DEVELOPMENT AND APPLICATION OF A MARKOV CHAIN MODEL FOR PREDICTING INFLUENZA EXPOSURE IN INDOOR ENVIRONMENTS

BERGs Summer Meeting Presentation

June/26/2014

Parham Azimi

INFLUENZA TRANSMISSION

- Exposure to airborne pathogens such as influenza remains a significant threat to public health.
- Influenza Transmission Routes

  - **Fomite:** any object or substance capable of carrying infectious organisms, germs or parasites, and hence transferring them from one individual to another. Skin cells, hair, clothing, and bedding are common hospital sources of contamination.

  - **Inhalation:** for respirable particles ($D_p \leq 10$ μm) which deposit throughout the upper and lower respiratory tract

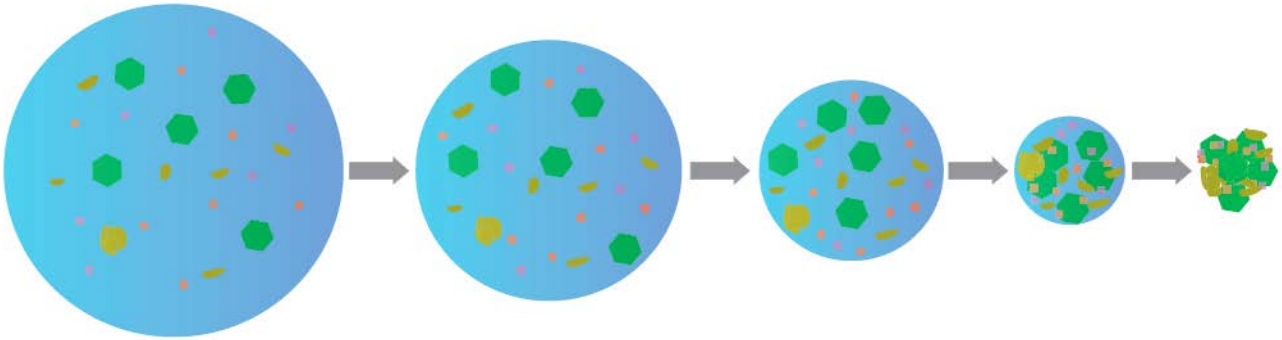
  - **Inspiration:** for particles with 10 μm $\leq D_p \leq$ 100 μm which deposit in the upper respiratory tract

  - **Direct spray:** the projection of virus carried in cough and sneeze particles (generally da > 100 μm) onto the eyes, nostrils, and lips.

What are the predominate pathways of influenza transmission?

DROPLET NUCLEUS

- Droplets rapidly (less than 1 sec for particles smaller than ~50 µm in diameter) decrease in size as the surrounding liquid evaporates, once expelled from the human body (very humid) to indoor environments (a relatively less humid environment)
- After rapid evaporation, a "**droplet nucleus**" containing the mix of solid particles (including any infectious particles) remains. Droplet nuclei typically have particle diameters that are 40-50% of the original droplet size

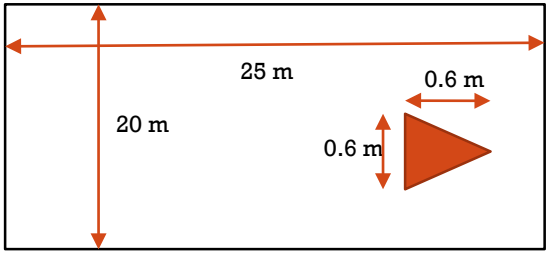


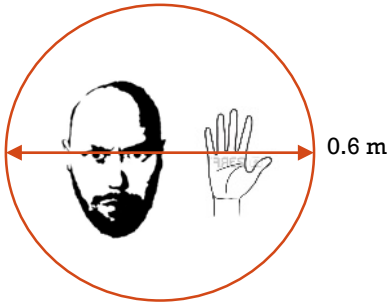
Evaporation of a liquid expelled *droplet* to a *droplet nucleus*(Image source: Verreault et al., 2008)

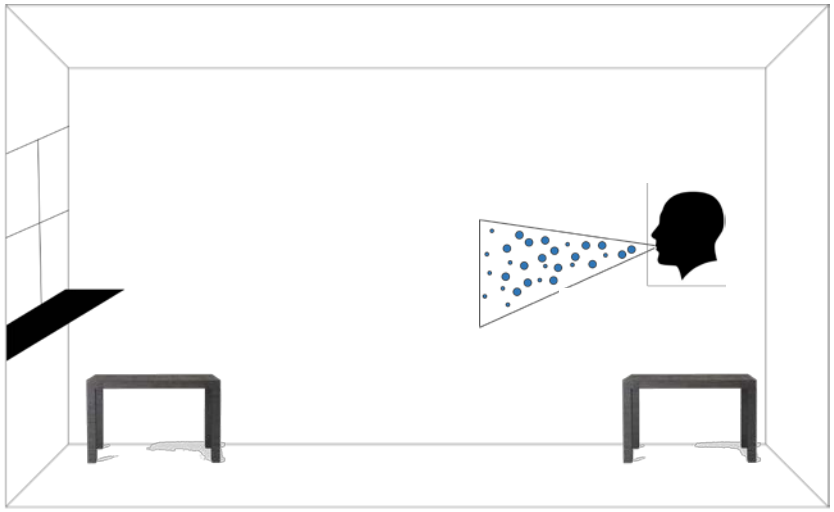
Verreault, D.et.al.; 2008. Methods for Sampling of Airborne Viruses. Microbiology and Molecular Biology Reviews 72, 413–444.

DIRECT SPRAY

- Direct spray would happen if a susceptible individual crosses the 0.6 m cone in front of the infector while he is coughing.
- The cough frequency is varied 6 to 215 coughs/hr with mean of 39 coughs/hr
- The chances of direct contact of finger skin, mucous membrane, and respiratory tracts with exhaled infectious particles are 5×10^{-3}% and 2×10^{-3}% respectively, assuming 10 cm^2 skin finger skin and 5 cm^2 the noise and mouth surface.







