Washington University in St. Louis

center for aerosol science and engineering

# CASE Researchers Tackling COVID-19

**Pratim Biswas:** Airborne Transmission of SARS-COV-2

**Rajan Chakrabarty:** Models to predict spread of the coronavirus in populations

**Richard Axelbaum:** Guidance to front line health care physicians on masks

**Brent Williams:** Facemask Filter Testing in the Laboratory

**Pratim Biswas & Rajan Chakrabarty :** Delivery of Antiviral Drugs for Treatment of COVID-19

***April 17, 2020***

# Airborne Transport of SARS-COV-2

## Projects Underway in AAQRL


**Pratim Biswas**
**Sukrant Dhawan (Airborne Transport)**
**David Dhanraj, Ben Kumfer (Filter testing)**
**Shruti Choudhary (Filter Testing & PM Sensors)**
**Hao Zhou (Espray Drug Delivery)**

pbiswas@wustl.edu


***April 17, 2020***

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AAQRL

# MODES OF TRANSMISSION OF SARS-COV-2 CAUSING COVID 19

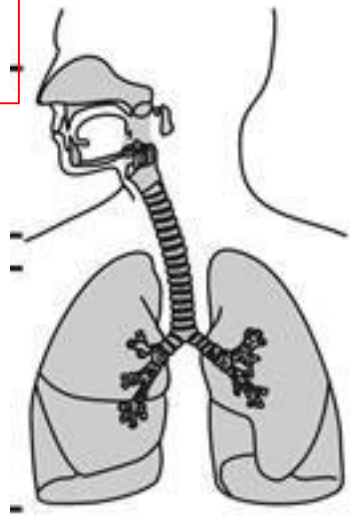
Talking
Breathing

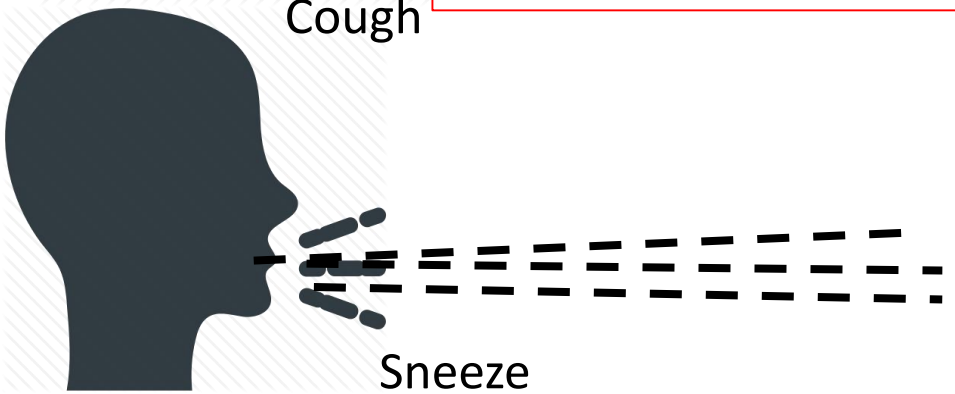
- Direct Contact (e.g Handshake)
- Indirect Mode via Fomite (Surfaces)
- Airborne Transmission (as Aerosols)

Cough

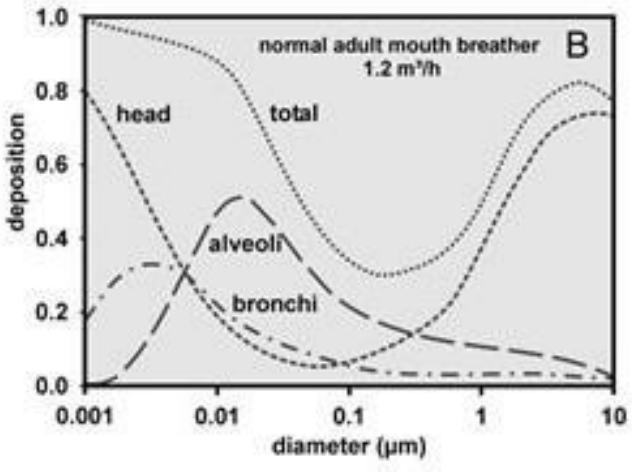
Important Considerations

- Virus has to be emitted
- Virus has to enter Respiratory Tract
- Remain Viable and Replicate



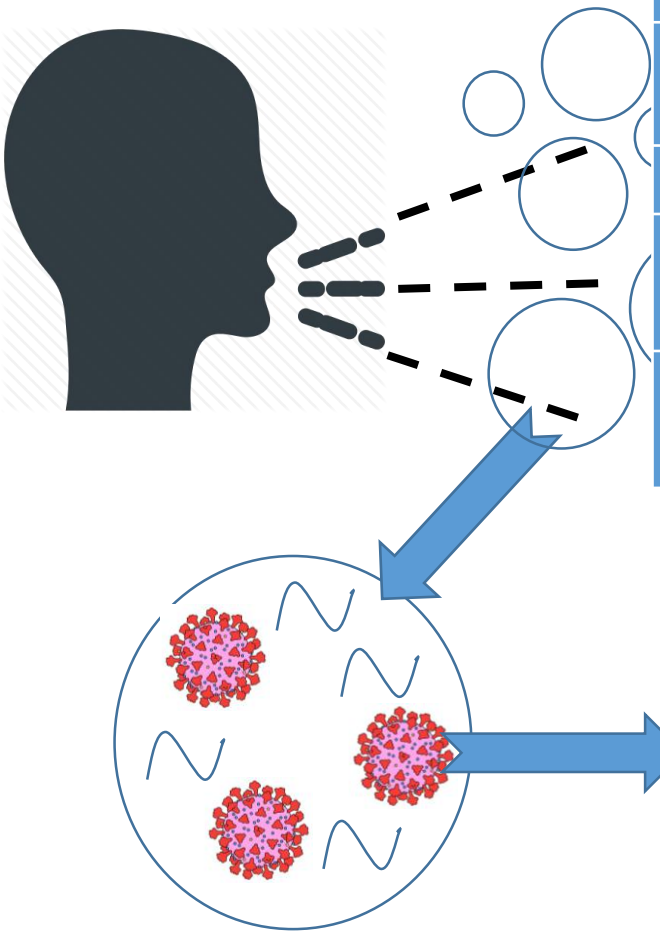


Sneeze

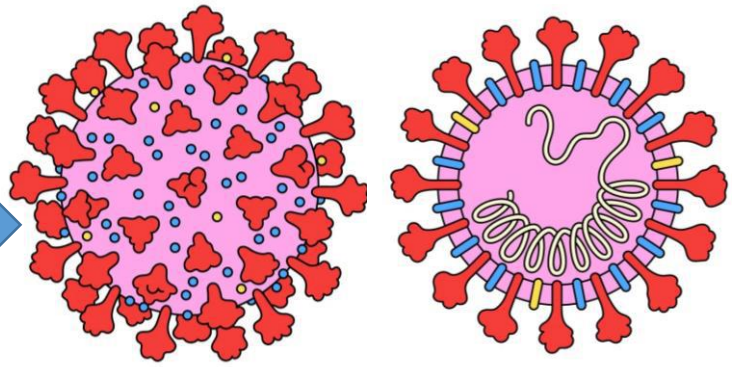



Symptomatic
& Asymptomatic Individuals

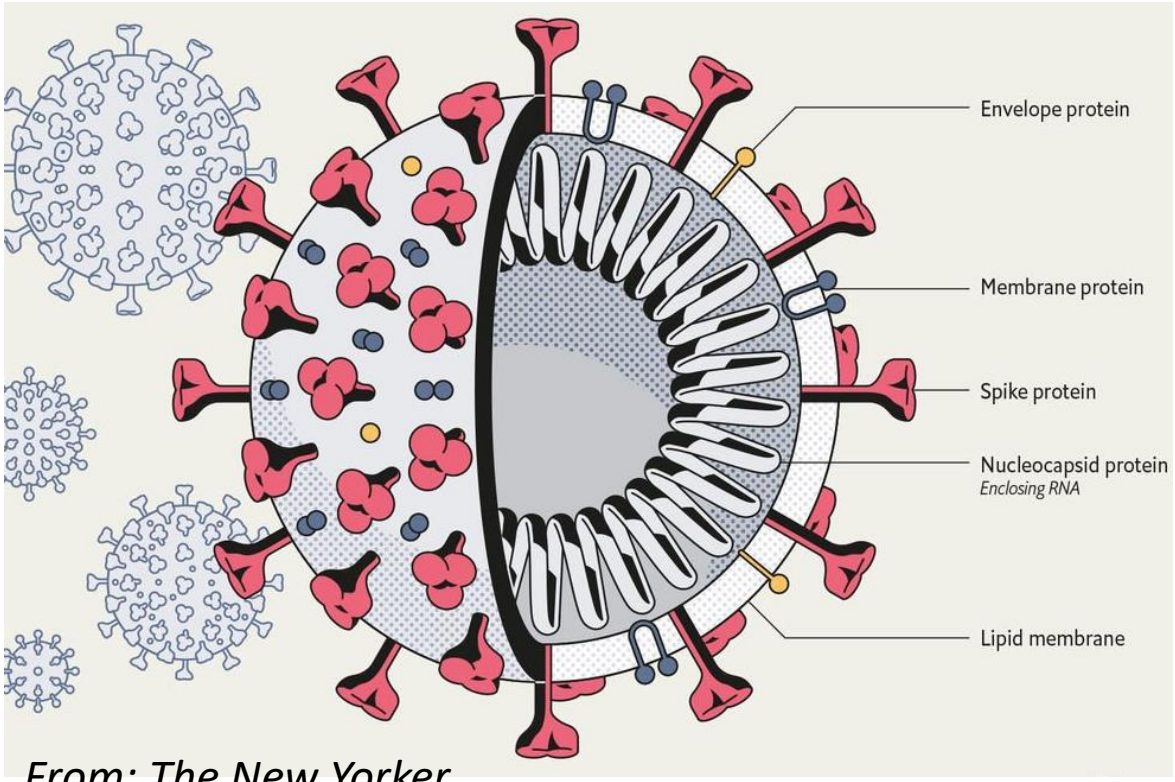
| | Particle Size Distribution of Emitted Droplets | | |
|---|---|---|---|
| | Speaking (Breathing) | Coughing | Sneezing |
| | Chao et al (2009) | Chao et al. (2009) | Duguid (1946) |
| $N_{total}$ (# / $m^3$) | 1.51 x $10^5$ | 2.37 x $10^6$ | 2.74 x $10^8$ |
| Geometric Mean Size(µm) | 16.3 | 13.4 | 8.86 |
| Geom. Std Deviation | 3.6 | 3.48 | 2.21 |



Range of Diameters
Mean Size ~ 10 µm



SARS – COV-2 Virus (~ 120 nm)




*From: The New Yorker*

The coronavirus's RNA, is swathed in three different kinds of proteins, one of which decorates the virus's surface with mushroom-like spikes, giving the virus the eponymous appearance of a crown.

