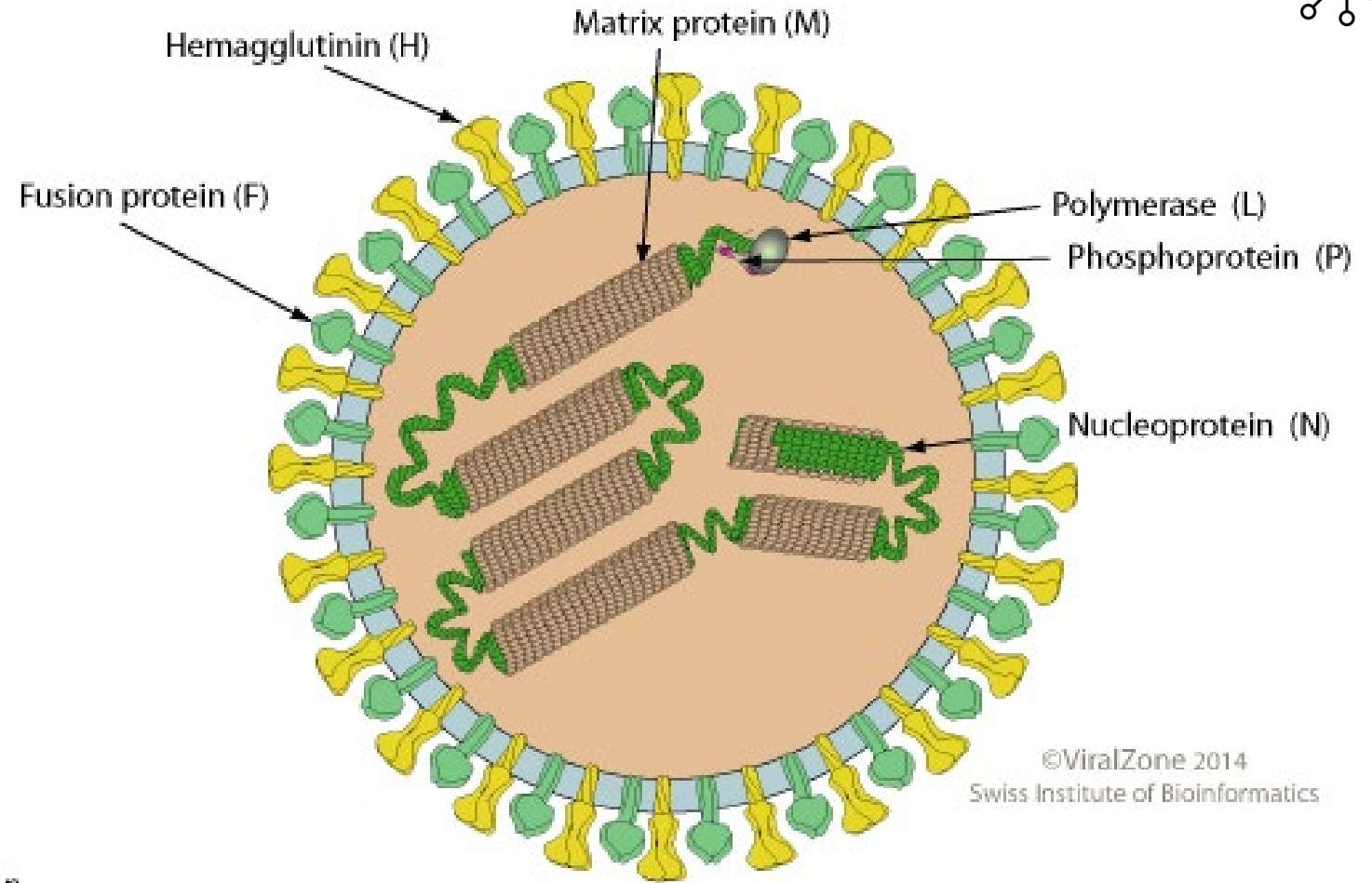
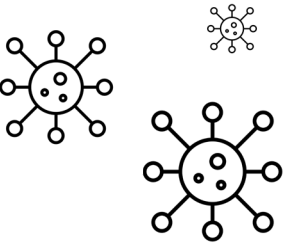
Monkeypox



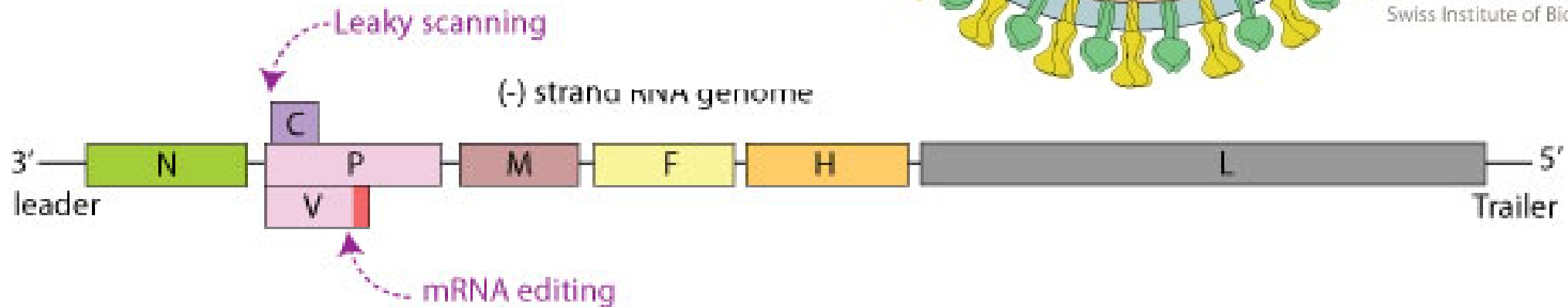


*Scenario:
Community, P2P*

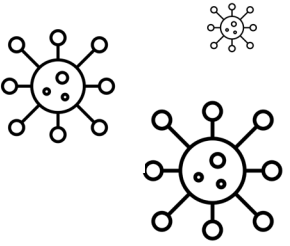
Measles virus



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Swiss Institute of Bioinformatics