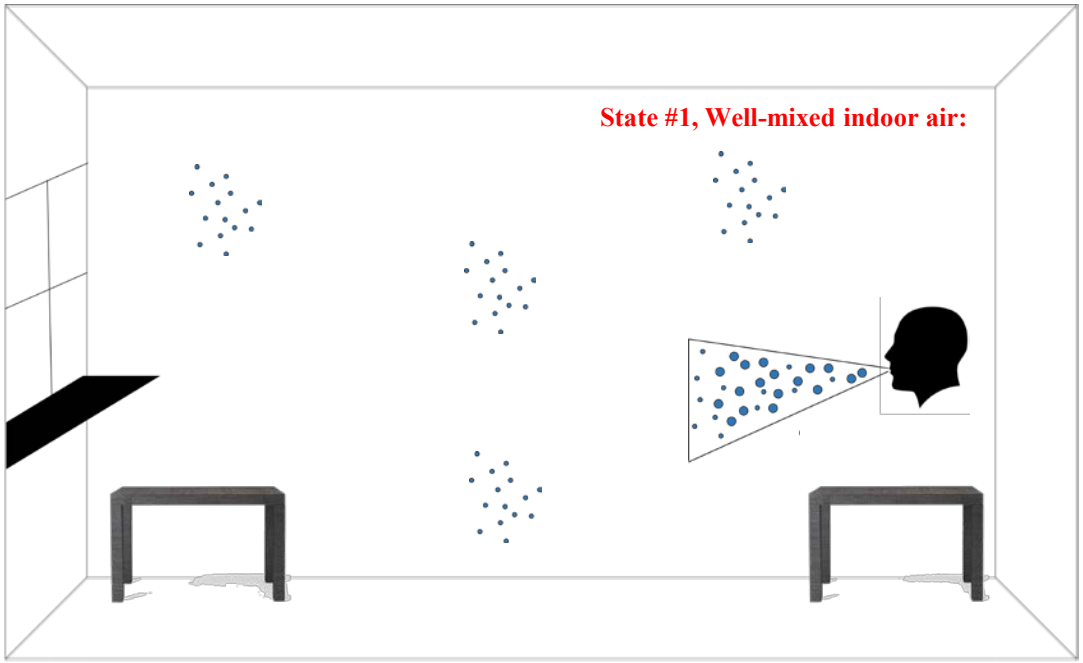
A 500 m^2 hypothetical office environment
1 infector
24 susceptible
8 hours exposure time

Milton DK., et.al.; "Influenza Virus Aerosols in Human Exhaled Breath:Particle Size, Culturability, and Effect of Surgical Masks", PLOS Pathogens, Volume 9, Issue 3, 2013.

STATE #1: WELL-MIXED INDOOR AIR

The number concentration of influenza viruses injected to indoor air ranged from 11 to 597 viruses per 30 mins. (Milton, 2013)

	Distribution of influenza virus in modified ranges for use with ASHRAE Standard 52.2							
	Mean	Lindsly 2010	Lindsly 2010	Lindsly 2010	Blachere 2009	Lindsly 2010	Yang 2011	Noti 2012
		Personal	Lower Stationary	Upper Stationary	Personal & Stationary	On face	Stationary	Stationary
0.3 - 1.0 µm	0.203	0.188	0.13	0.09	0.04	0.42	0.36	0.195
1.0 - 3.0 µm	0.281	0.197	0.239	0.174	0.327	0.153	0.373	0.503
3.0 - 10 µm	0.516	0.615	0.631	0.736	0.633	0.427	0.267	0.302



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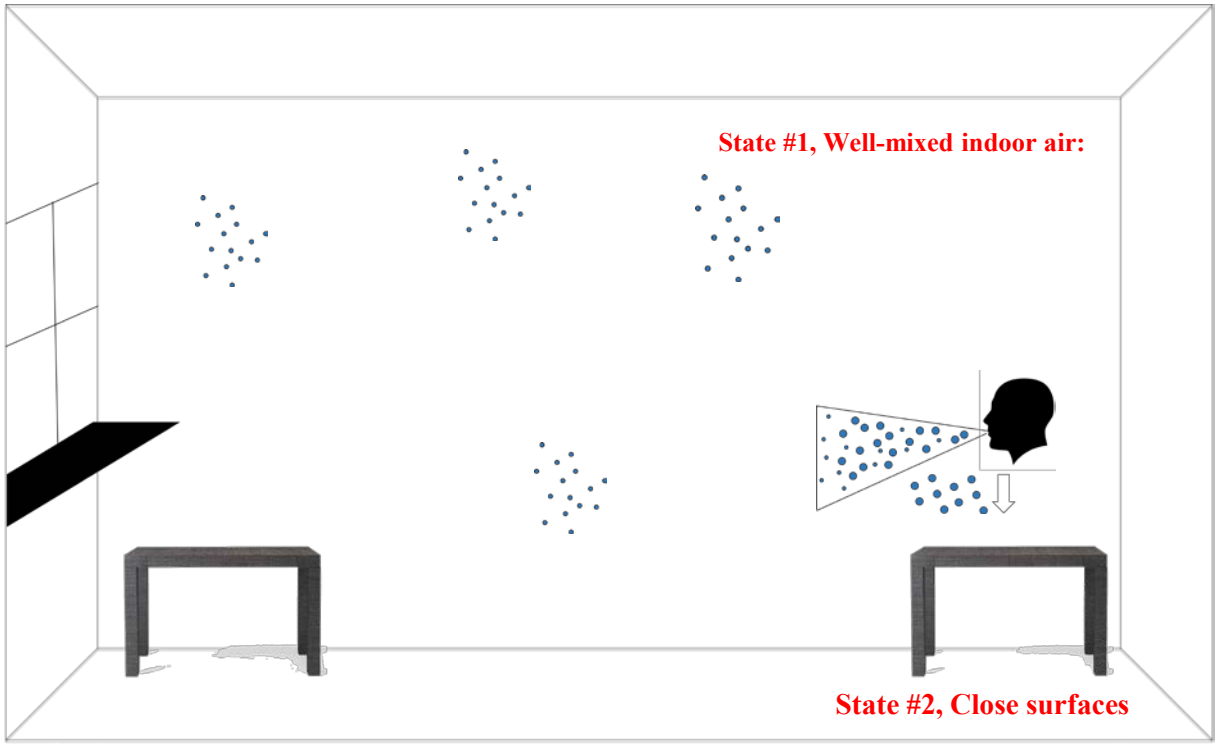
STATE #2: CLOSE SURFACES:

- Surfaces in 1 meter far from the infector has been considered as close surfaces.
- Droplet nucleuses larger than 10 μm deposit rapidly on closed surfaces.
- Number of influenza viruses ranged from 83000 to 1800000 viruses per 30 mins. (Milton, 2013).