## Pathway to Causing Infection

- **Binding and Fusing** to Lung Cells (Mushroom shaped spikes bind to a receptor called ACE-2 easily accessible in the lung)
- **Replication** successful (self correcting mechanism during self assembly)
- **Shedding** mechanism (released with mucus, phlegm)
- Stays virulent (infective) for a certain time outside the host cell after it is released– after which the structure denatures

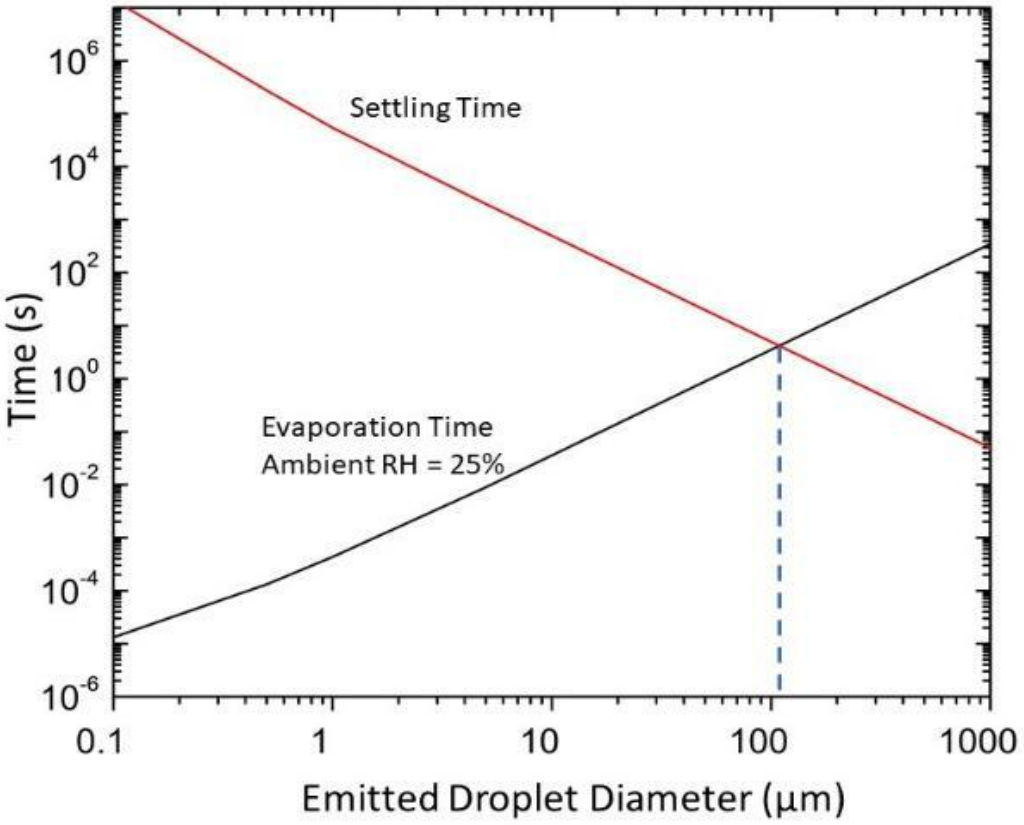
# AIRBORNE TRANSMISSION MODEL TO DETERMINE SARS-COV-2 SPREAD

$$\frac{\partial n}{\partial t} = \nabla^2(Dn) - \frac{\partial(Gn)}{\partial v} - \nabla.(\overrightarrow{v_p} n)$$

$$\overrightarrow{v_p} = (\overrightarrow{u_{air}} - \overrightarrow{u_{ext}})$$

Aerosol dynamic phenomena important

Evaporation of droplet should be considered

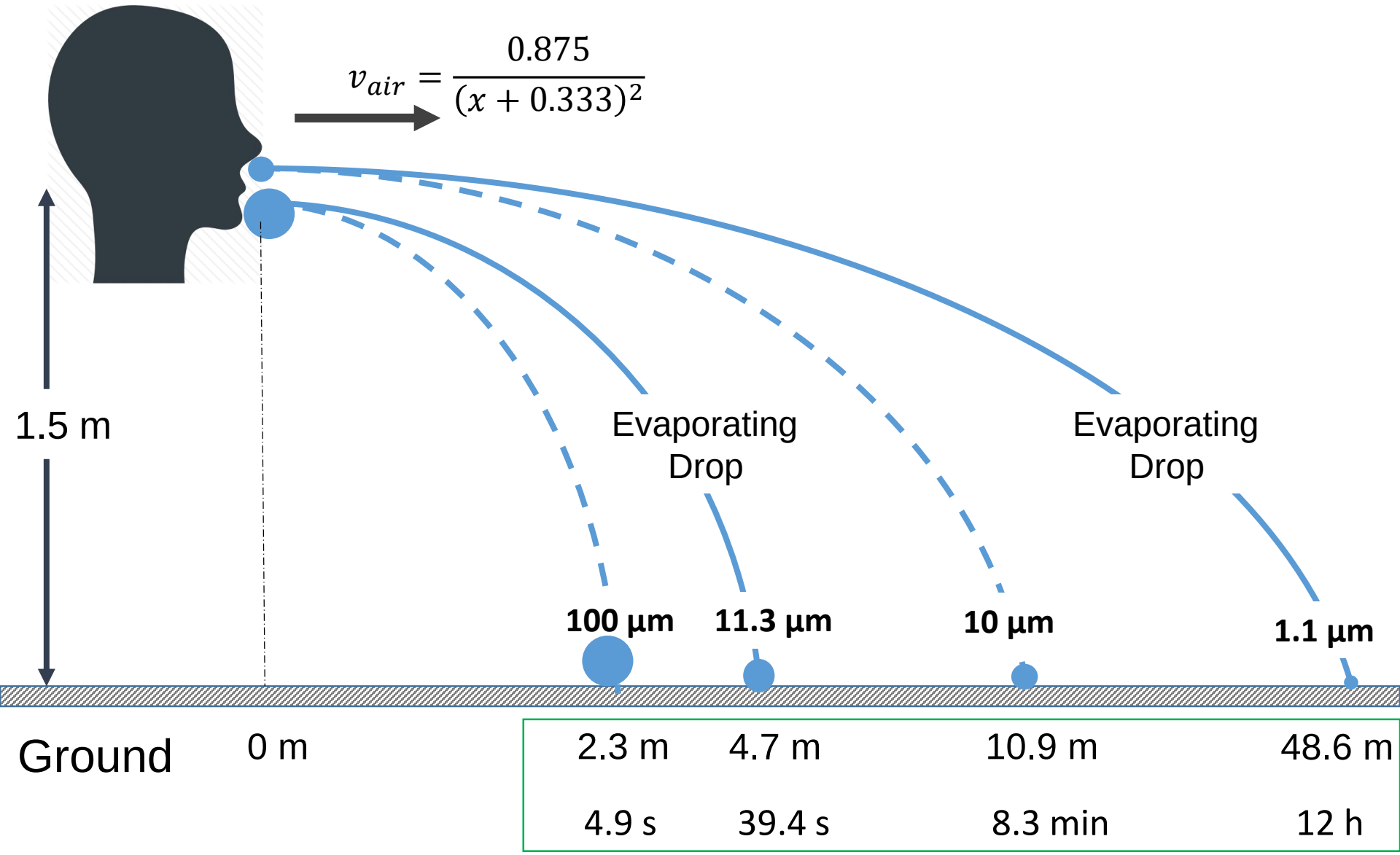



## Current Work

- Number of Viruses per droplet
- Incorporating Virus Shedding
- Viability of virus (denaturing kinetics)
- Size distribution of resultant viable aerosol
- Respiratory deposition