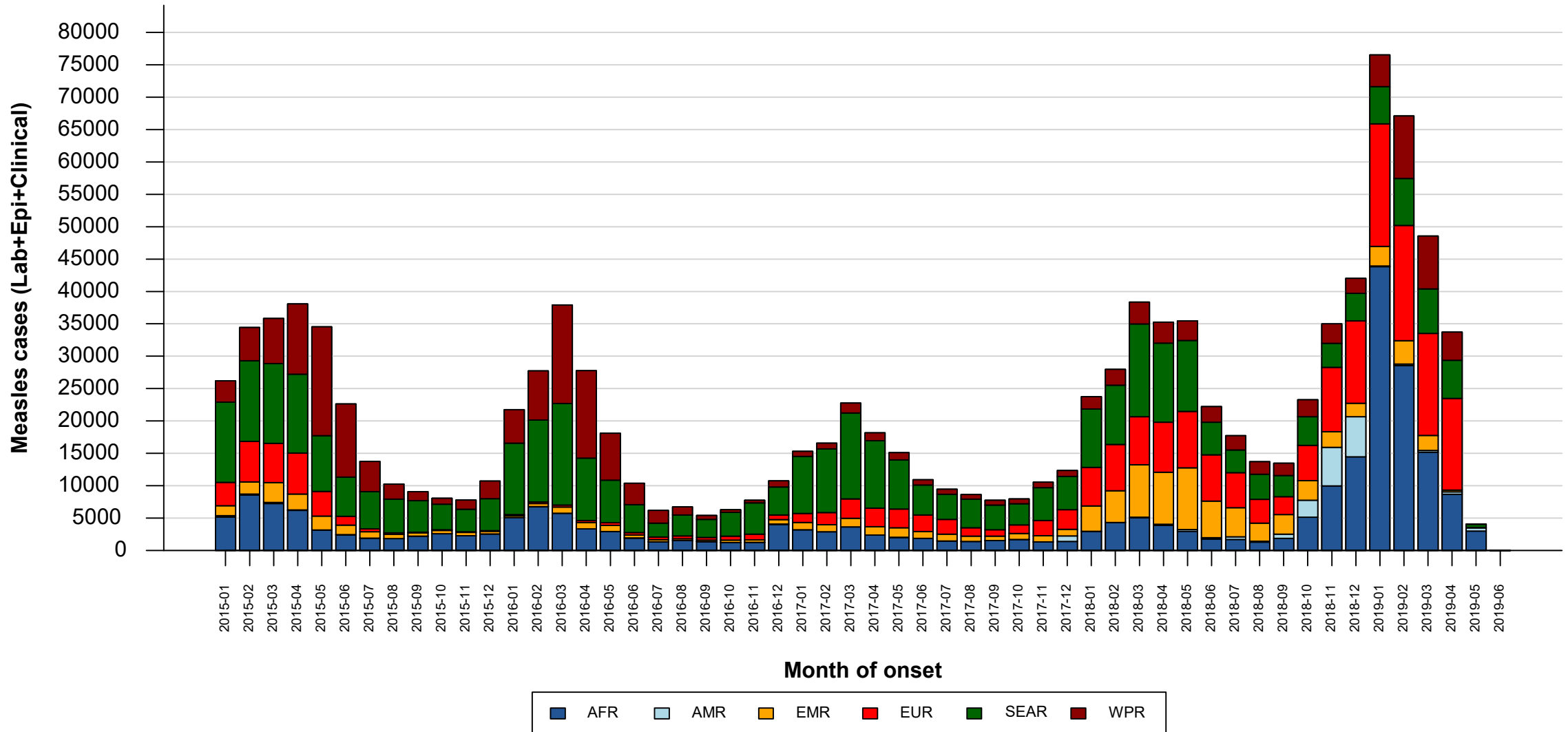
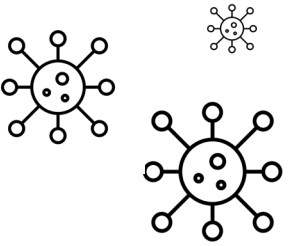
Measles reproduction rate



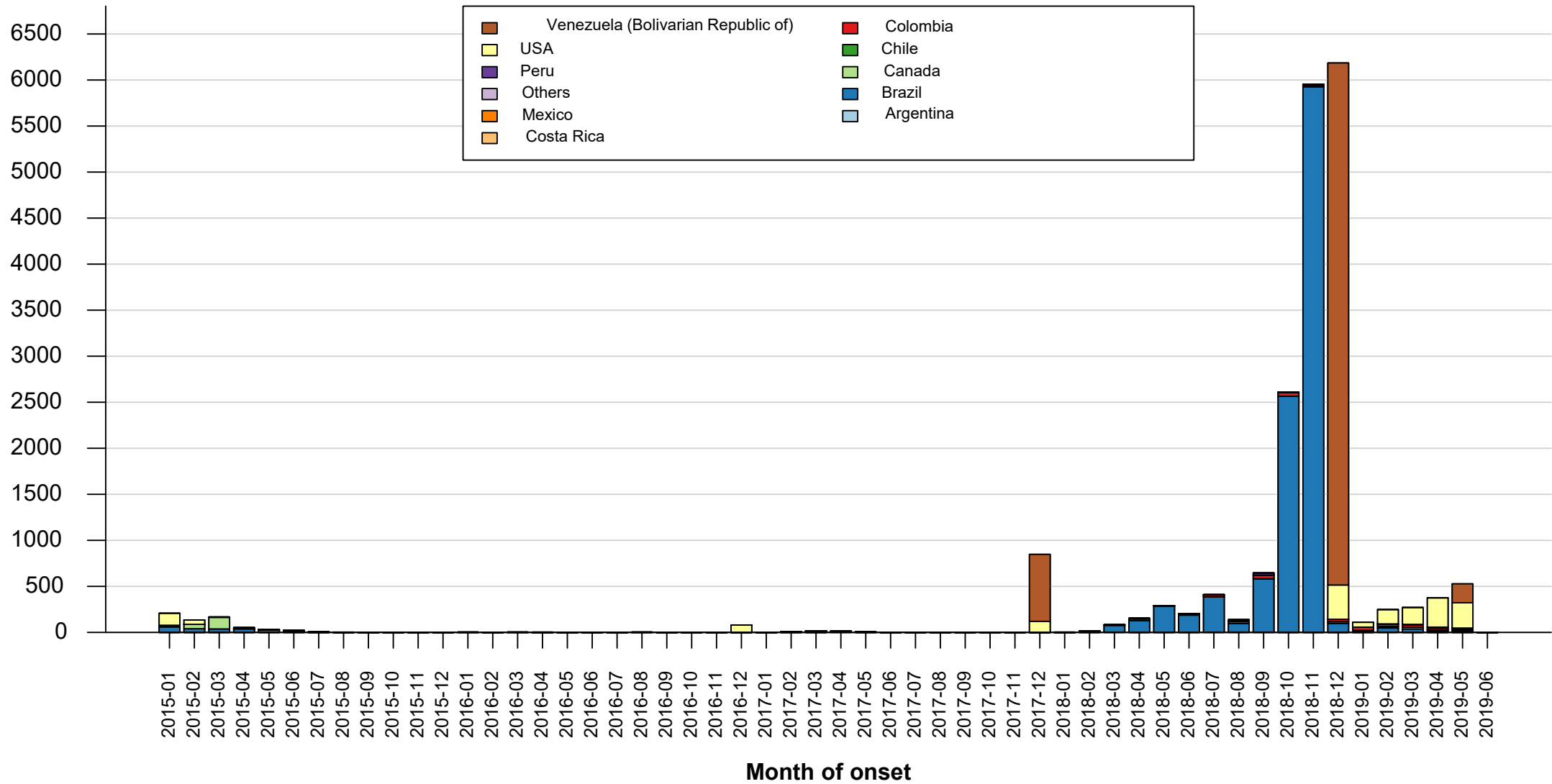
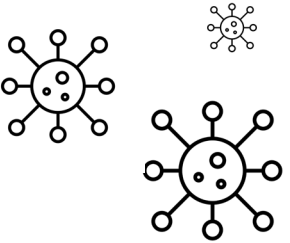
$$R_0 = 8 - 12$$

(give or take)