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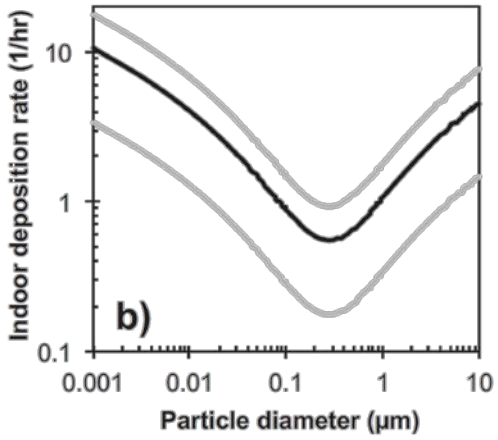
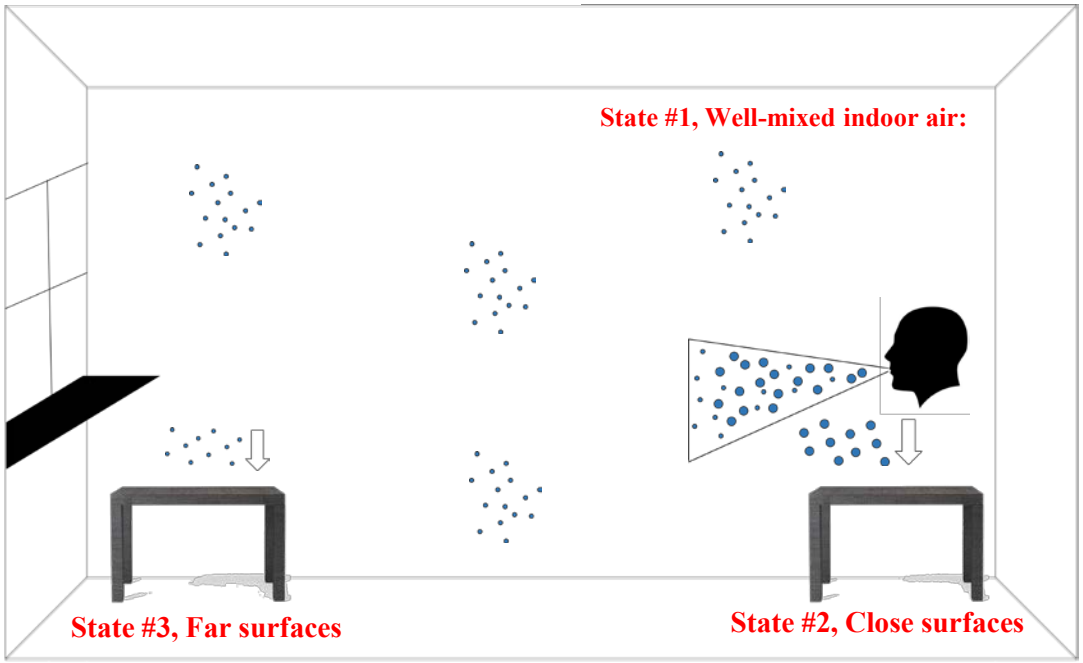
STATE #2: FAR SURFACES:

- Infectious particles in the indoor air deposit on all surfaces.
- The deposition rate is based on the size of particles.
- Assuming the mentioned influenza viruses size distribution the mean deposition rate is ~1.69 1/hr.



(El Orch et.al, 2014)



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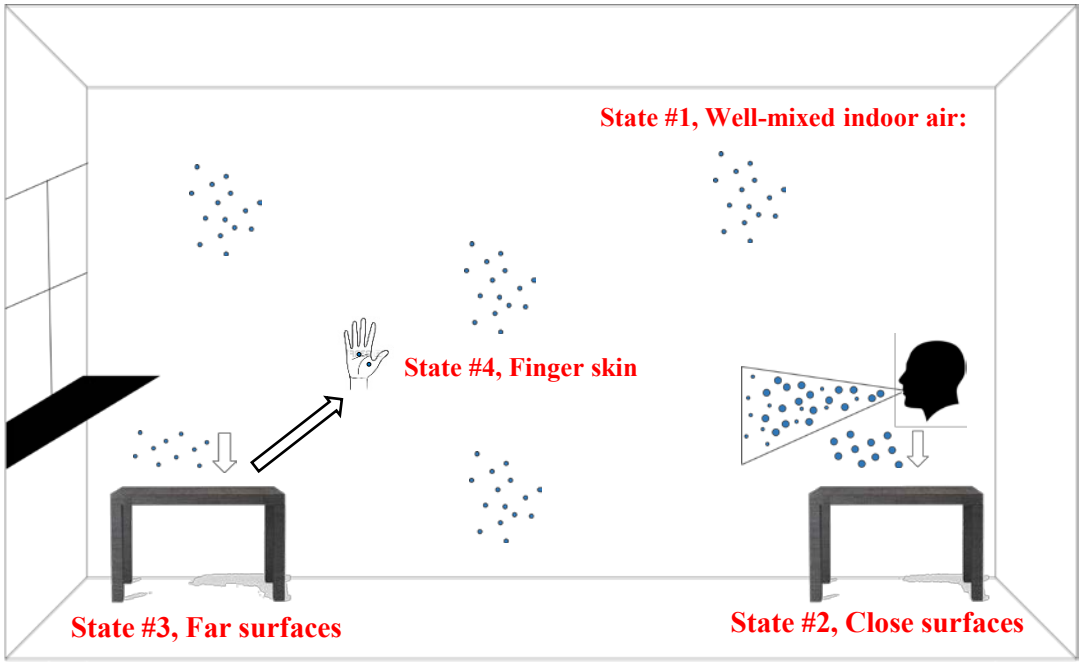
El Orch, Z., Stephens, B., Waring, M.; Predictions and determinants of size-resolved particle infiltration factors in single-family homes in the U.S., Building and Environment, Volume 74, April 2014, Pages 106-118, 2014

STATE #4, FINGER SKIN

- The contact rate of hand to face and hand to surfaces is 1.5 per min with range of 0.3 1/min to 3.7 1/min
- The contact rate of hand to surfaces is 1.5 per min with range of 1.0 1/min to 2.3 1/min respectively.
- The transfer efficiencies of skin-to-surface and skin-to-skin are 7.9% (5.1% to 12.2%) and 4.6% (3.0% to 7.1%) respectively



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Jones RM., Adida E.; "Influenza Infection Risk and Predominate Exposure Route: Uncertainty Analysis", Risk Anal. 2011, Oct;31(10):1622-31.