*Work being done by PhD Student: Sukrant Dhawan*

# AIRBORNE TRANSMISSION MODEL TO DETERMINE SARS-COV2 SPREAD




*Dhawan and Biswas (2020)*

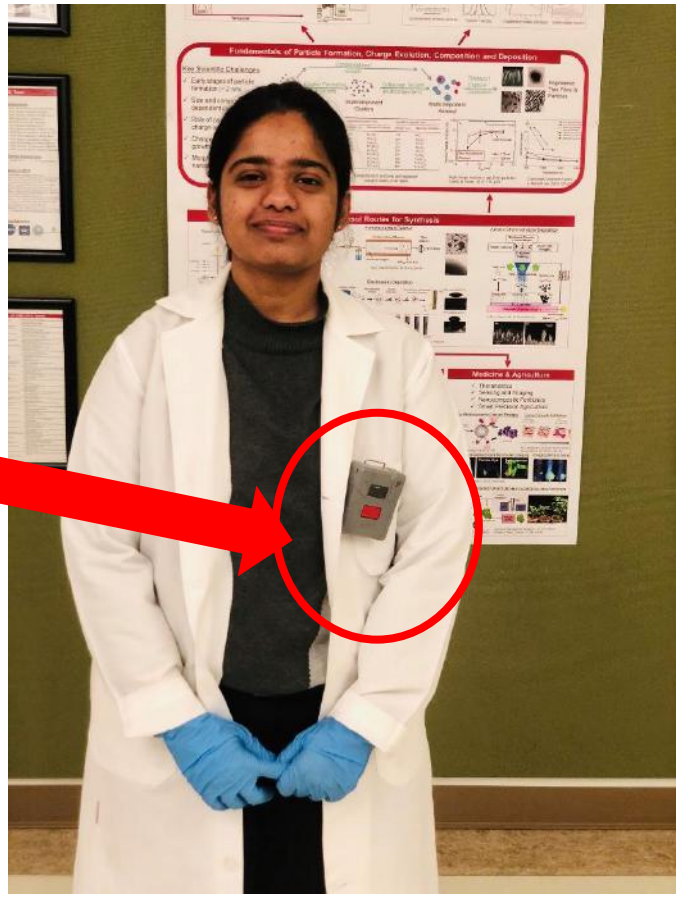
# AIRBORNE SPREAD : MEASUREMENTS IN COVID-19 PATIENT ROOMS


15 cm

**M A X I M A**

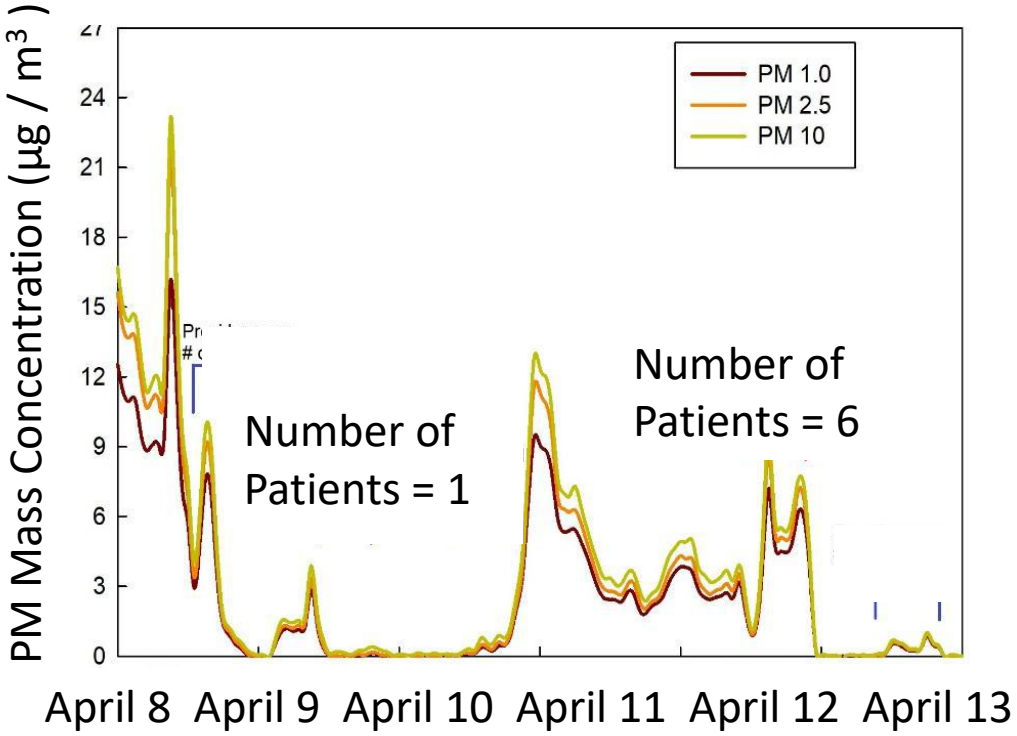
**M I N I M A**

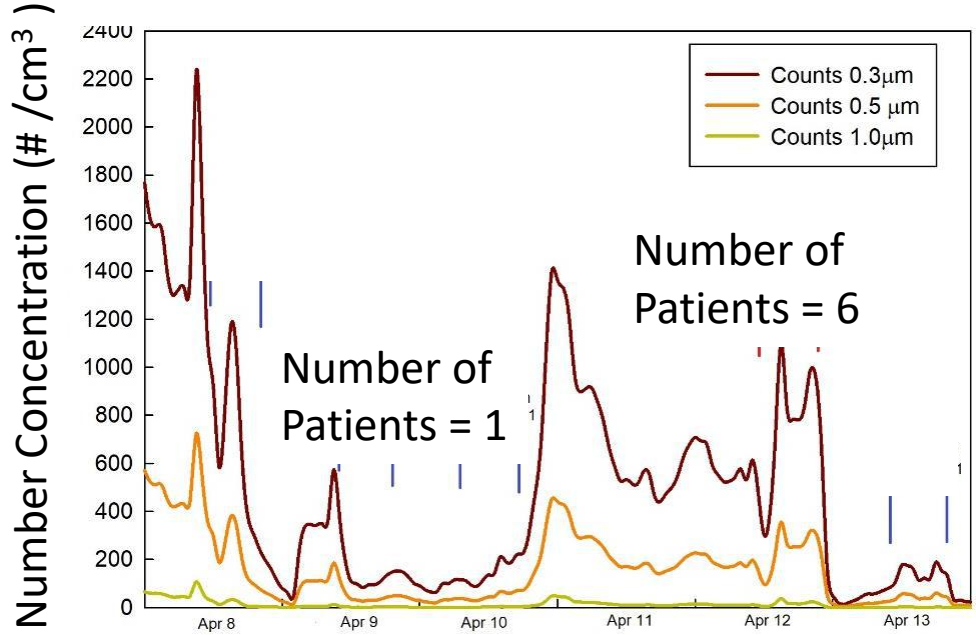
**APT Low Cost Sensor:**
**Real time, Cloud Based**



- OBTAIN DATA FOR AIRBORNE TRANSMISSION MODELS
- INDICATOR TO HEALTH CARE WORKER AND PHYSICIANS FOR PROTECTION

*Work by Shruti Choudhary*
*Drs S. Liang, Laura Marks*




# PM DATA FROM COVID-19 PATIENT WAITING ROOMS MONITORED REMOTELY ON OUR COVID-19 DASHBOARD

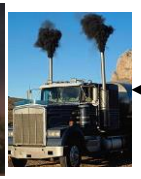
Plan to use VIVAS BioSpot Sampler
To selectively identify airborne SARS-COV-2

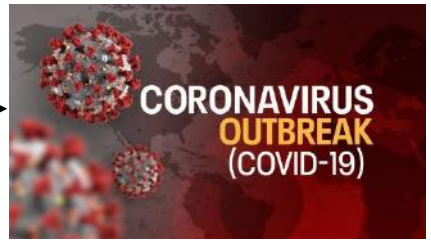
# Modeling to predict spread of coronavirus in populations

Pai Liu (Postdoc), Payton Beeler
(2nd year PhD student)
&
Rajan Chakrabarty (PI)

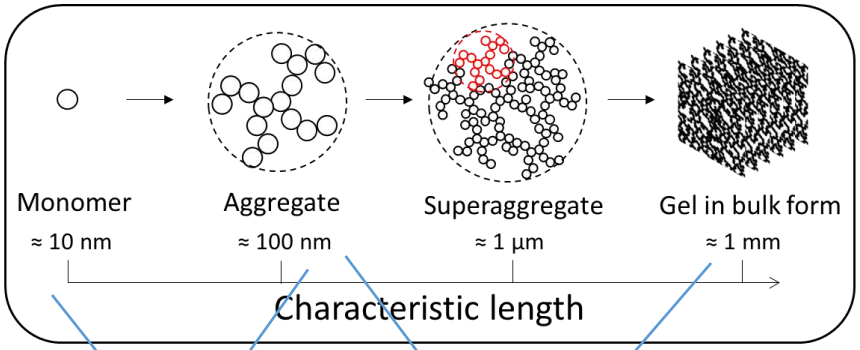
Complex Aerosol Systems
Research Laboratory

Special Thanks: Vince Ruppert (IT Support) & Dean's staff



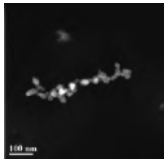


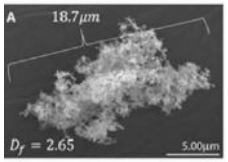

Aggregation Kernel $\beta_{ij} = (ij)^{\lambda}$

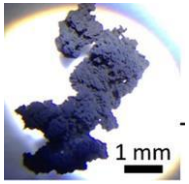


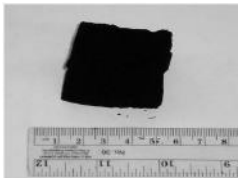

$\lambda = 0$

$\lambda > 0$





Radius of gyration

$R_g$ (µm)

$10^{-3}$

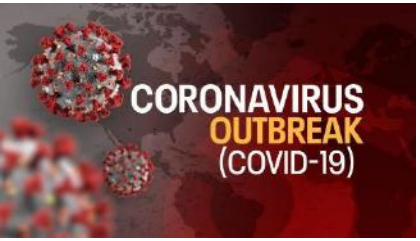
**Aggregation,**

$10^{0}$ **Gelation,**

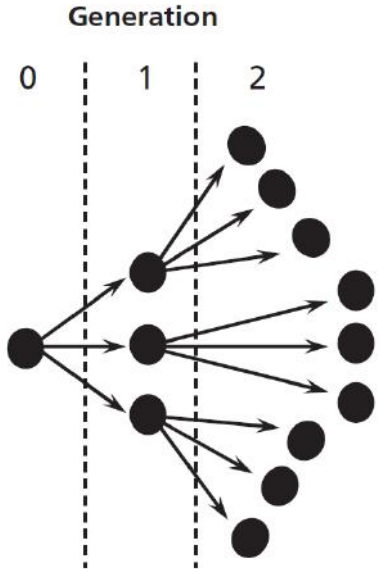
$10^{3}$

**…and Beyond**

$10^{6}$




# Reproductive number $R_0$ analogous to $\beta_{ij}$




Initial phase of epidemic ($R_0 = 3$)

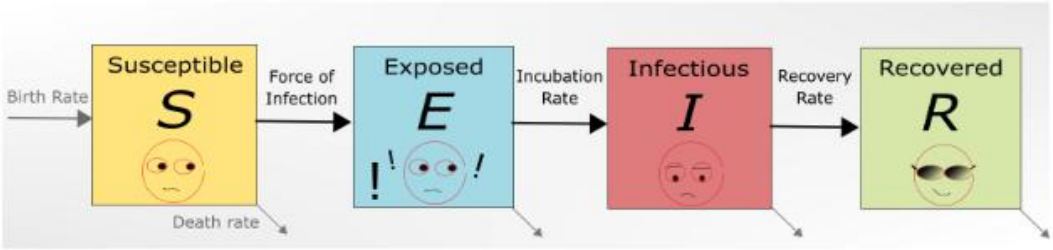
The basic reproductive number, $R_0$, is the number of secondary infections that one infected person would produce in a fully susceptible population through the entire duration of the infectious period.