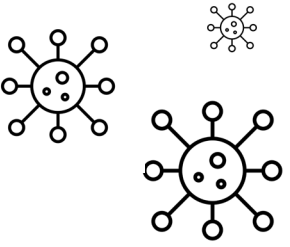
Measles case distribution by WHO Region



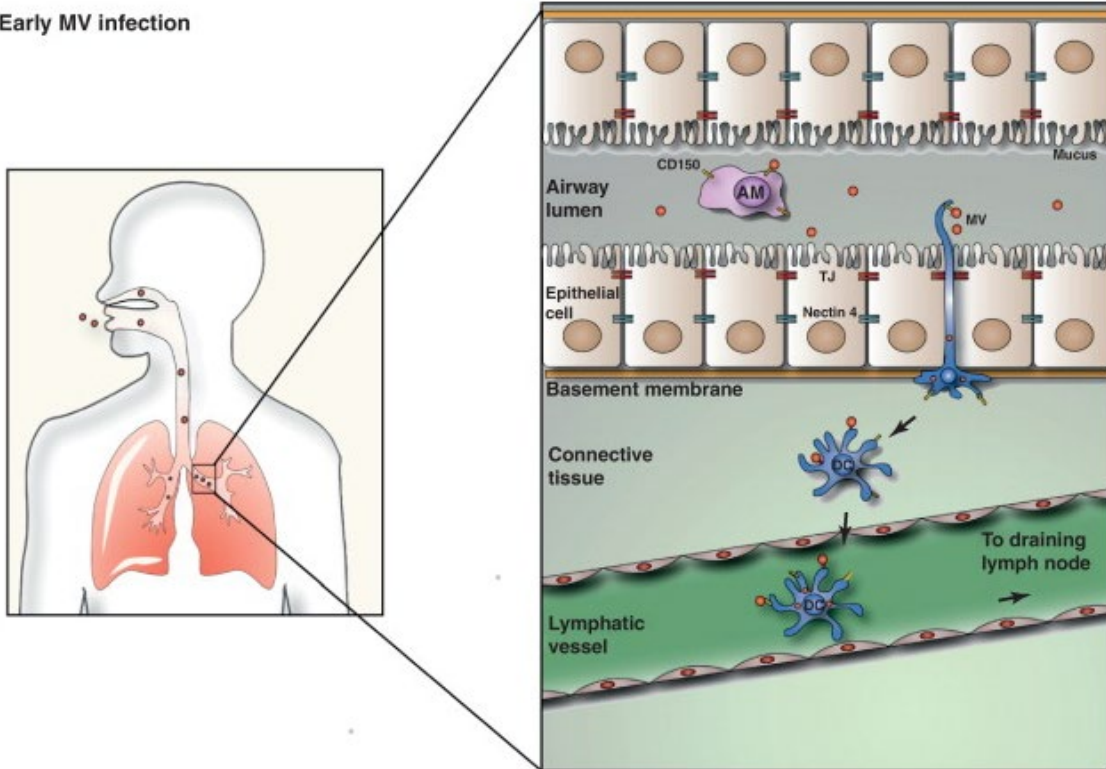
Measles case distribution AMR



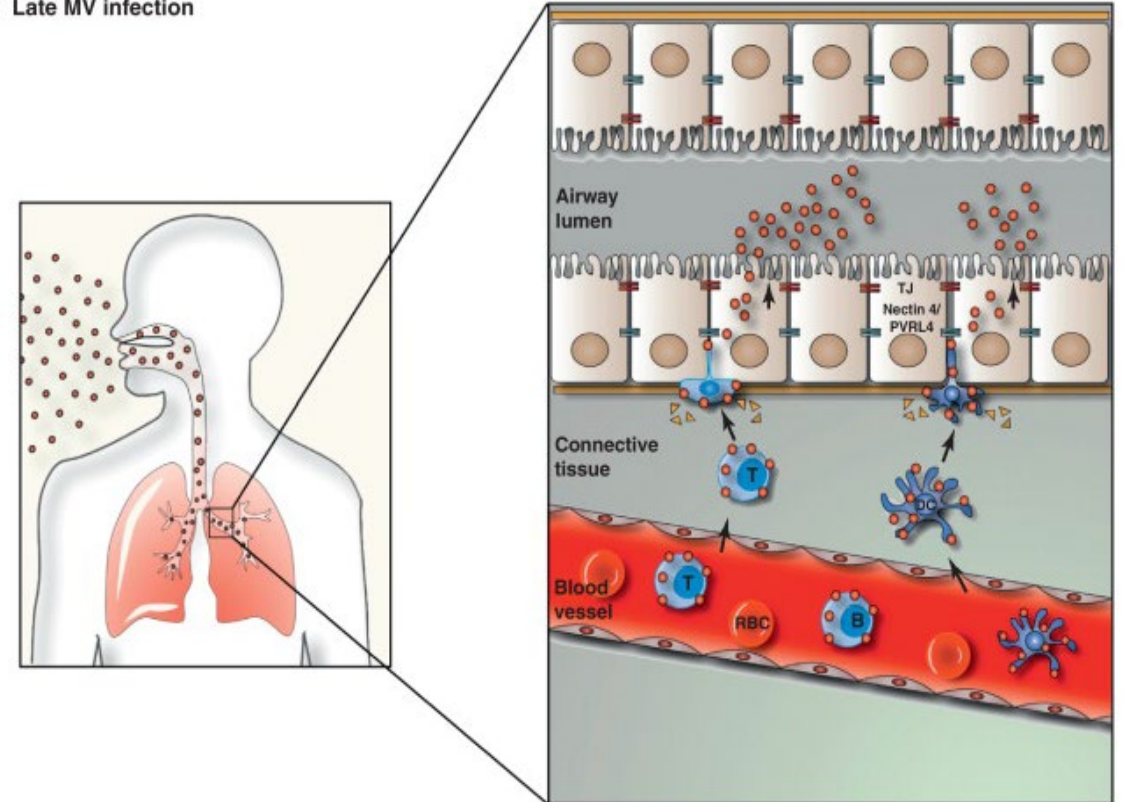