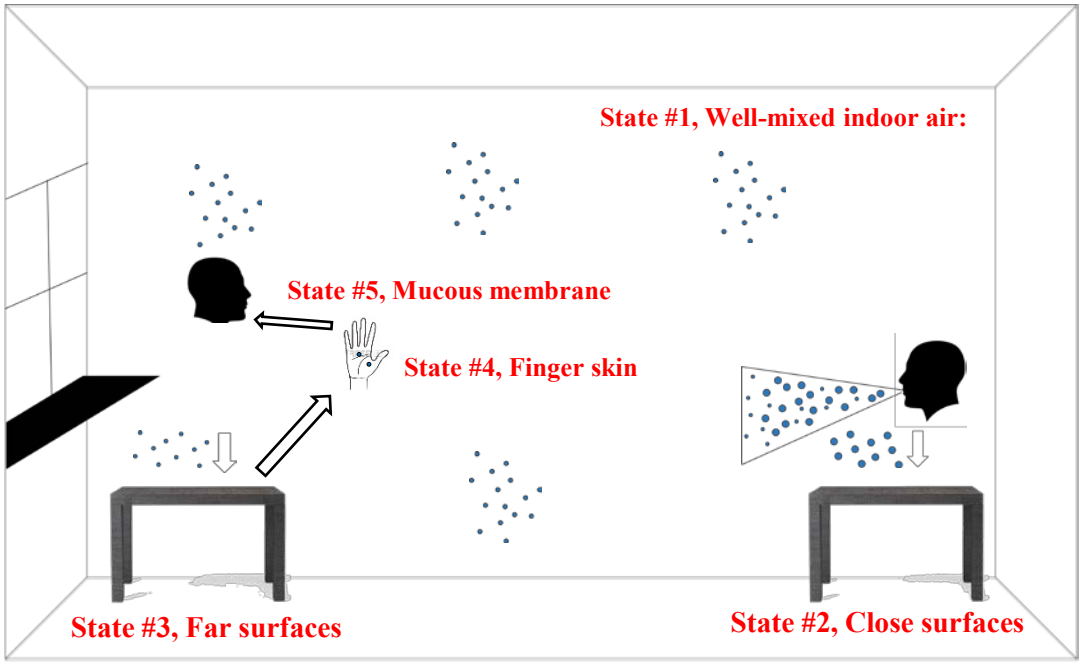
STATE #5, MUCOUS MEMBRANE

- **HID50: human infectious dose-50%** , is the amount of pathogen (measured in number of microorganisms) required to cause an infection in the host with of 50% chance.

$$P_{infection} = 1 - \exp(-\alpha_{MM} N)$$

$\alpha_{RN} = Ln(2) / HID50$
N: Intake dose

Parameter	Low	Median	High
HID50 for influenza for Mucous membrane	297	198	132
alpha for Mucous membrane	0.002	0.004	0.005



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STATE #6, RESPIRATORY TRACT

- The infectious particles enter the lower respiratory tracts when the susceptible individuals breath.

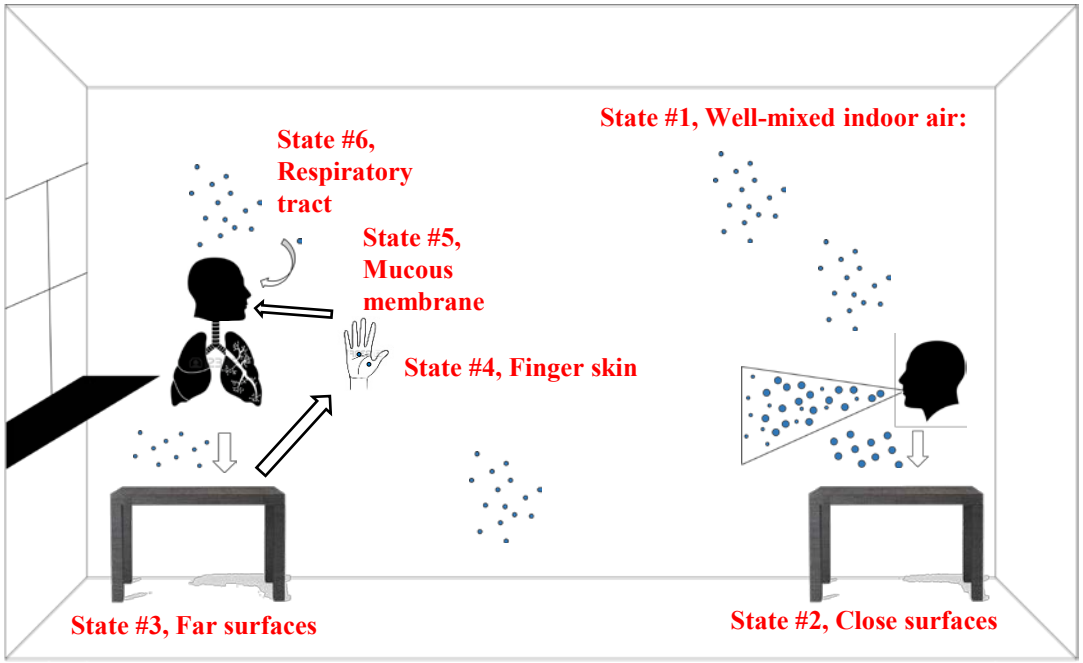
$\lambda_{inhalation} = N_{occ} \times P / V$

$P_{infection} = 1 - \exp(-\alpha_{RT} N)$

Parameter	Low	Median	High
HID50 for influenza for lower respiratory tract	27	10.8	2.4
alpha for lower respiratory tract	0.026	0.064	0.289

N_{occ}: Number of occupants =25

P: pulmonary ventilation rate of a person = 0.67 m^3/hr



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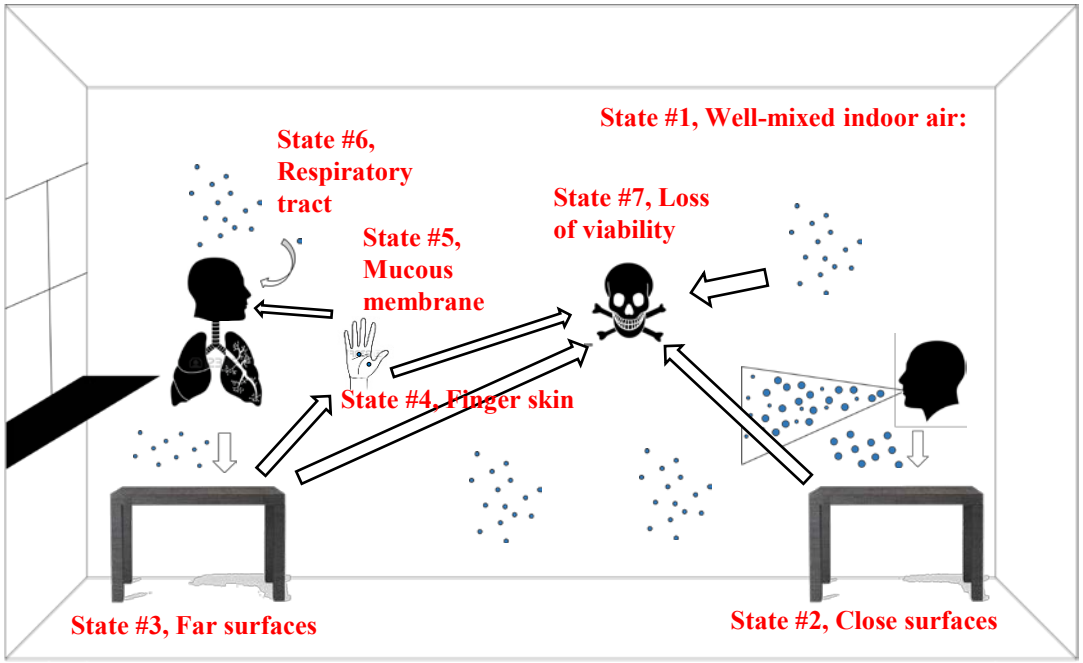
STATE #7, LOSS OF VIABILITY

- Infectious particles loose their viability during time with various rates depend on their location.