Pan-InfORM (2009)

$$R_0 = \left( \begin{array}{c} \text{Number of} \\ \text{contacts} \\ \text{per unit time} \end{array} \right) \left( \begin{array}{c} \text{Probability of} \\ \text{transmission} \\ \text{per contact} \end{array} \right) \left( \begin{array}{c} \text{Duration of} \\ \text{infection} \end{array} \right) \times \left( \begin{array}{c} \text{Probabililty of} \\ \text{surviving} \\ \text{exposed stage} \end{array} \right)$$

- If $R_0 < 1$, the disease-free equilibrium point is globally asymptotically stable and there is no endemic equilibrium point (the disease dies out).
- If $R_0 > 1$, the disease-free equilibrium point is unstable and a globally asymptotically stable endemic equilibrium point exists.

# Susceptible-Exposed-Infectious-Recovered Model



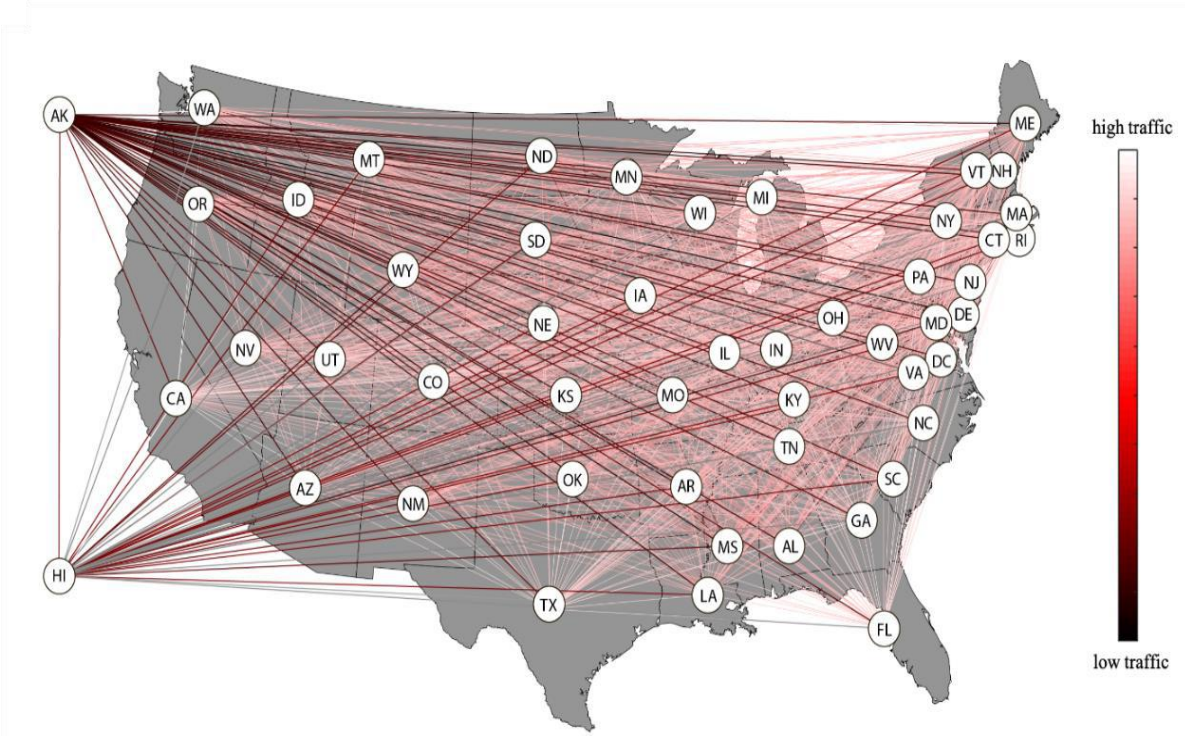

Divide the population into different groups based on infection status:

- $S$: Susceptible humans
- $E$: Exposed (infected but not yet infectious) humans
- $I$: Infectious humans
- $R$: Recovered humans.

- Can include time-dependent parameters to include the effects of seasonality.
- Can include additional compartments to model vaccinated and asymptomatic individuals, and different stages of disease progression.
- Can include multiple groups to model heterogeneity, age, spatial structure or host species.

WUStL SEIR model:

# Mobility Network-Driven Dynamics



# Metapopulation Social Interaction Dynamics

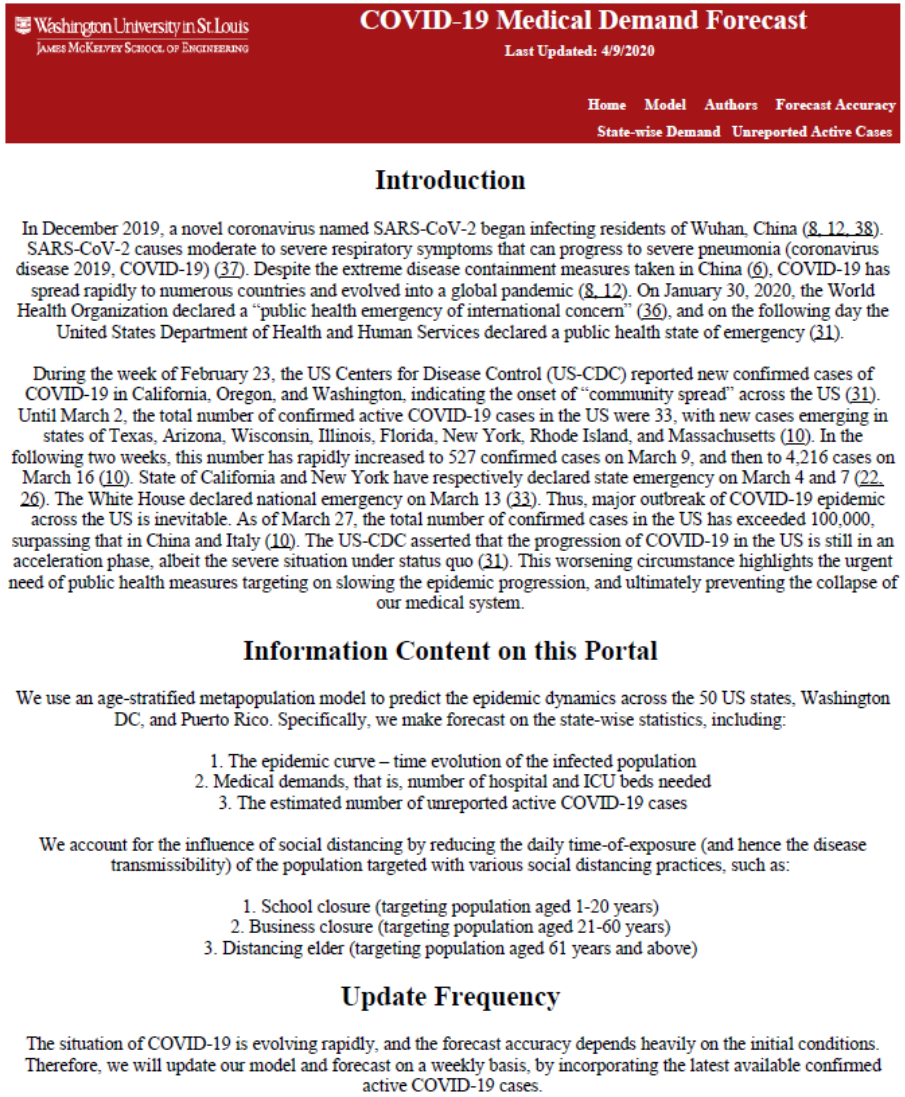
WUStL SEIR model:

| | 0-9 years | 10-19 | 20-29 | 30-39 | 40-49 | 50-59 | 60-69 | 70-79 |
|---|---|---|---|---|---|---|---|---|
| 0-9 years | 144.5 | 84.25 | 135.5 | 198.5 | 79.5 | 20.75 | 12.5 | 7 |
| 10-19 | 80.5 | 174.25 | 44.25 | 85.75 | 104.25 | 36.75 | 11.5 | 5.25 |
| 20-29 | 137.75 | 51 | 105 | 60.5 | 59 | 48 | 13.5 | 4.75 |
| 30-39 | 199 | 89.25 | 55.5 | 124.5 | 66 | 39.75 | 15.25 | 5.75 |
| 40-49 | 78.75 | 111.25 | 51 | 63 | 121.25 | 52.5 | 15.25 | 6.75 |
| 50-59 | 22 | 44.25 | 48.75 | 48.75 | 70.75 | 119 | 32.75 | 10 |
| 60-69 | 16.5 | 22 | 27.25 | 32.5 | 36.75 | 55 | 131.25 | 41.25 |
| 70-79 | 10.5 | 13.75 | 13.5 | 18.5 | 30.5 | 22.75 | 49.5 | 159.5 |

Daily time of exposure (mins) between people in age-group $k$ (column) and people in age-group $i$ (row)

URL: https://eece.wustl.edu/chakrabarty-group/covid/

# WUStL SEIR model:



Washington University in St. Louis
James McKelvey School of Engineering

## COVID-19 Medical Demand Forecast

Last Updated: 4/9/2020

Home Model Authors Forecast Accuracy
State-wise Demand Unreported Active Cases

### Introduction

In December 2019, a novel coronavirus named SARS-CoV-2 began infecting residents of Wuhan, China (8, 12, 38). SARS-CoV-2 causes moderate to severe respiratory symptoms that can progress to severe pneumonia (coronavirus disease 2019, COVID-19) (37). Despite the extreme disease containment measures taken in China (6), COVID-19 has spread rapidly to numerous countries and evolved into a global pandemic (8, 12). On January 30, 2020, the World Health Organization declared a "public health emergency of international concern" (36), and on the following day the United States Department of Health and Human Services declared a public health state of emergency (31).

During the week of February 23, the US Centers for Disease Control (US-CDC) reported new confirmed cases of COVID-19 in California, Oregon, and Washington, indicating the onset of "community spread" across the US (31). Until March 2, the total number of confirmed active COVID-19 cases in the US were 33, with new cases emerging in states of Texas, Arizona, Wisconsin, Illinois, Florida, New York, Rhode Island, and Massachusetts (10). In the following two weeks, this number has rapidly increased to 527 confirmed cases on March 9, and then to 4,216 cases on March 16 (10). State of California and New York have respectively declared state emergency on March 4 and 7 (22, 26). The White House declared national emergency on March 13 (33). Thus, major outbreak of COVID-19 epidemic across the US is inevitable. As of March 27, the total number of confirmed cases in the US has exceeded 100,000, surpassing that in China and Italy (10). The US-CDC asserted that the progression of COVID-19 in the US is still in an acceleration phase, albeit the severe situation under status quo (31). This worsening circumstance highlights the urgent need of public health measures targeting on slowing the epidemic progression, and ultimately preventing the collapse of our medical system.