Measles virus biology



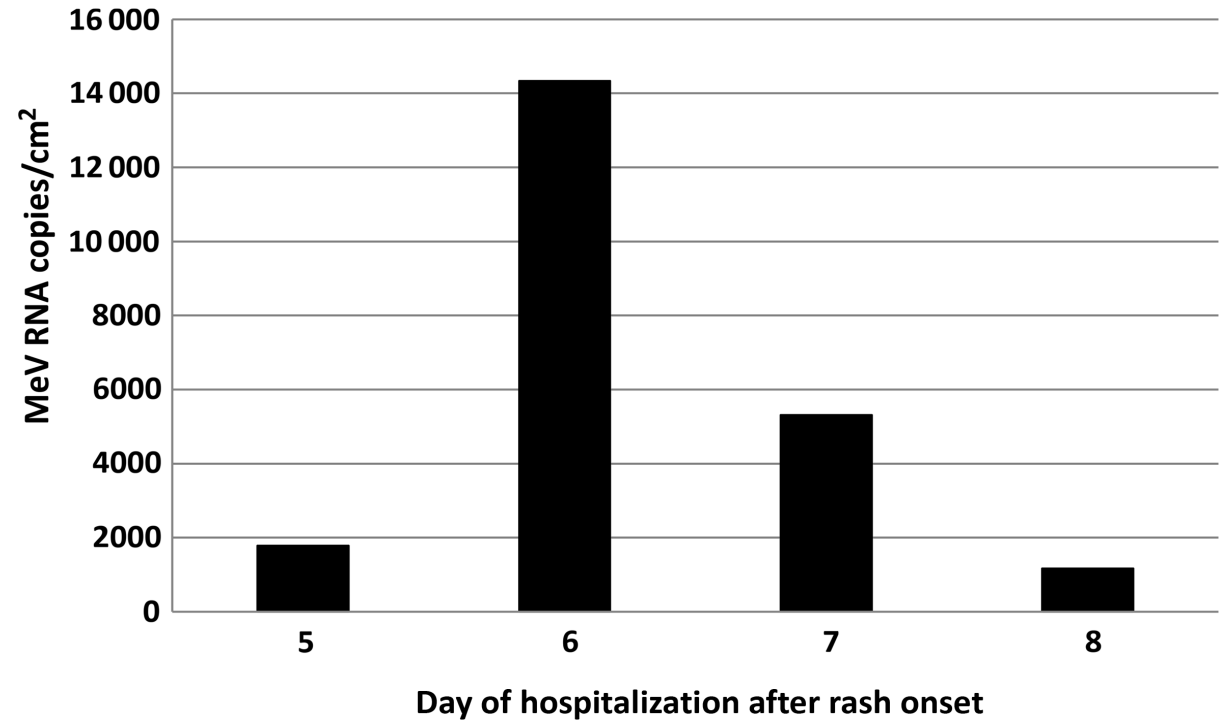
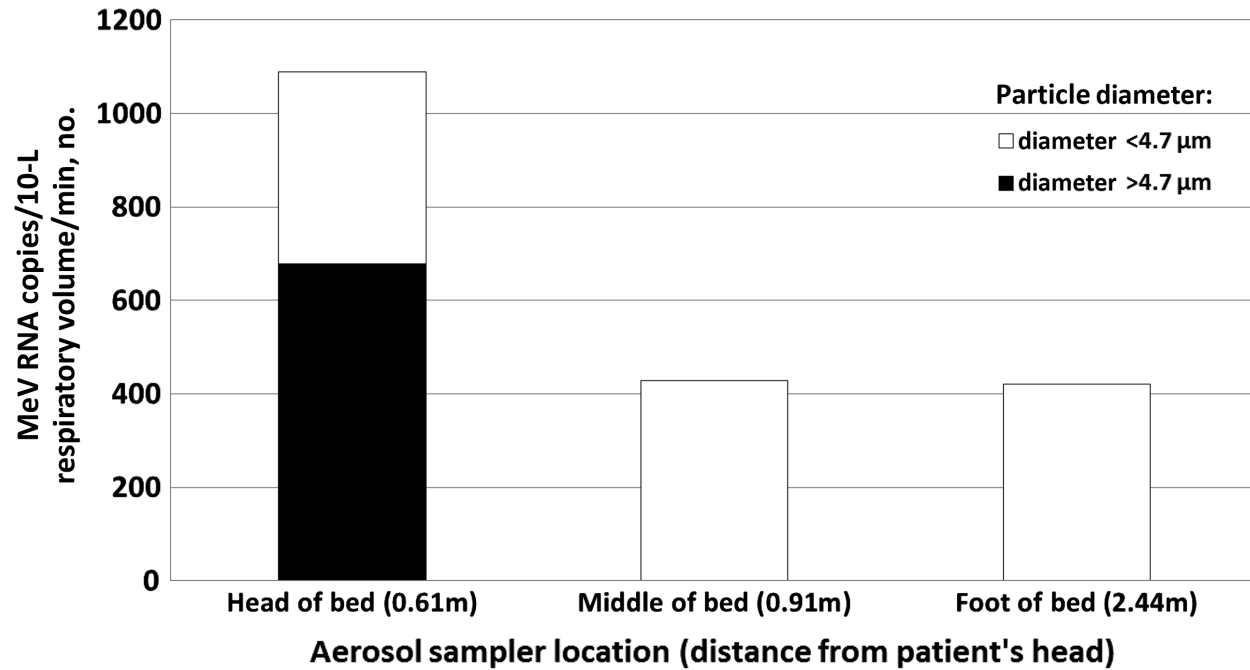
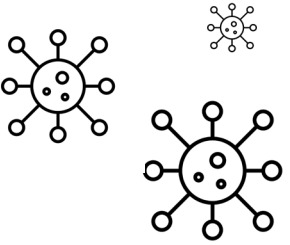
(a) Early MV infection