Inactivation rate of viruses	Unit	Percentile		
		10th	50th	90th
Indoor air	1/min	0.095	0.0075	0.00095
Office surfaces	1/min	0.0047	0.0022	0.000733
Human skin	1/min	1.7	1.2	0.698



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STATE #8, HVAC SYSTEM

- Infectious particles removal rate by filtration is depend on the recirculation rate through the HVAC filter and particle removal efficiency of the filter.

	Removal efficiency				Removal rate due to filtration
Filter Type	0.3 - 1.0 μm	1.0 - 3.0 μm	3.0 - 10 μm	Mean	
MERV 4	1%	9%	15%	10.5%	0.16
MERV 7	17%	46%	50%	42.2%	0.64
MERV 11	30%	65%	85%	68.2%	1.04
MERV 13	70%	90%	90%	85.9%	1.31
MERV 14	80%	90%	90%	88.0%	1.34
MERV 15	90%	90%	90%	90.0%	1.37
MERV 16	95%	95%	95%	95.0%	1.45
HEPA	99.90%	99.90%	99.90%	99.9%	1.52

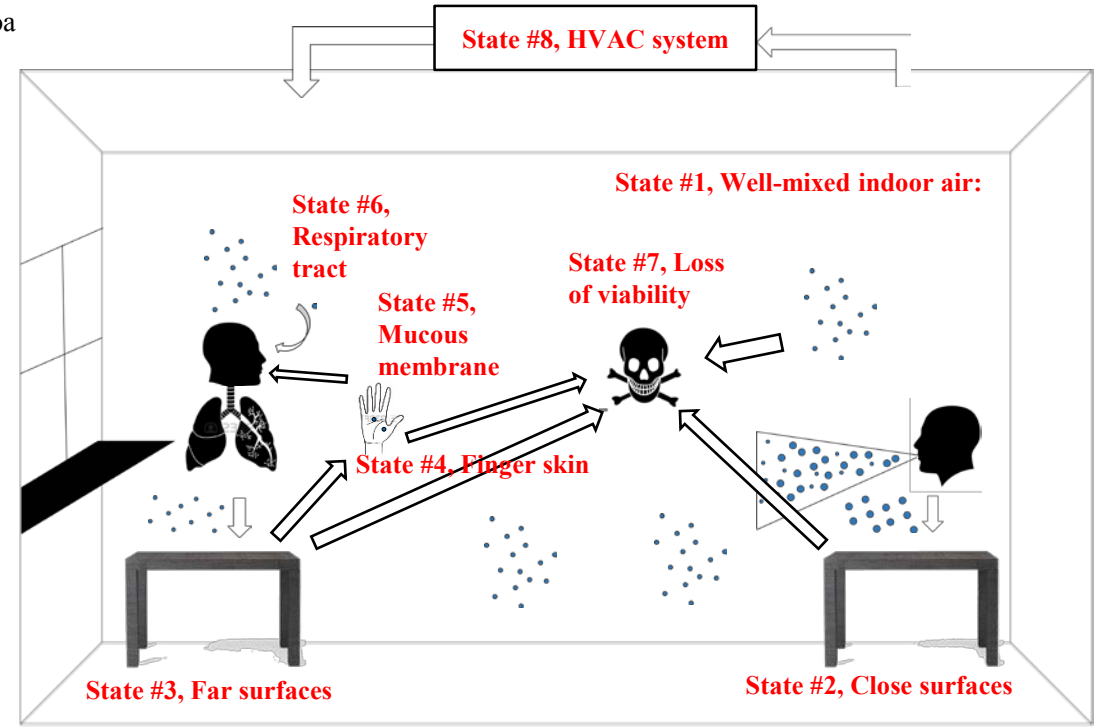
$K_{filtration} = \eta_{filter} \times \lambda_{recirculated}$

$\lambda_{recirculated} = F_{HVAC} \times Q_{filter} / V$

$Q_{filter} = (Q_{oa}/F_{oa}) - Q_{oa}$

$\lambda_{recirculated}$: Recirculation rate = 1.52 1/hr
F_{HVAC}: fractional HVAC operation time = 1
V: Indoor air volume = 1500 m^3

Q_{filter} : Recirculation flow = 2300 m^3/hr
Q_{oa}:Room ventilation rate with clean air
F_{oa}:Outdoor air supply fraction = 0.25