### Information Content on this Portal

We use an age-stratified metapopulation model to predict the epidemic dynamics across the 50 US states, Washington DC, and Puerto Rico. Specifically, we make forecast on the state-wise statistics, including:

1. The epidemic curve – time evolution of the infected population
2. Medical demands, that is, number of hospital and ICU beds needed
3. The estimated number of unreported active COVID-19 cases

We account for the influence of social distancing by reducing the daily time-of-exposure (and hence the disease transmissibility) of the population targeted with various social distancing practices, such as:

1. School closure (targeting population aged 1-20 years)
2. Business closure (targeting population aged 21-60 years)
3. Distancing elder (targeting population aged 61 years and above)

### Update Frequency

The situation of COVID-19 is evolving rapidly, and the forecast accuracy depends heavily on the initial conditions. Therefore, we will update our model and forecast on a weekly basis, by incorporating the latest available confirmed active COVID-19 cases.

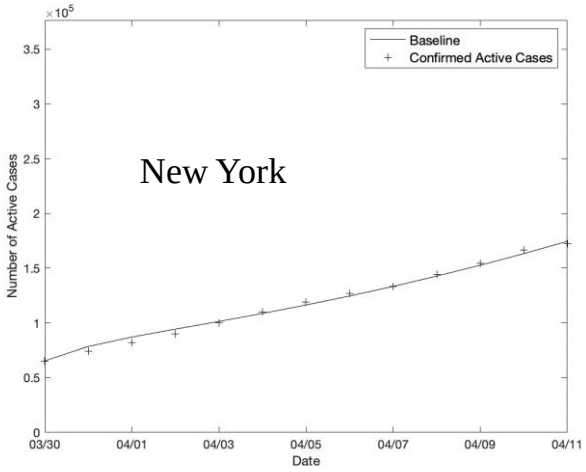
For all 50 US States

- Epidemiological Parameters
  - Medical Demands*
- Effects of Social Distancing

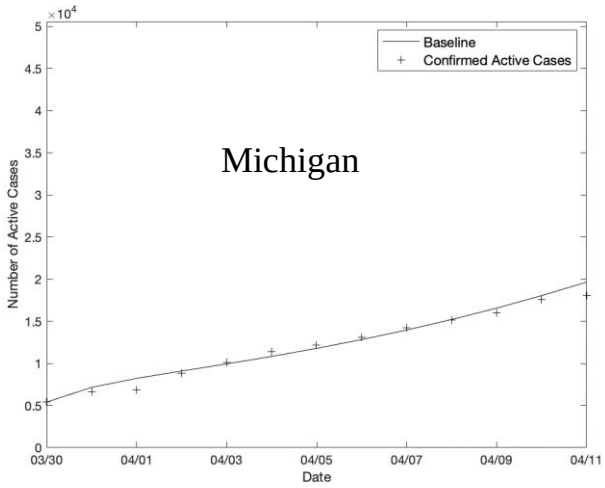
*Harvard Global Health Institute

URL: https://eece.wustl.edu/chakrabarty-group/covid/

# WUStL SEIR model:

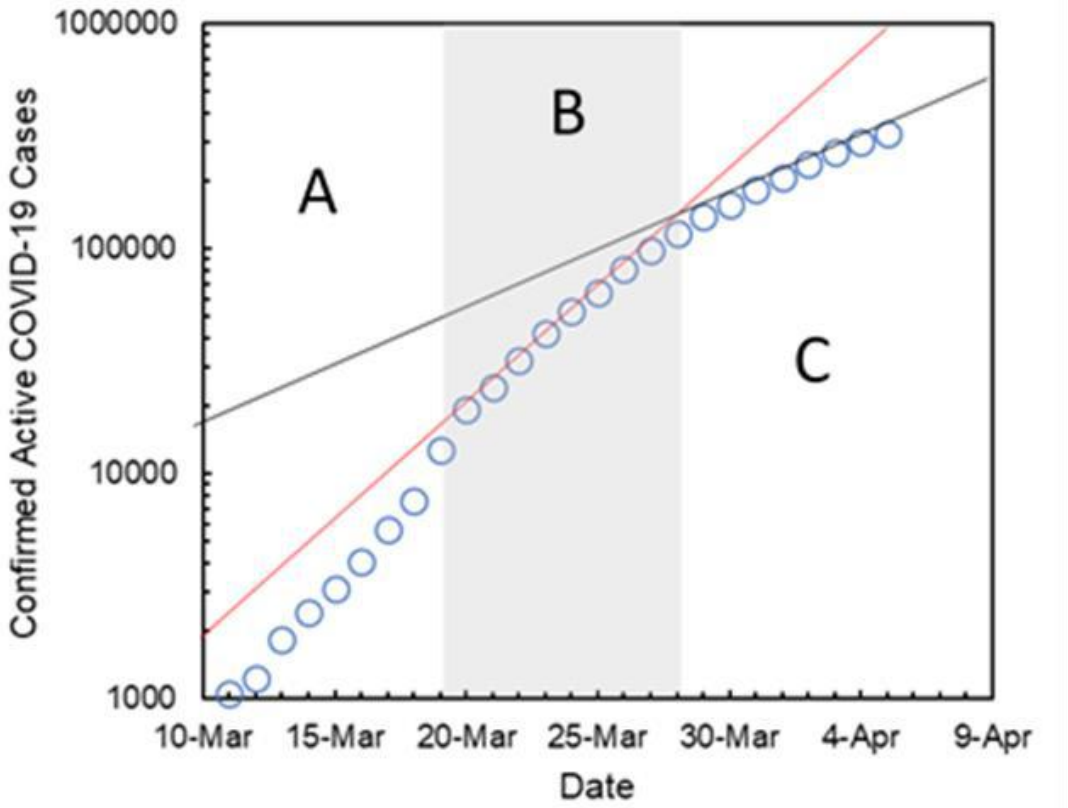




New York




Michigan

# Preliminary Analysis (in the US)

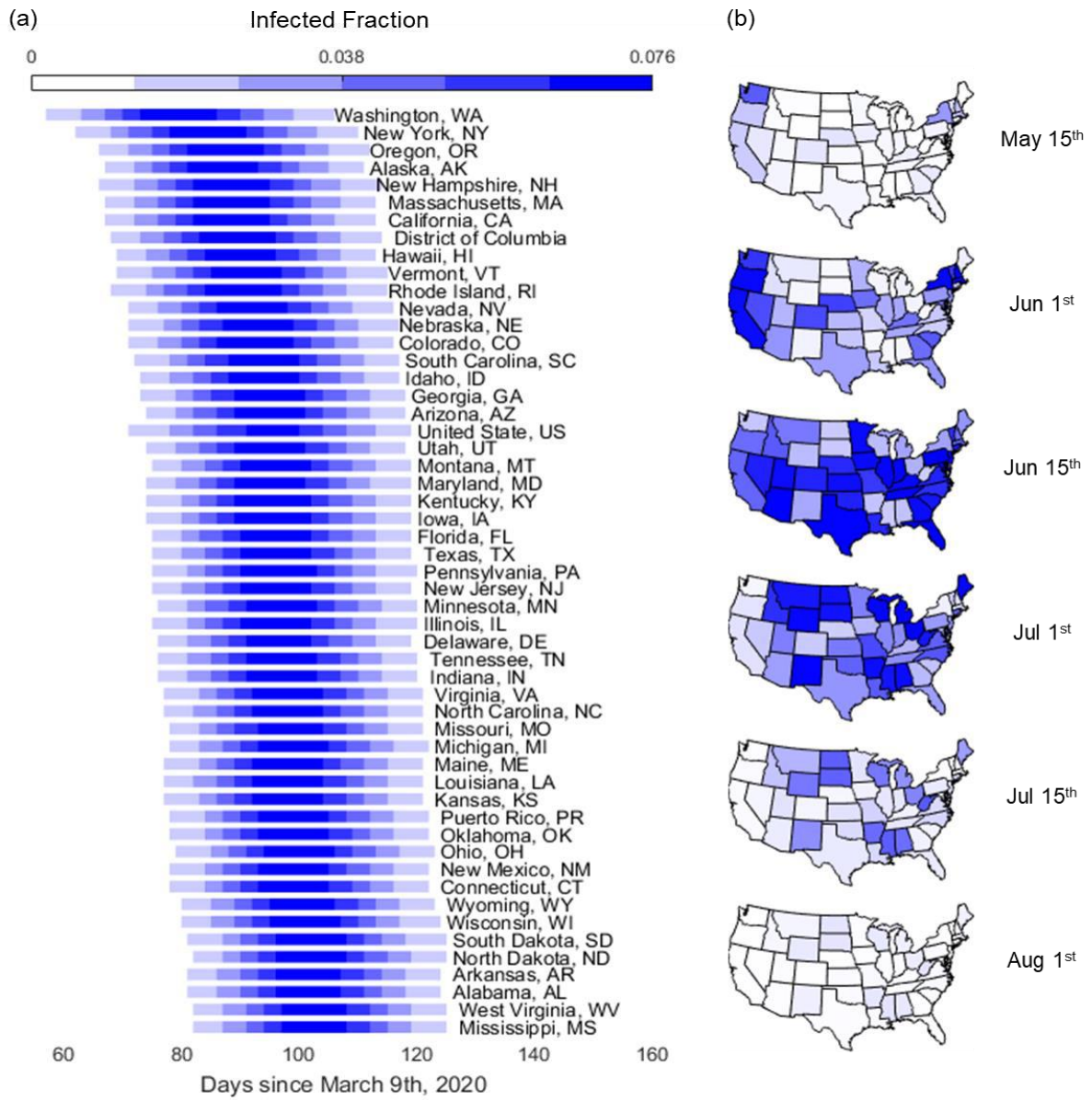



**A -** Limited Testing Phase

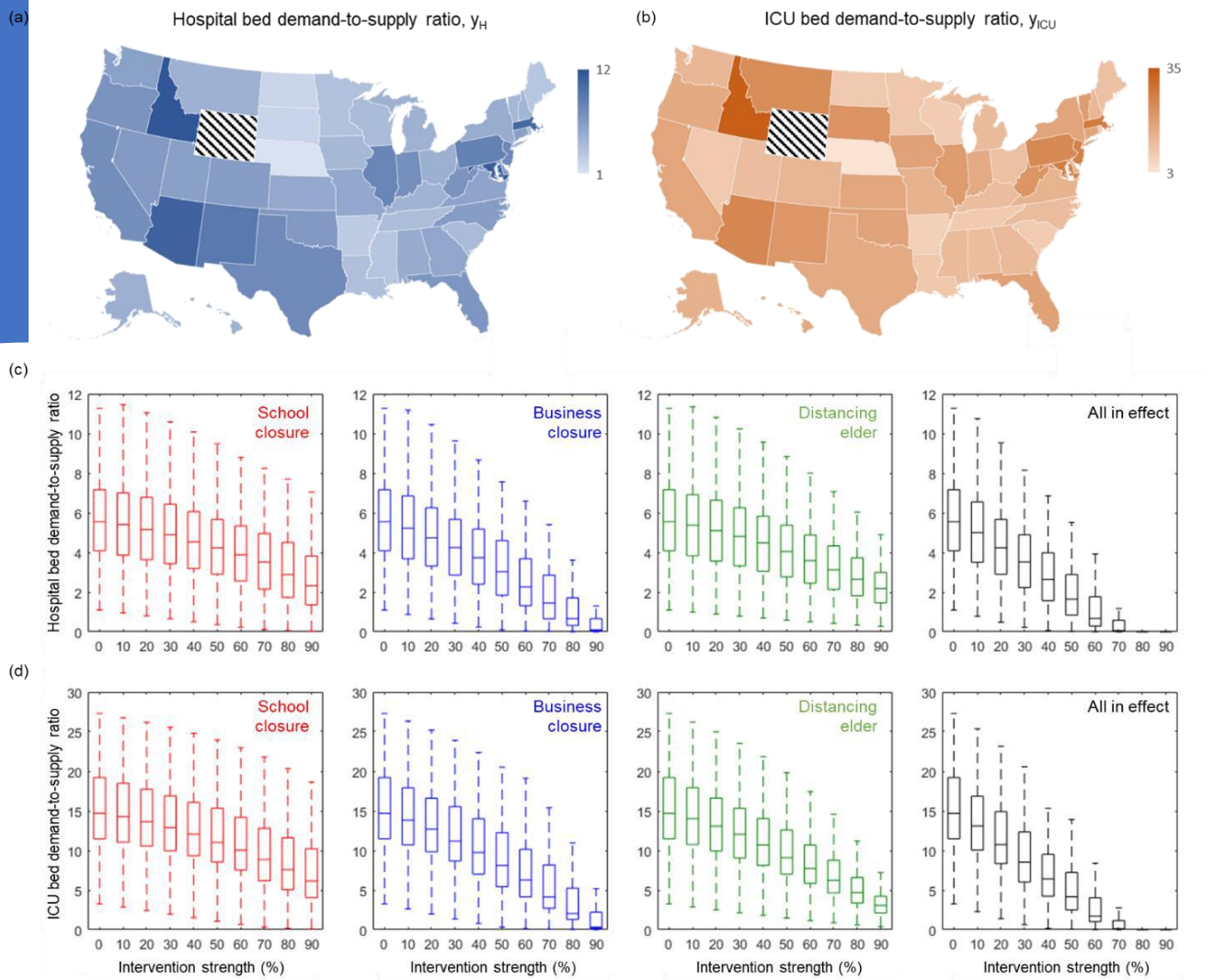
**B -** Ramp-up in Testing and Social Distancing

**C -** Effects of Social Distancing

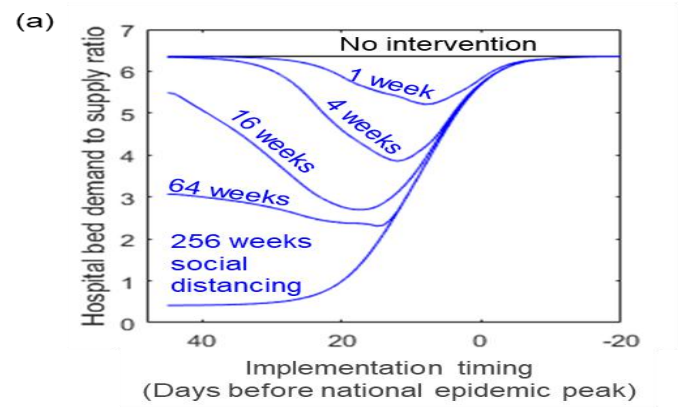
# Limited Testing Phase (till March 17)

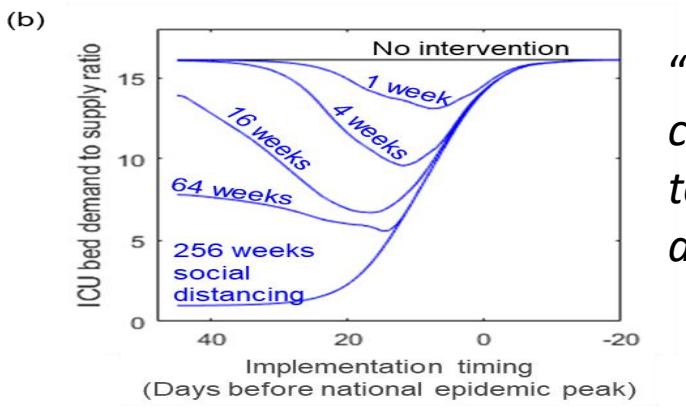


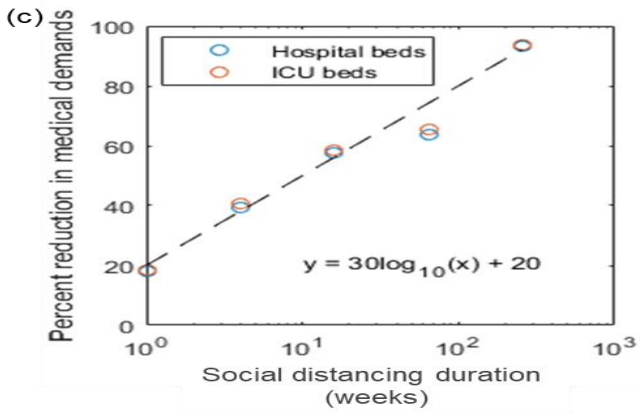
# Ramp-up Social Distancing + Testing (March 18 - 30)



# Effects of Social Distancing + Testing (April 1 onward)




*"How long and at what cost benefit does US need to implement social distancing intervention?"*

Thank you for your attention!

**Pre-prints on medRxiv:**

1. Liu, P., P. Beeler, & R. K. Chakrabarty (2020). COVID-19 Progression Timeline and Effectiveness of Response-to-Spread Interventions across the United States. medRxiv, March 20, https://doi.org/10.1101/2020.03.17.20037770.