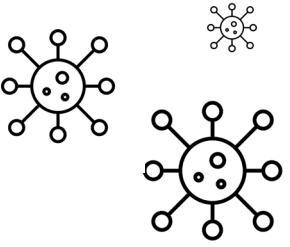
(b) Late MV infection



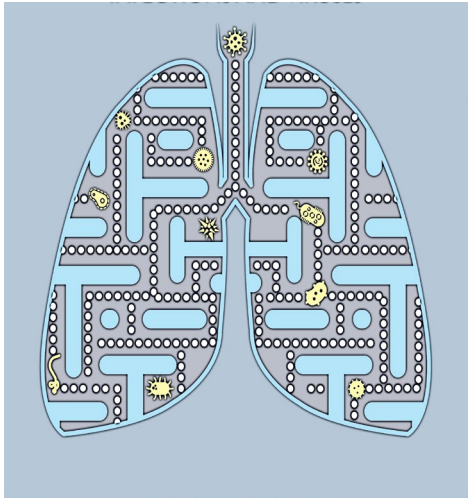
Measles virus recovery from air

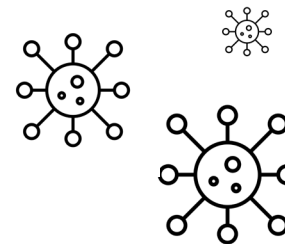


4/134 respirators (3%) tested positive for MeV RNA



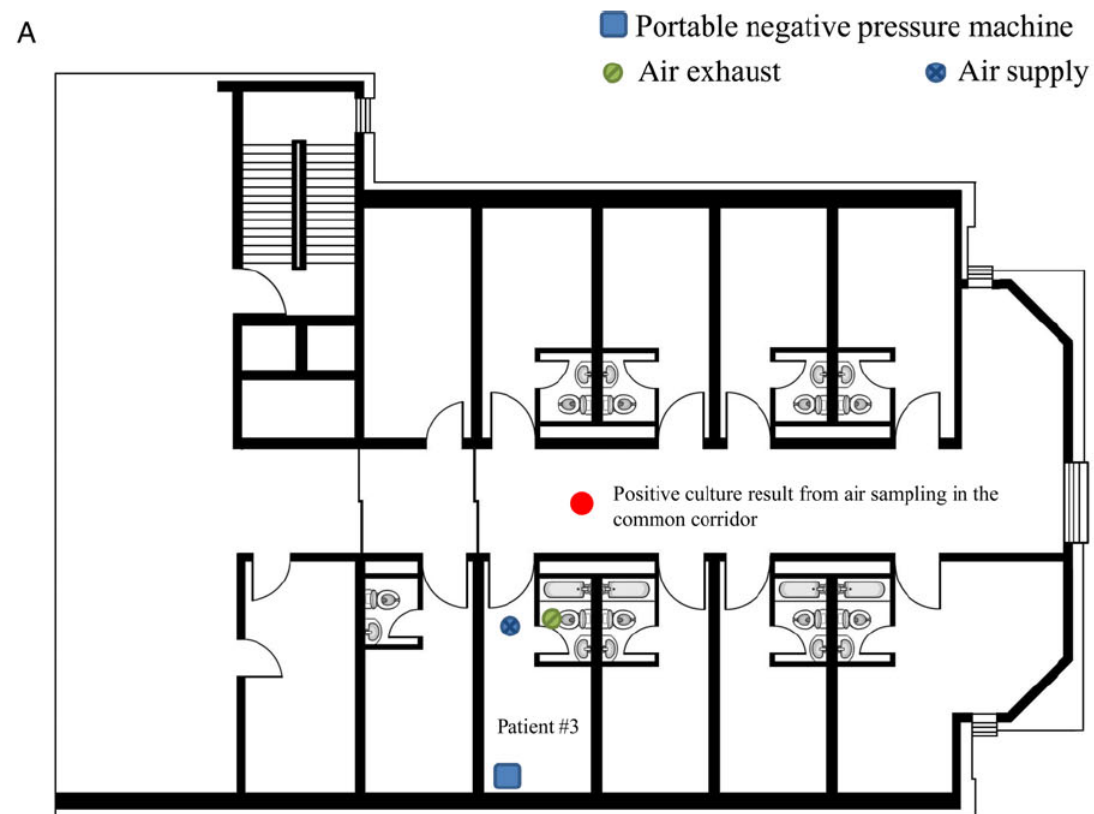
Scenario:
Healthcare, P2P





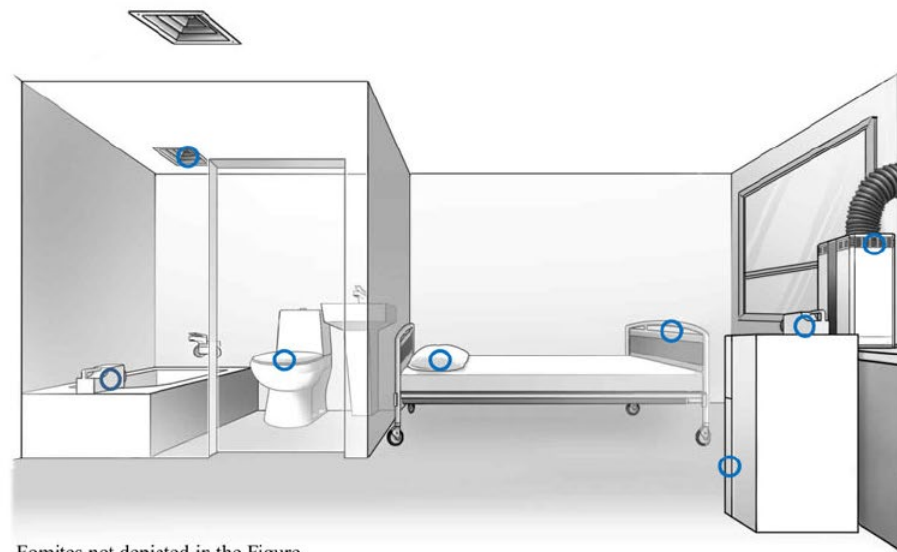
Extensive Viable Middle East Respiratory Syndrome (MERS) Coronavirus Contamination in Air and Surrounding Environment in MERS Isolation Wards

Sung-Han Kim,^{1,ab} So Young Chang,^{2,a} Minki Sung,^{3,a} Ji Hoon Park,² Hong Bin Kim,⁴ Heeyoung Lee,⁵ Jae-Phil Choi,⁶ Won Suk Choi,⁷ et al



B

- Positive from viral culture
- Negative from viral culture



Fomites not depicted in the Figure

- Nasal prong, telephone button
- Blood pressure cuff, moving cart, hand washer tip

Fixed structure not depicted in the Figure

- Door knob in the room, door knob in the restroom, the patient's opposite corner of the floor, call button & handrail, floor, exit door knob in common corridor

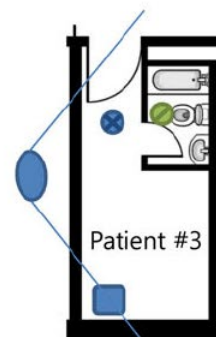


Table 1. Patient Case Status and Environmental Test Results in 2 Middle East Respiratory Syndrome–Designated Hospitals, Republic of Korea

Patient Data			Environmental Data				
Hospital	No.	Case Status	Time of Sampling for PCR (Days After Symptom Onset)	MERS-CoV PCR Results	Environmental Sampling	RT-PCR From Samples	RT-PCR From Viral Culture
A ^a	1	Pneumonia on mechanical ventilation and ECMO	22	(+) at the time of sampling	Air sampling ^b	2/2	1/2
					Fomites swab	4/6	2/6
					Fixed-structure swab	7/13	2/13
	2	Pneumonia on mechanical ventilation	16	(+) at the time of sampling	Air sampling ^b	2/2	2/2
					Fomites swab	4/4	3/4
Elevator	Fixed-structure swab	12/12	5/12				
B ^c	3	Pneumonia and bedridden	19	(–) at the time of sampling	Air sampling ^d	3/3 ^c	1/3
					Fomites swab	5/6	2/6
					Fixed-structure swab	8/17	0/17
					Fixed-structure swab	1/5	0/5
	Elevator	Fixed-structure swab	1/5	1/5			