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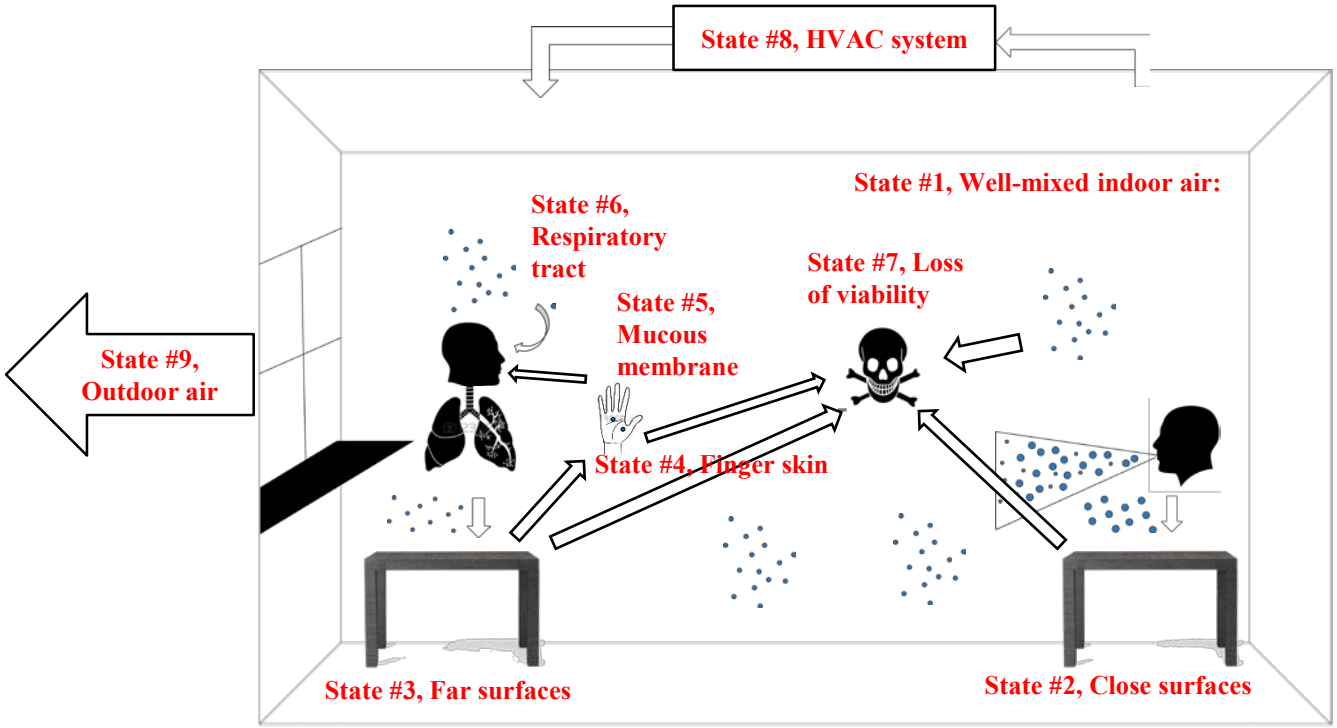
[1] ASHRAE Standard 52.2
[2] Stephens B, Siegel JA. Comparison of test methods for determining the particle removal efficiency of filters in residential and light-commercial central HVAC systems. Aerosol Sci Technol 2012;46(5):504–13

STATE #9, OUTDOOR AIR

We assumed the minimum required ventilation rate for an office environment which is:

$$\lambda_{ventilation} = 5 \text{ cfm per person} + 0.06 \text{ cfm/ft}^2$$

$$Q_{oa} = 761 \text{ m}^3/\text{hr}$$



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ASHRAE. Standard 62.1: Ventilation for acceptable indoor air quality. American Society of Heating, Refrigerating and Air-Conditioning Engineers; 2010.

MOVING RATE MATRIX

- The moving rates within states are shown in a matrix like the following.

λ (1/hr)	1	2	3	4	5	6	7	8	9
1	0	0.013558	1.328821537	0	0	0.011166667	0.45	1.33953784	0.507343044
2	0	0	0	0.000068256	0	0	0.132	0	0
3	0	0	0	0.000273024	0	0	0.132		
4	0	0.0068256	0.0273024	0	0.802416	0	72	0	0
5	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0

MARKOV MATRIX

- Markov matrix is showing the movement probability of a pathogen from one state to the other one or staying in the same state in a very short time interval (e.g. 10^{-7} hr).

$$\lambda_i = \sum_j \lambda_{ij} \qquad P_{ii} = e^{(-\lambda_i \times \Delta t)} \qquad P_{ij} = \frac{\lambda_{ij}}{\lambda_i} \times (1 - P_{ii})$$

Markov Matrix for median values of variables in the model, assuming Minimum Efficiency Reporting Value (MERV) 14 filters and 10^{-7} hour time steps

0.9999999	1.36E−09	1.68E−07	0.00E−01	0.00E−01	1.12E−09	5.7E−0.9	1.34E−07	5.07E−08
0.00E−01	0.99999996	0.00E−01	1.62E−11	0.00E−01	0.00E−01	4.4E−09	0.00E−01	0.00E−01
0.00E−01	0.00E−01	0.99999996	6.49E−11	0.00E−01	0.00E−01	4.4E−09	0.00E−01	0.00E−01
0.00E−01	1.62E−9	6.49E−9	0.999995	6.49E−11	0.00E−01	4.19E−06	0.00E−01	0.00E−010
0.00E−01	0.00E−01	0.00E−01	0.00E−01	1	0.00E−01	0.00E−01	0.00E−01	0.00E−01
0.00E−01	0.00E−01	0.00E−01	0.00E−01	0.00E−01	1	0.00E−01	0.00E−01	0.00E−01
0.00E−01	0.00E−01	0.00E−01	0.00E−01	0.00E−01	0.00E−01	1	0.00E−01	0.00E−01
0.00E−01	0.00E−01	0.00E−01	0.00E−01	0.00E−01	0.00E−01	0.00E−01	1	0.00E−01
0.00E−01	0.00E−01	0.00E−01	0.00E−01	0.00E−01	0.00E−01	00.00E−01	00.00E−01	1

FINAL NUMBER CONCENTRATION OF INFECTIOUS PARTICLES IN EACH STATE

- Assume we breath every 5 sec and cough 38 times per hour.
- We calculate the number concentration of infectious particles which goes to indoor air, close surfaces and mucous and respiratory tracts after each cough and breath

	1 indoor air	2 close surfaces	3 far surfaces	4 finger skin	5 mucous membrane	6 respiratory tracts	7 viability loss	8 HVAC system	9 outdoor air
Nbrearh	0.107843137	411.7647059	0	0	0	0	0	0	0
Ncough	1.833333333	6999.38848	0	0.34944	0.13104	0.13104	0	0	0

- We have 13889 and 263158 time intervals between each breath and cough respectively
- The final number concentration of infectious particles in each state is calculated as the following for 8 hours exposure time:

❖ $[N_{i,breath}]_{1\times9} = ([N_{i-1,breath}]_{1\times9} + [N_{breath}]_{1\times9}) \times [MM]_{9\times9}^{13889}$

Repeat it 5760 times

❖ $[N_{i,cough}]_{1\times9} = ([N_{i-1,cough}]_{1\times9} + [N_{cough}]_{1\times9}) \times [MM]_{9\times9}^{263158}$

Repeat it 304 times

❖ $[N_{final}]_{1\times9} = [N_{5760,breath}]_{1\times9} + [N_{304,cough}]_{1\times9}$