2. Liu, P., P. Beeler, & R. K. Chakrabarty (2020). Diminishing Marginal Benefit of Social Distancing in Balancing COVID-19 Medical Demand-to-Supply. medRxiv, April 14, https://doi.org/10.1101/2020.04.09.20059550

# Guidance to front line health care physicians on masks…

and guidance to the rest of us when it comes to wearing masks

Richard Axelbaum
Center for Aerosol Science and Engineering
Energy, Environmental and Chemical Engineering
Washington University in St. Louis

*Associated Press*

April 16, 2020

# Ten nurses suspended for refusing to work without N95 masks

Nurses in Santa Monica, California, refused to care for Covid-19 patients after they say hospital didn't provide essential protective gear

Nurses at Providence Saint John's health center in Santa Monica raise their fists in solidarity after telling managers they can't care for coronavirus patients without N95 masks. Photograph: Lizabeth Baker Wade/AP

# N95 Respirator

Worn to protect ***wearer*** from inhaling hazardous particles


https://articulo.mercadolibre.com.mx/MLM-555056897-3m-8210-respirador-industrial-filtro-n95-caja-con-20-pz-_JM

https://www.medonthego.com/Cardinal-Health-Flat-Fold-N95-Surgical-Mask-Small-USAN95S-Box50_p_133146.html

# Surgical Mask

Worn to protect ***patients*** from the wearers' respiratory emissions

https://www.grainger.com/product/ALPHA-PROTECH-Surgical-Mask-29DZ42

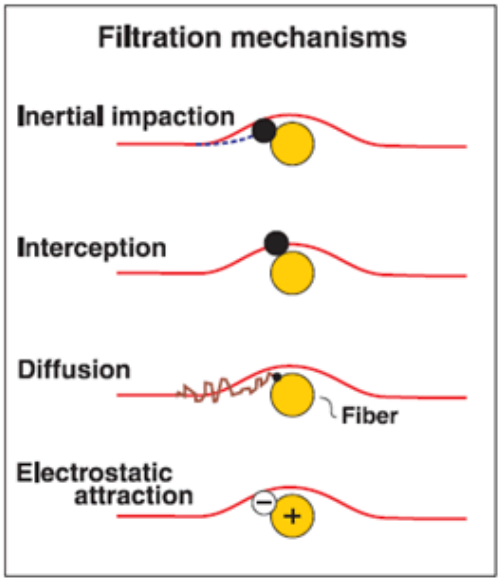
https://www.medsales.com.au/products/proshield-surgical-mask-box-50

# Requirements for a Respirator

- Filter must be able to capture the full range of hazardous particles, typically within a wide range of sizes (<1 to >100 µm) over a range of airflow (approximately 10 to 100 L/min).

- Leakage must be prevented at the boundary of the facepiece and the face.

Filters do NOT act as sieves




NIOSH Science Blog

# Respirators versus surgical masks

## Filtration:

- Respirator filters are tested by NIOSH

- The FDA does not perform an independent evaluation of surgical mask filter performance.

## Fit:

- Respirator must have a fit factor of at least 100 (1% leakage).
  (Fit factor = Outside particle concentration/inside concentration)
- Laboratory study of five surgical masks with "good" filters:
  - 80–100% of subjects failed an OSHA-accepted qualitative fit test using Bitrex (a bitter tasting aerosol)
  - Quantitative fit factors ranged from 4–8 (12–25% leakage) using a TSI Portacount.[1]

1. Oberg, T., and L. M. Brosseau. 2008. Surgical mask filter and fit performance. American Journal of Infection Control 36, (4) (May): 276-82.