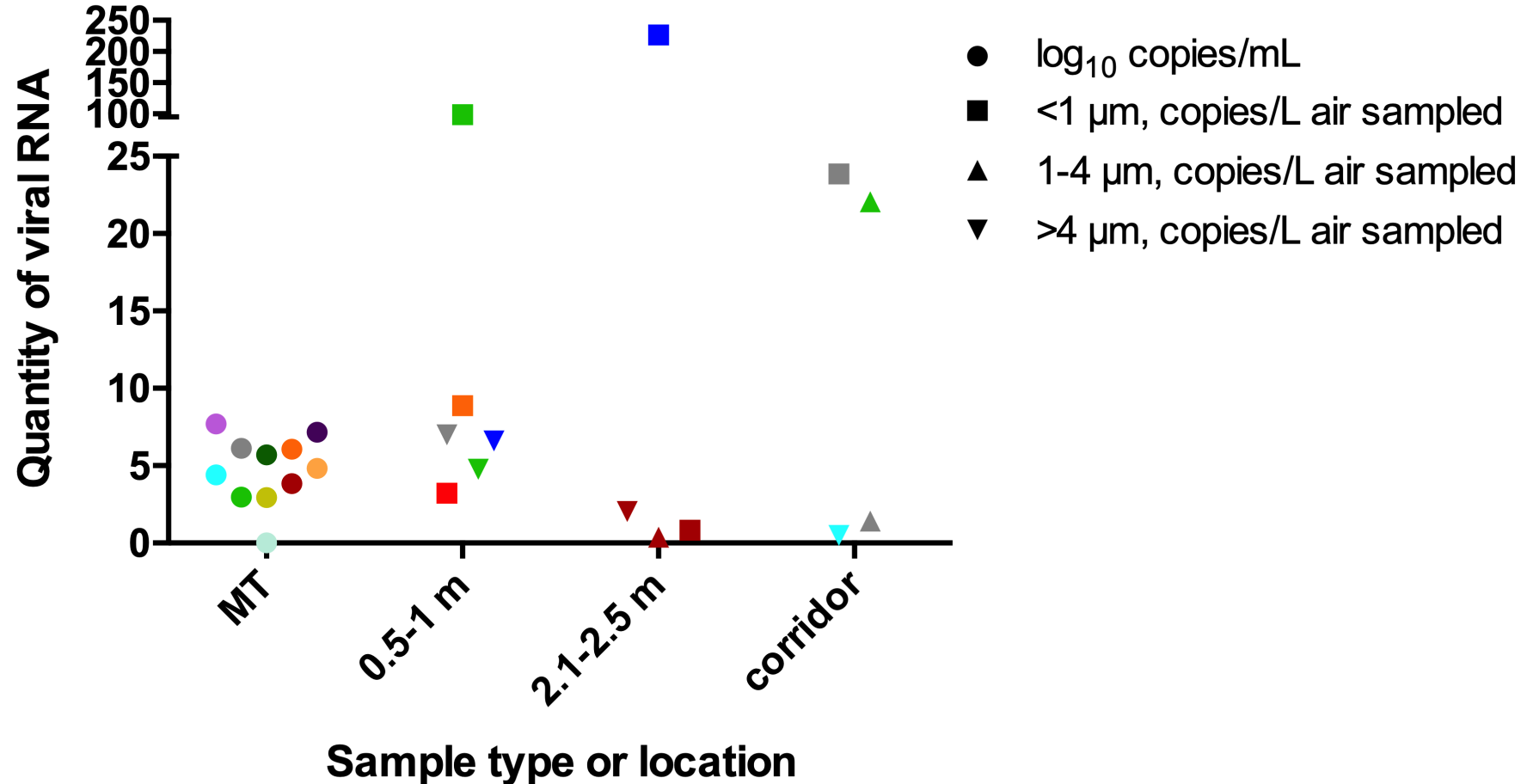
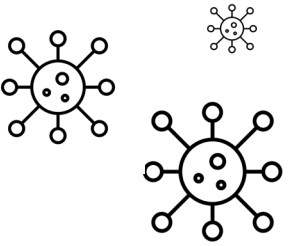
FIGURE

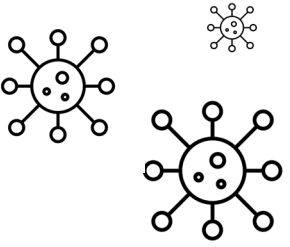
Milking camels according to local customs, Al Shahaniya barn complex, Qatar, April 2014



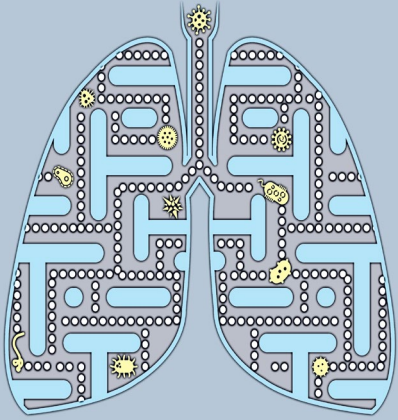
Milk production is triggered by the calf: the calf is then set aside and the milk is collected.
Photographs by E. Farag.

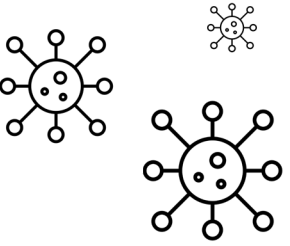
Influenza virus RNA emitted by naturally-infected patients





Scenario:
Human-animal-environment



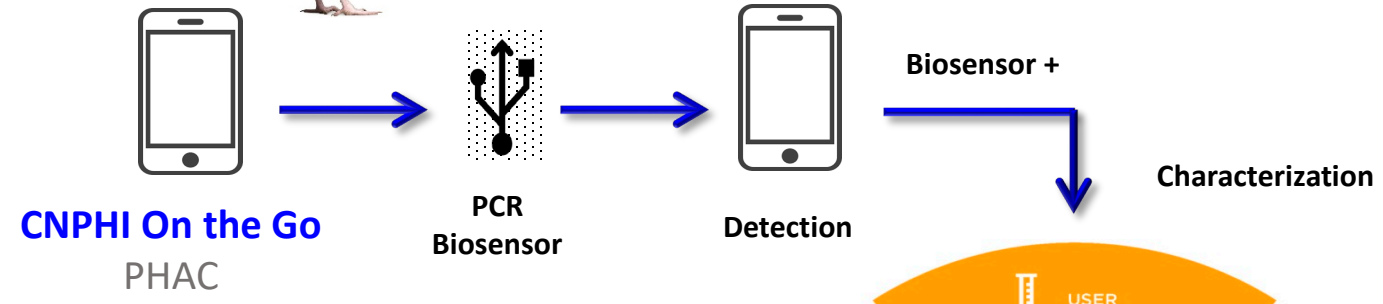
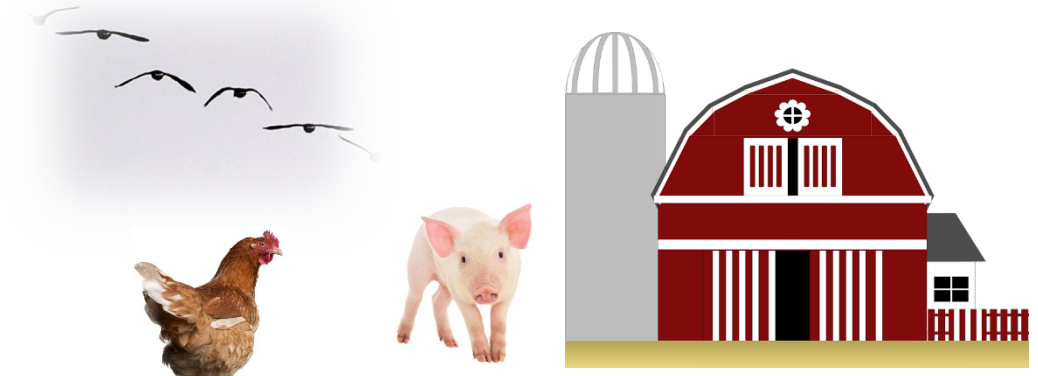
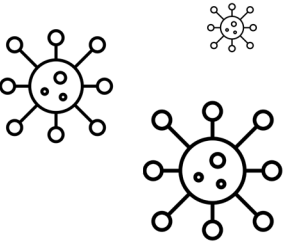


Why swine?