DOMINANT TRANSMISSION PATHWAY

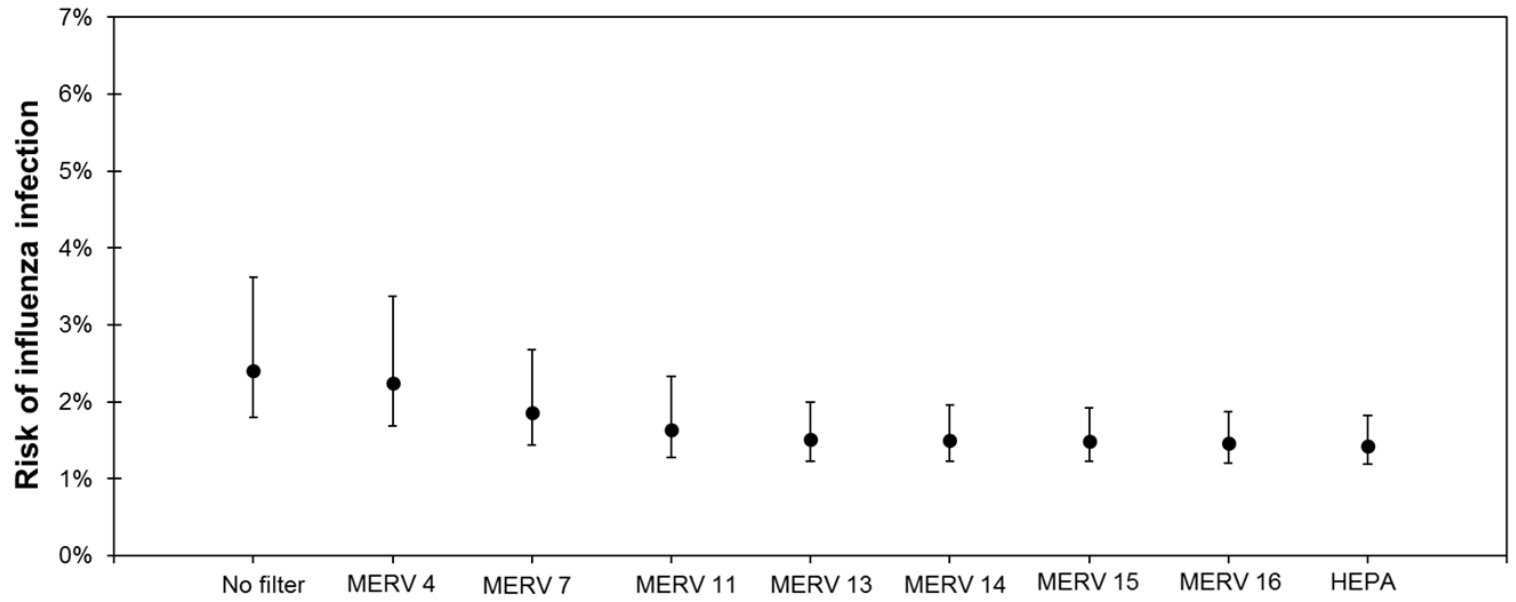
- Using MATLAB the intake dose range of infectious particles in respiratory tracts and mucous membranes has been calculated considering direct spray and also without it.

Describtion	parameter	Unit	low risk	median Risk	high Risk
the probability of infection	$P_{infection}$	-	0.01	0.12	1.01
Intake dose to respiratory Tracts by breath	FRTB	#	0.10	2.60	14.26
Intake dose to mucous membrane by breath	FMMB	#	0.05	7.33	586.73
Intake dose to respiratory Tracts by cough without direct contact	FRTC'	#	0.73	1.67	10.86
Intake dose to mucous membrane by cough without direct contact	FMMC'	#	2.56	4.86	37.91
Intake dose to respiratory Tracts by cough with direct contact	FRTC	#	8.07	42.16	182.70
Intake dose to mucous membrane by cough with direct contact	FMMC	#	8.06	46.39	583.32

The results show the **direct spray** is likely the **dominant transmission pathway** of influenza in the office. If there is not any chance of direct contact with infector and susceptible individuals, **then inhalation** is the dominate pathway

AVERAGE INFECTION RISK

- Assuming the direct spray, the **average infection risk** is approximately the same for **all MERV** filters and it is equal to **11.5 ± 0.2%**.
- 11.5% infection risk for influenza yielded an equivalent quanta generation rate in a transient Wells-Riley model of **125 per hour**, which is generally in line with assumptions from the literature.
- The predicted risk of infection by influenza virus in the hypothetical office environment with **various HVAC filters** installed, **without considering the direct contact.**



FUTURE WORK

- It will be with Zach and Stephanie

- Develop and apply a system for measuring the fate, transport, and control of droplets and droplet nuclei in an indoor environment (StudioE).

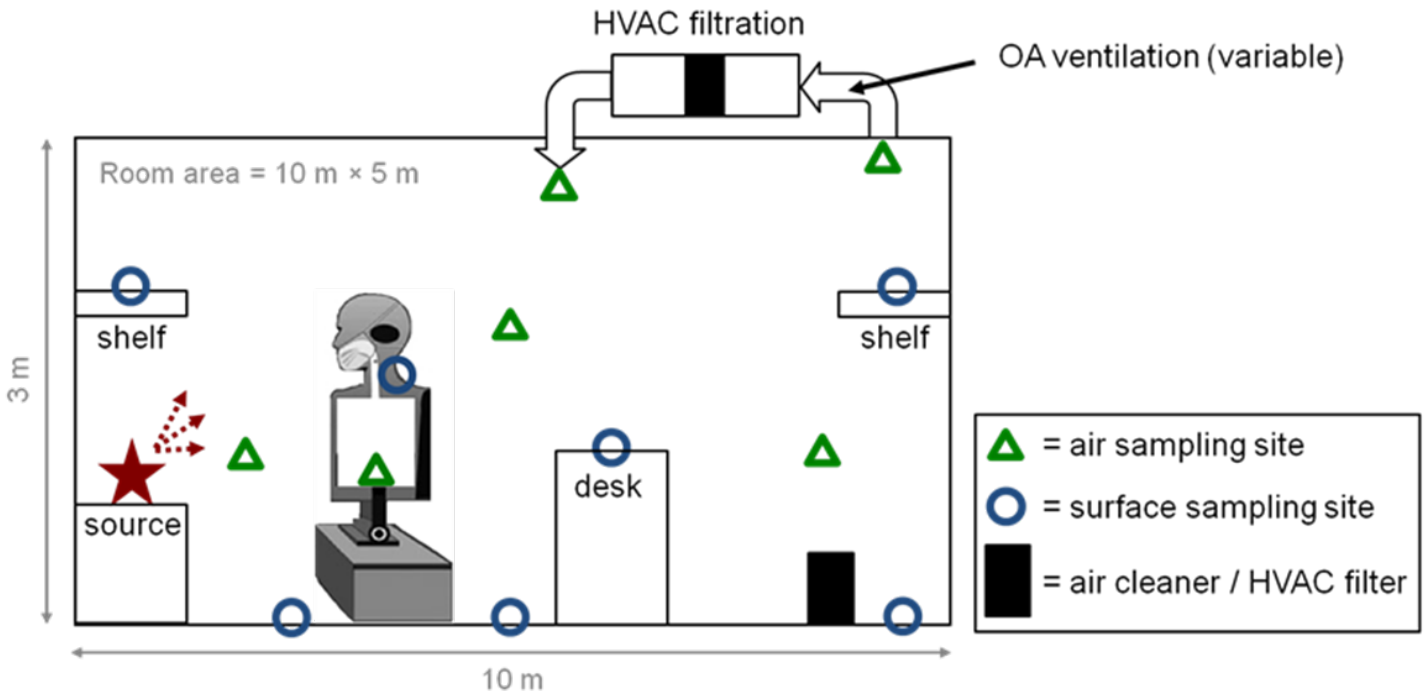
- It would be safe in the dorm because we the we won't use any pathogenic organisms

- We can mimic the airborne transmission of pathogenic viruses resulting from human coughing because the physical characteristics of particles will be keep the same.