# WashU Filter/Mask Testing Operations

## Center for Aerosol Science & Engineering (CASE)

## McKelvey School of Engineering

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Assistance and consultation from many **CASE students**

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Washington University in St. Louis

center for aerosol science and engineering

# Filter/Mask Testing Questions

**Can we help to inform on possible solutions for the following needs:**

1) Creating N95-quality masks for health care providers during an N95 mask shortage

1) Determine effectiveness and durability of masks that have undergone sterilization treatment processes for mask reuse

1) Low-tech mask designs and materials for use by general public

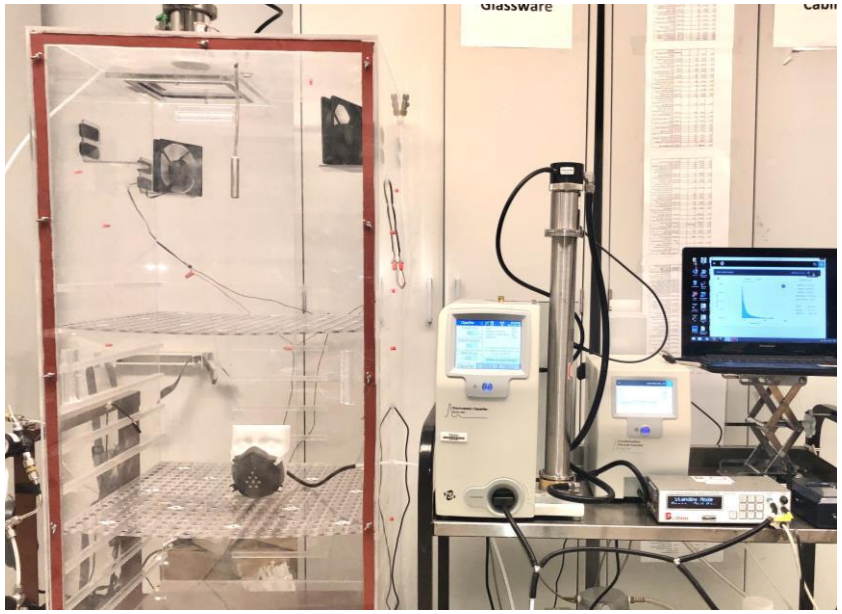
## Filter/Mask Testing Challenges

- Small and large particles captured by different mechanisms (diffusion and impaction, respectively)
- A difficult size range exists between 100-500nm
- N95 masks are tested by NIOSH standards to capture >95% particles at the size of **300nm** and at a flowrate of 85 LPM through an entire mask surface area (in the range of **10 cm/s** face velocity depending on mask design)
- Some historical testing has also been done at lower flowrates (lighter breathing) of 30-35 LPM (in the range of **4 cm/s** face velocity)
- We test all material at a similar **High flowrate** and a **Low flowrate** (scaled to surface area of test material to maintain face velocities)

# Filter/Mask Testing Stations

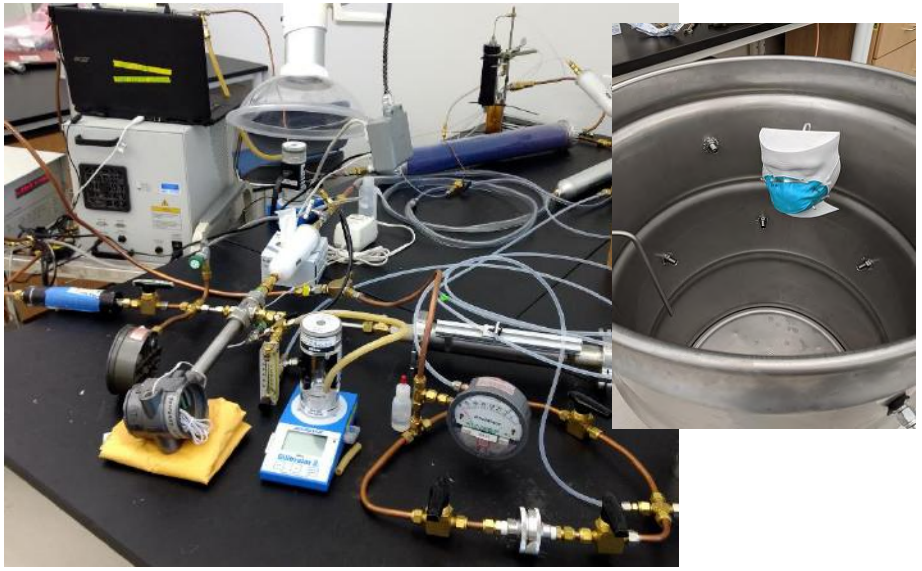
- **Two test stations**
- **Both could test punches of filter material, or full masks**
- **Initial focus more on materials and combinations of materials**

Test Station #1
AAQRL lab
Fast scanning of full size distribution



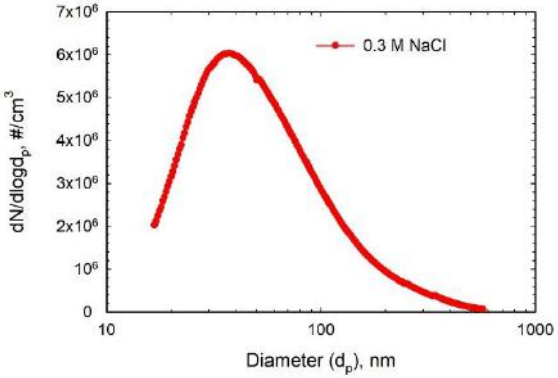
Can analyze entire size distribution and cycle through test materials fast

Test Station #2
CASE shared lab facility
Discrete particle sizes

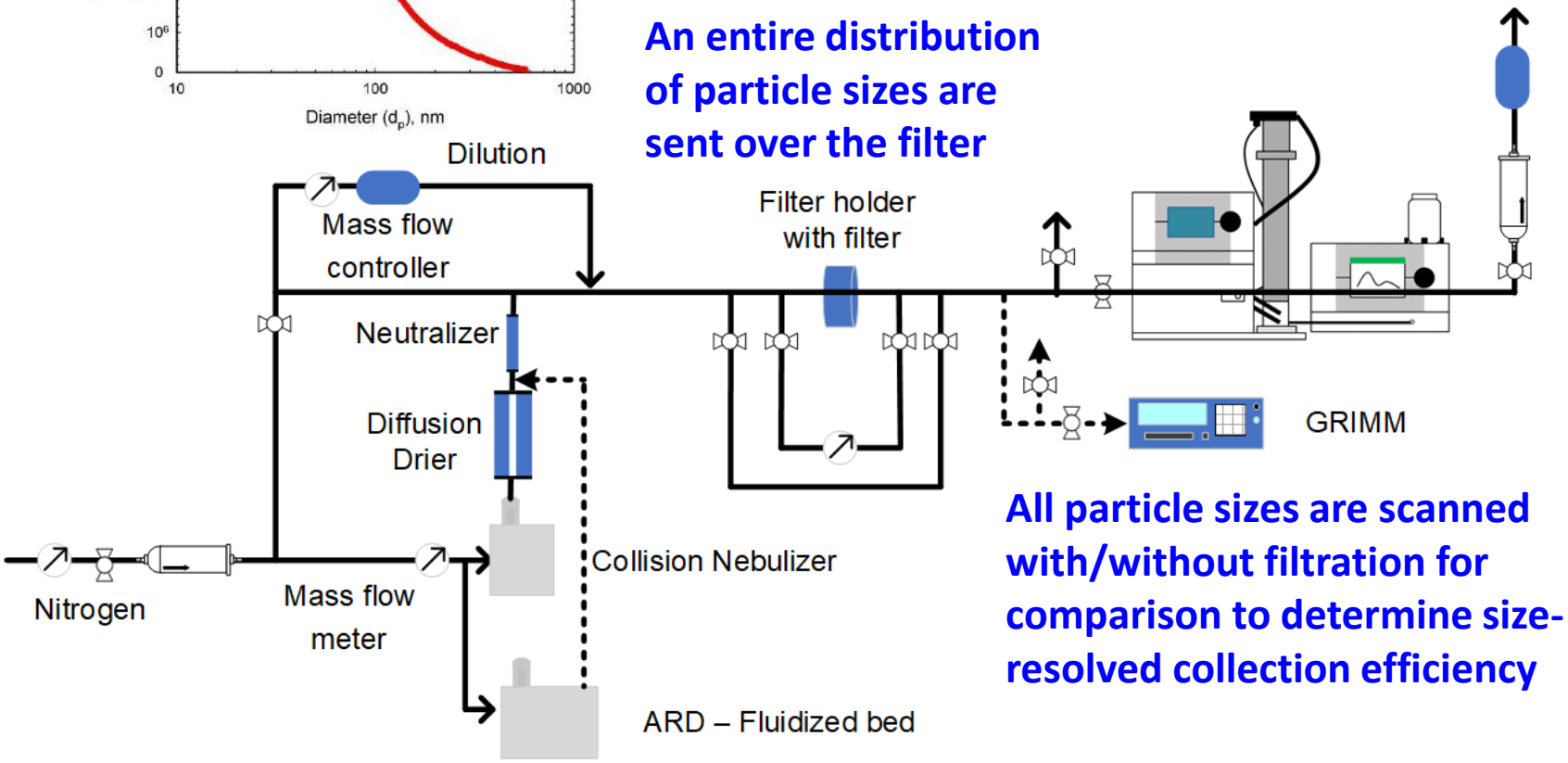


Can run extended tests due to low particle loading – allows good statistics and minimizes uncertainty (important for N95-type performance evaluation)