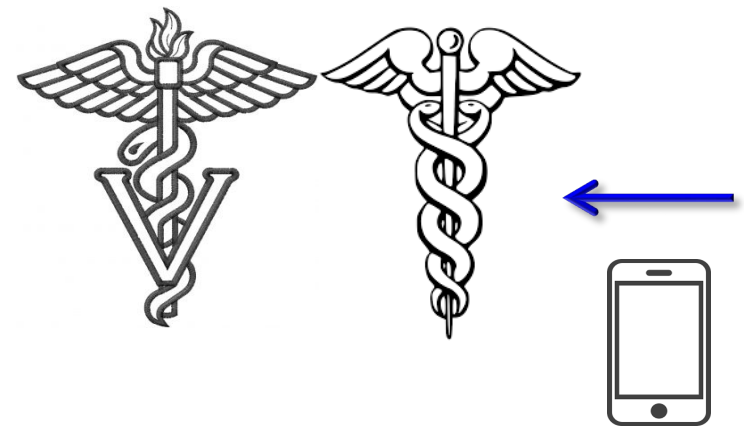
- Biological relevance
- Endemicity of influenza (model)
- Surveillance gaps
- Economic importance to Canada

Specific objective

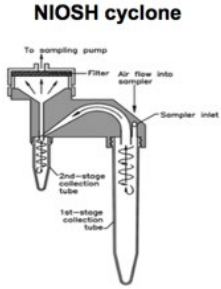
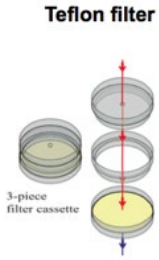
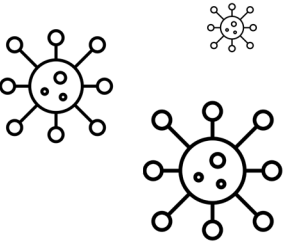
To validate DNA/RNA target-capture NGS-based technology for the enrichment and characterization of influenza genomes in *environmental* samples for surveillance and early warning



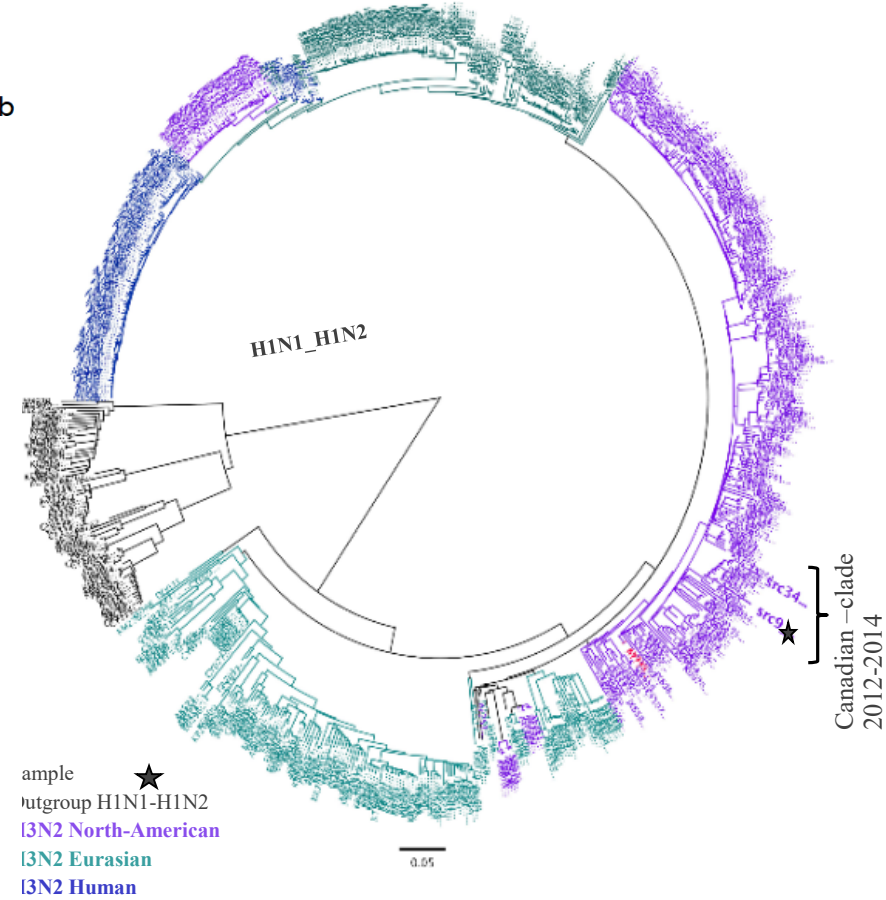
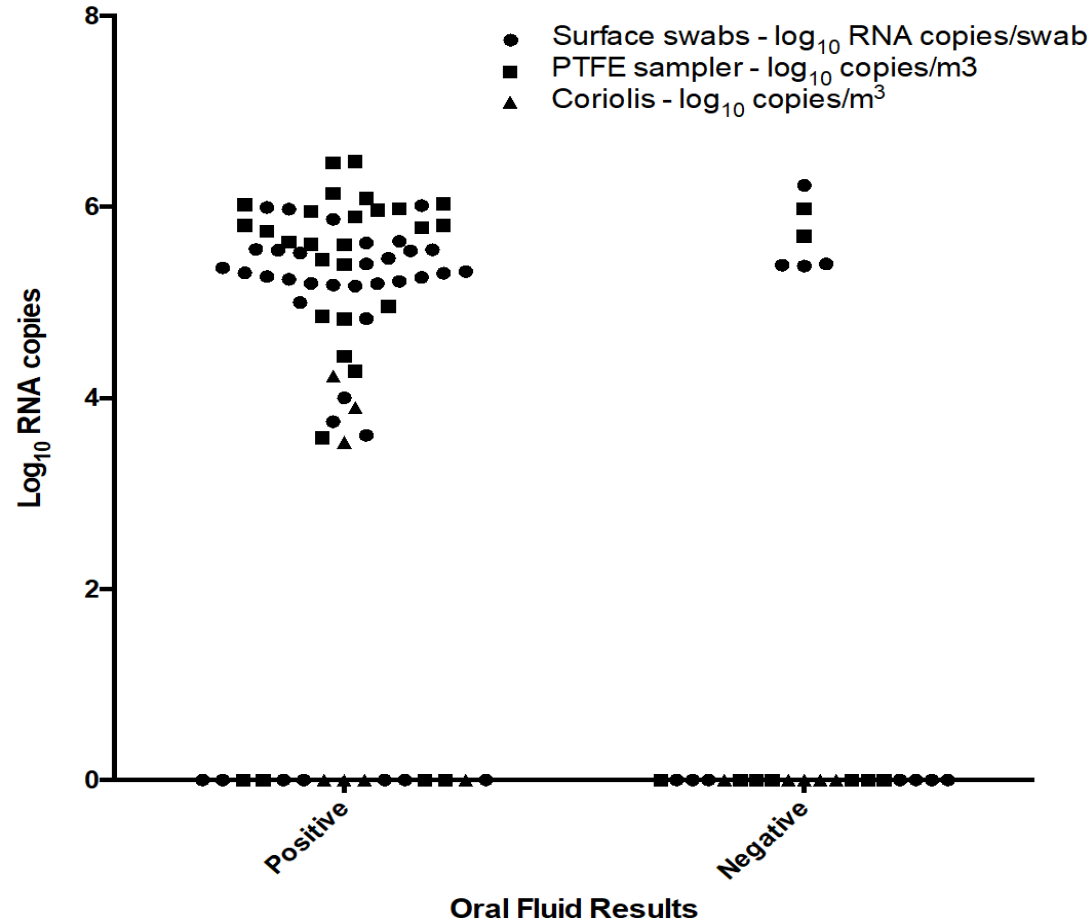
**National Centre for
Foreign Animal
Disease**
Canadian Food
Inspection Agency