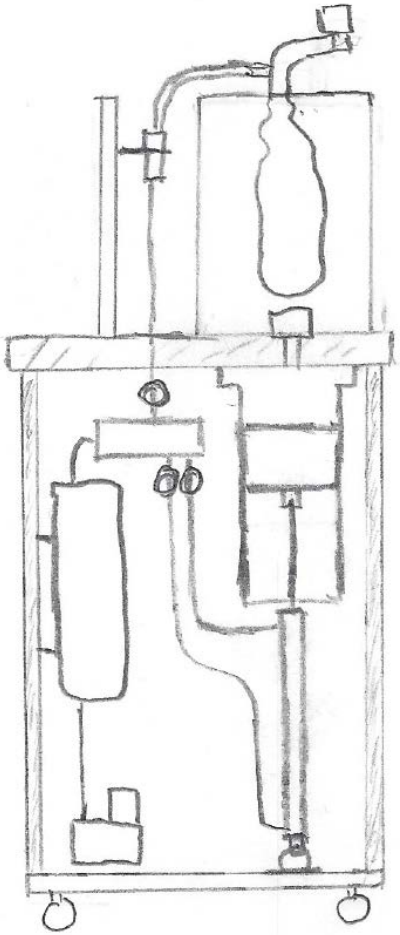
FUTURE WORK

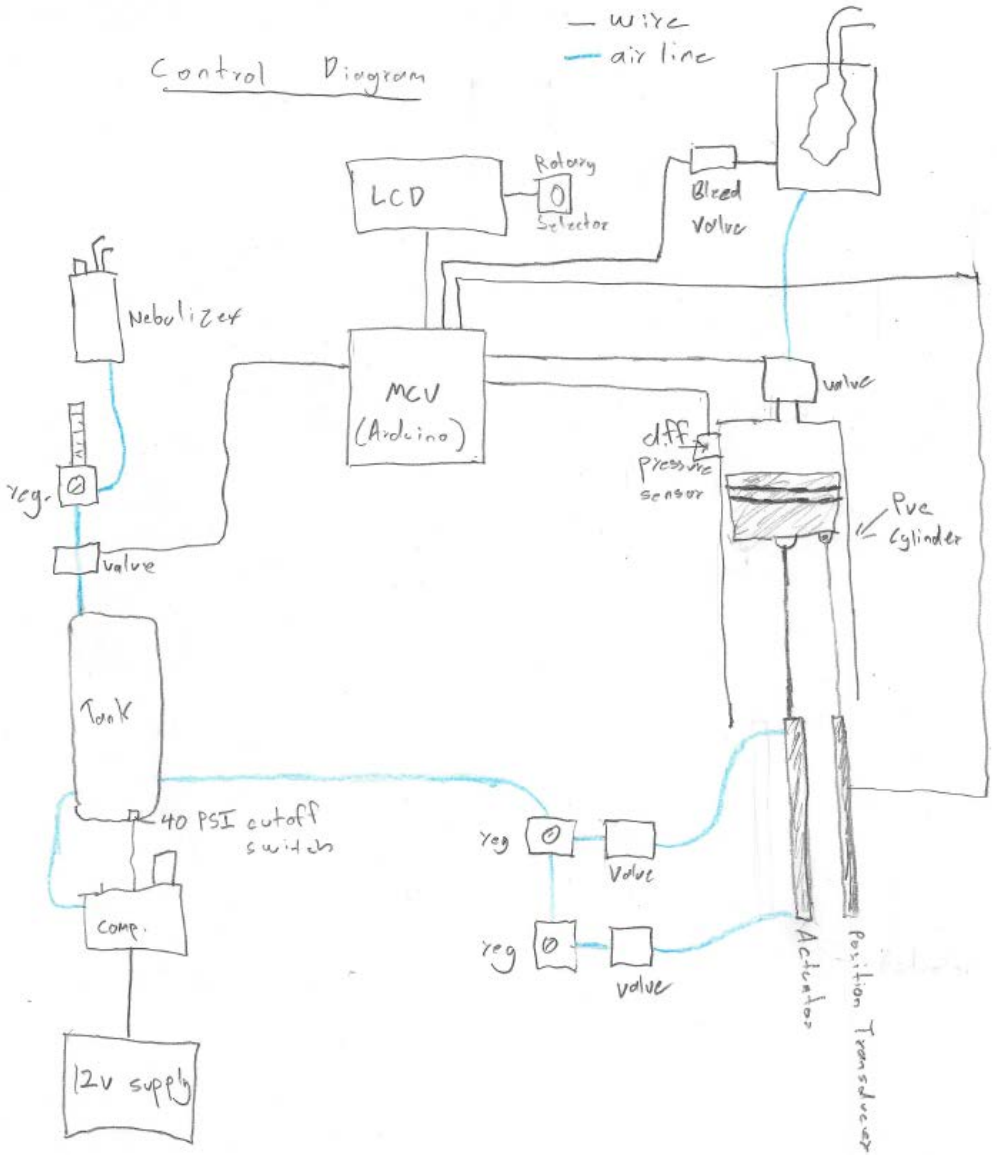
- **Phase 1:** Measuring size-resolved concentrations of bioaerosols and the impact of ventilation and filtration.

- **Phase 2:** Modeling airborne infectious particle concentrations and transmission pathways and comparison with measured data



COUGH BOX




wire
air line
Control Diagram
LCD
Rotary Selector
Bleed Valve
Nebulizer
MCV (Arduino)
valve
reg.
diff. pressure sensor
Pve Cylinder
valve
Tank
40 PSI cutoff switch
reg
Valve
comp.
reg
valve
Actuator
Position Transducer
12v supply

THANKS FOR YOUR ATTENTION

Questions