Influenza virus RNA recovered from bioaerosols



RNA Copies for Sampling Methods by Oral Fluid results

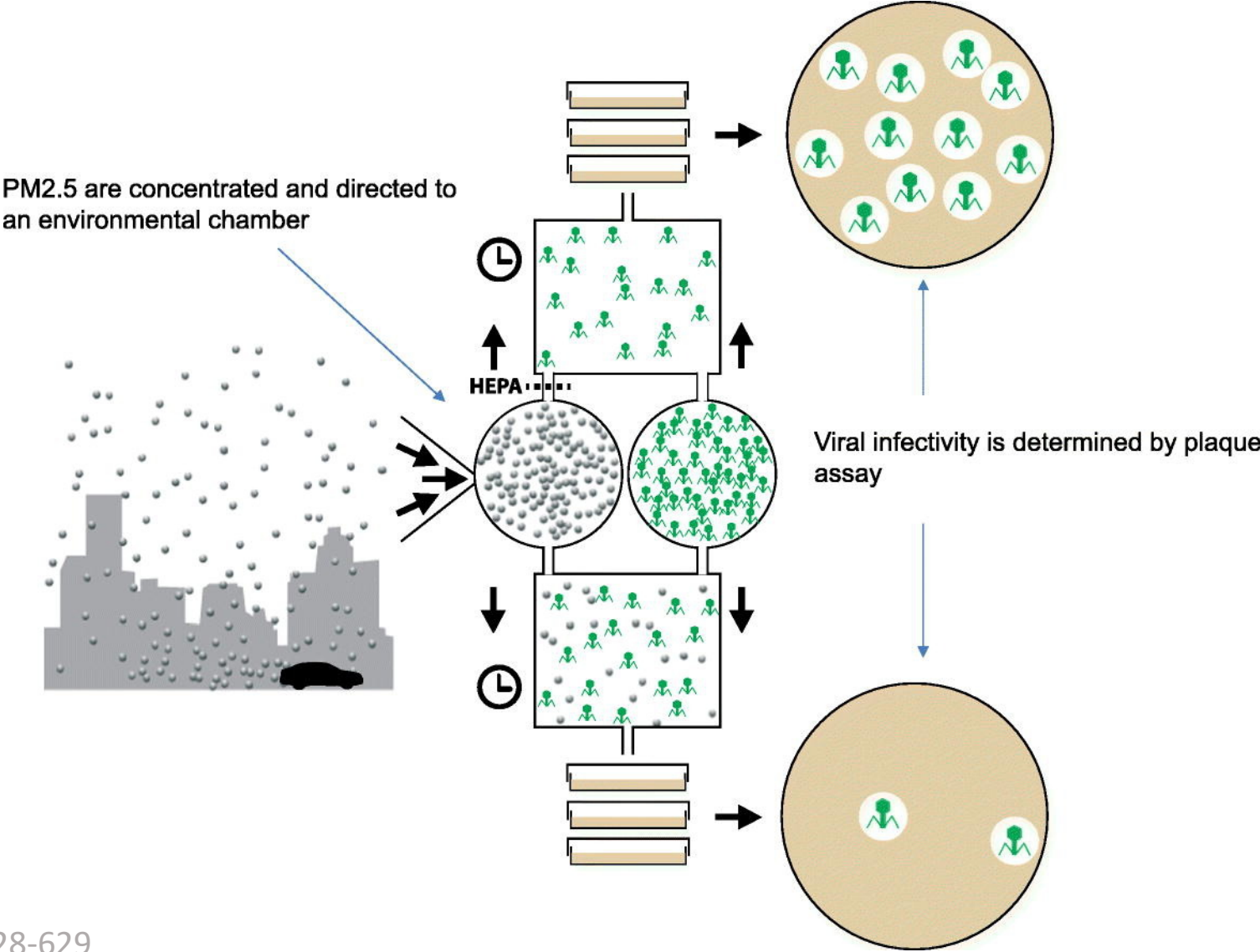
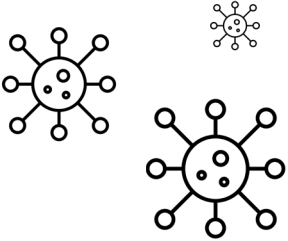


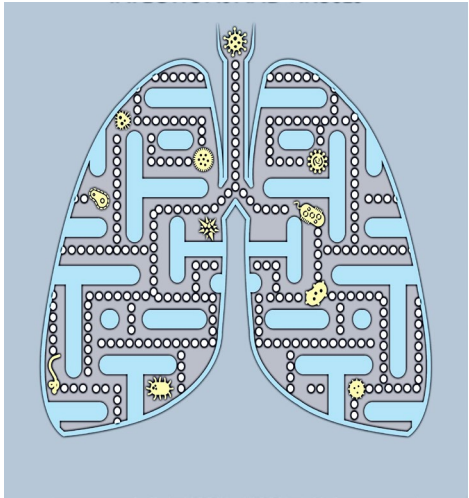
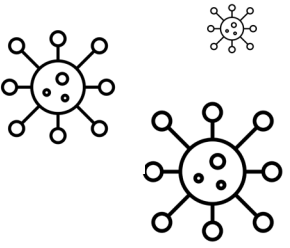
Influenza virus sequences recovered from bioaerosols and oral fluids

		PB2	PB1	PA	HA	NP	NA	M1	NS1
Oral Fluids (N=23)	Complete	23	19	22	22	22	22	23	22
	Partial	0	2	1	1	1	1	0	1
	Missing	0	2	0	0	0	0	0	0
PTFE (N=10)	Complete	4	3	4	3	5	2	7	7
	Partial	2	3	2	4	3	4	2	3
	Missing	4	4	4	3	2	4	1	0

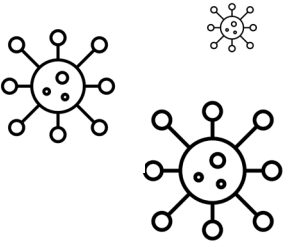
- 33 samples sent to NCFAD sequenced by next-generation sequencing
- 23 Oral fluid samples (average Ct value = 30.29)
 - 13 Complete genomes (H1N2 and H3N2)
 - 10 partial genomes
- 10 PTFE Samples (average Ct value = 35.23)
 - 1 complete genome sequenced (H1N2)
 - 9 partial genomes

The Pollution Particulate Concentrator (PopCon)





Summary



Take home points

- Understanding ecology and biology of specific viral pathogens is essential for mitigation; transmission & dispersion
- Opportunities exist to improve methodology and instrumentation for viral bioaerosol sampling, analysis and integration with metadata
- Multidisciplinary, collaborative efforts are required to fill the significant knowledge gaps that persist around bioaerosols and transmission of viral agents

Russia

Blast sparks fire at Russian laboratory housing smallpox virus

Facility known as Vector is one of only two sites holding virus, and also houses Ebola samples

Andrew Roth in Moscow

Tue 17 Sep 2019 12.43 BST



1,174



▲ A gas explosion at a Russian lab sparked a fire that was later put out. It is one of only two places on Earth to store the smallpox virus. Photograph: Christian Charisius/Reuters

A gas explosion has sparked a fire at a Russian laboratory complex stockpiling viruses ranging from smallpox to Ebola, authorities have said.

The State Research Centre of Virology and Biotechnology denied that the fire had exposed the public to the pathogens stored inside, some of the deadliest on Earth.

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