# Test Station #1 (AAQRL lab – fast scanning of full size distribution)



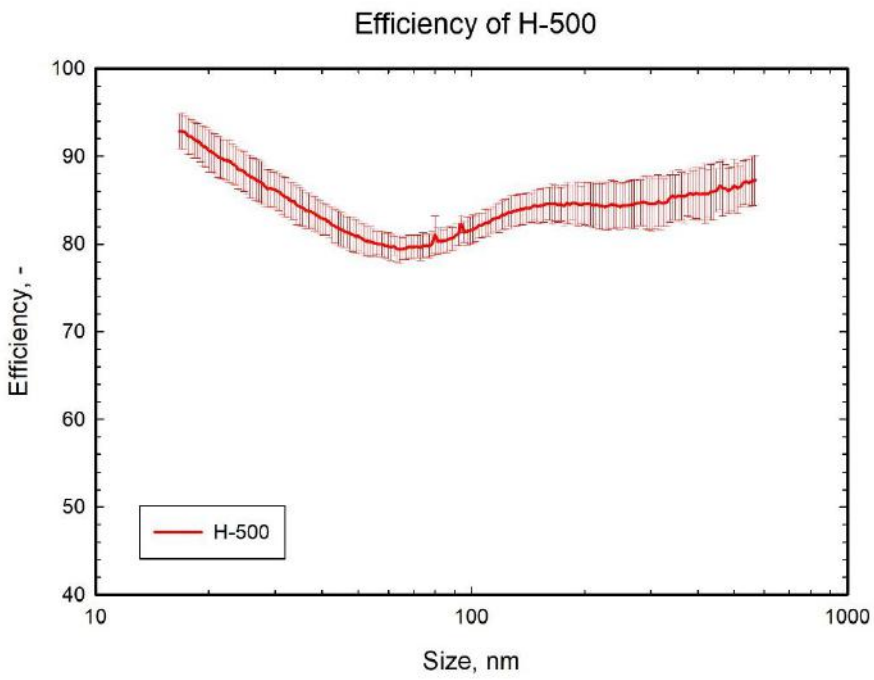

**An entire distribution of particle sizes are sent over the filter**




**All particle sizes are scanned with/without filtration for comparison to determine size-resolved collection efficiency**

Schematic for filter holder-based system

# Standard Operating Procedures




Conditions:

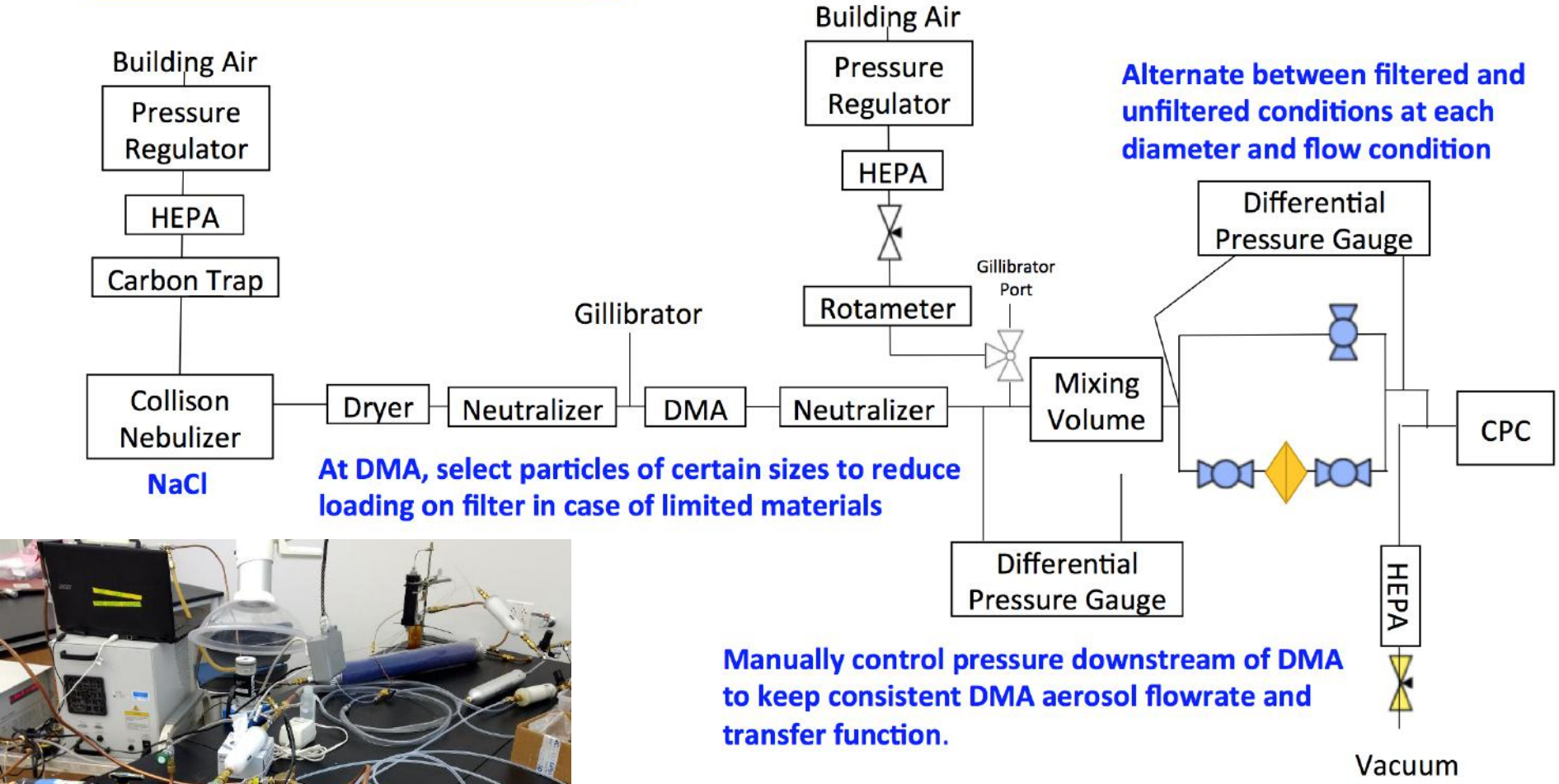
- Filter holder
- 1.8 LPM (Low Flow)
- $N_{TOT}$ ~ 4 x $10^6$ #/$cm^3$
- Single Layer
- Scan 1, averaged between three sets of filter data

Protocol

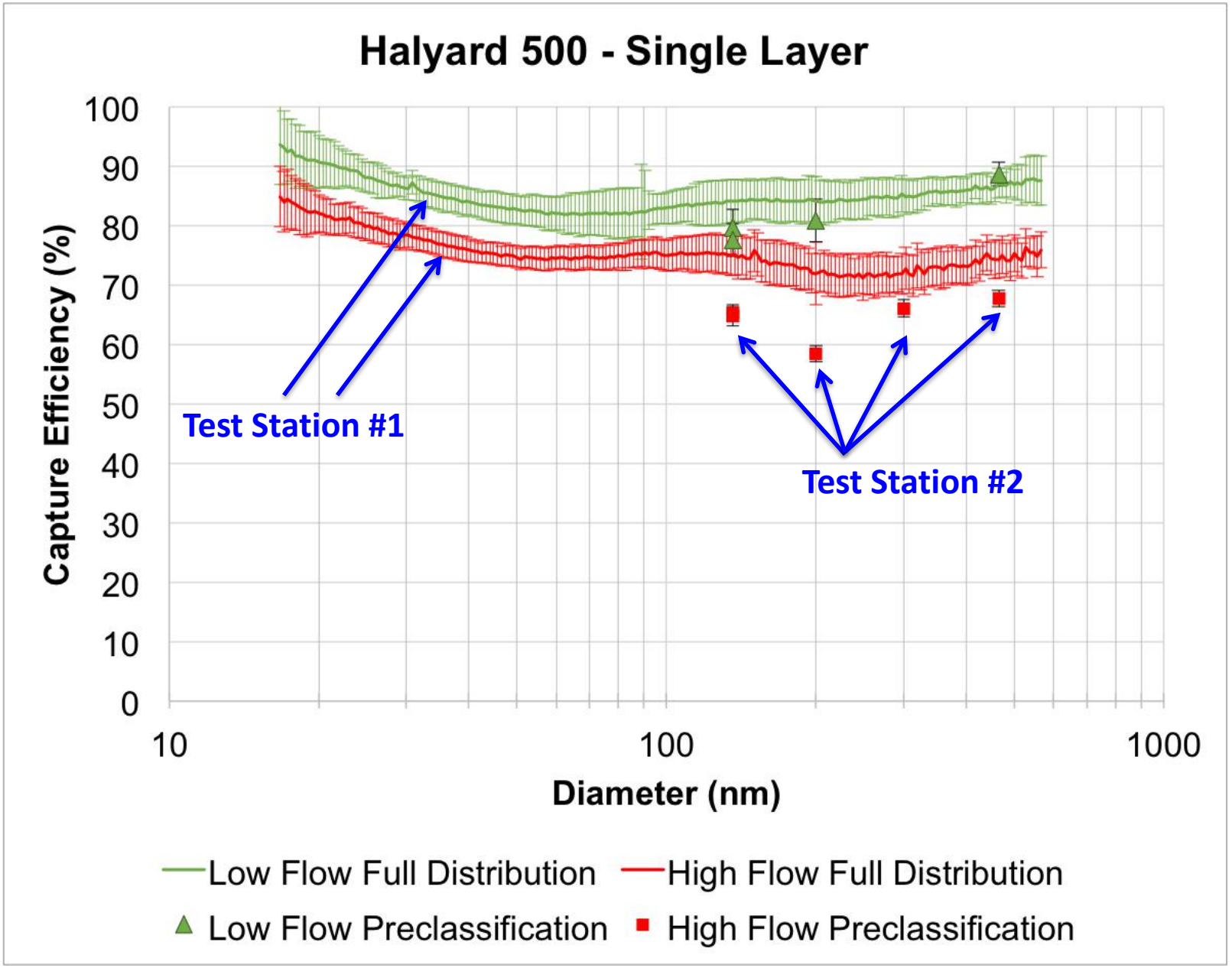
1. Set pressure to Nebulizer as 10 psi
2. Clean and Sonicate nebulizer metal parts and fill 0.3 M NaCl up to 2.6 cm in the container (ensure level remains constant for the entire experiment)
3. Wait for Nebulizer concentration to achieve steady state and then take 5 scans (Blanks, with no filter)
4. Place Filter in the holder and take 5 filter scans
5. Retake 5 blank scans
6. Repeat steps 3-5 for three different filter punch outs (we obtain 3 sets of data) for the same material
7. Calculate average blank by averaging the 10 scans
8. Calculate efficiency by using the average blank and 1-5 filter scans to obtain 5 sets of efficiency data (for each set).
9. Calculate average efficiency between corresponding scans in each set (e.g. scan 1 in set 1, scan 1 in set 2, and scan 1 in set 3) to obtain average efficiency and standard deviation. The figure here is the efficiency thus obtained for scan 1, with standard deviation estimated between three sets).
10. Average between corresponding scans to obtain efficiency as a function of scan or time (each scan is a minute) . See next slide for the plot.

# Test Station #2 (CASE shared lab facility – discrete particle sizes)

**Pre-Classification Measurement Strategy**

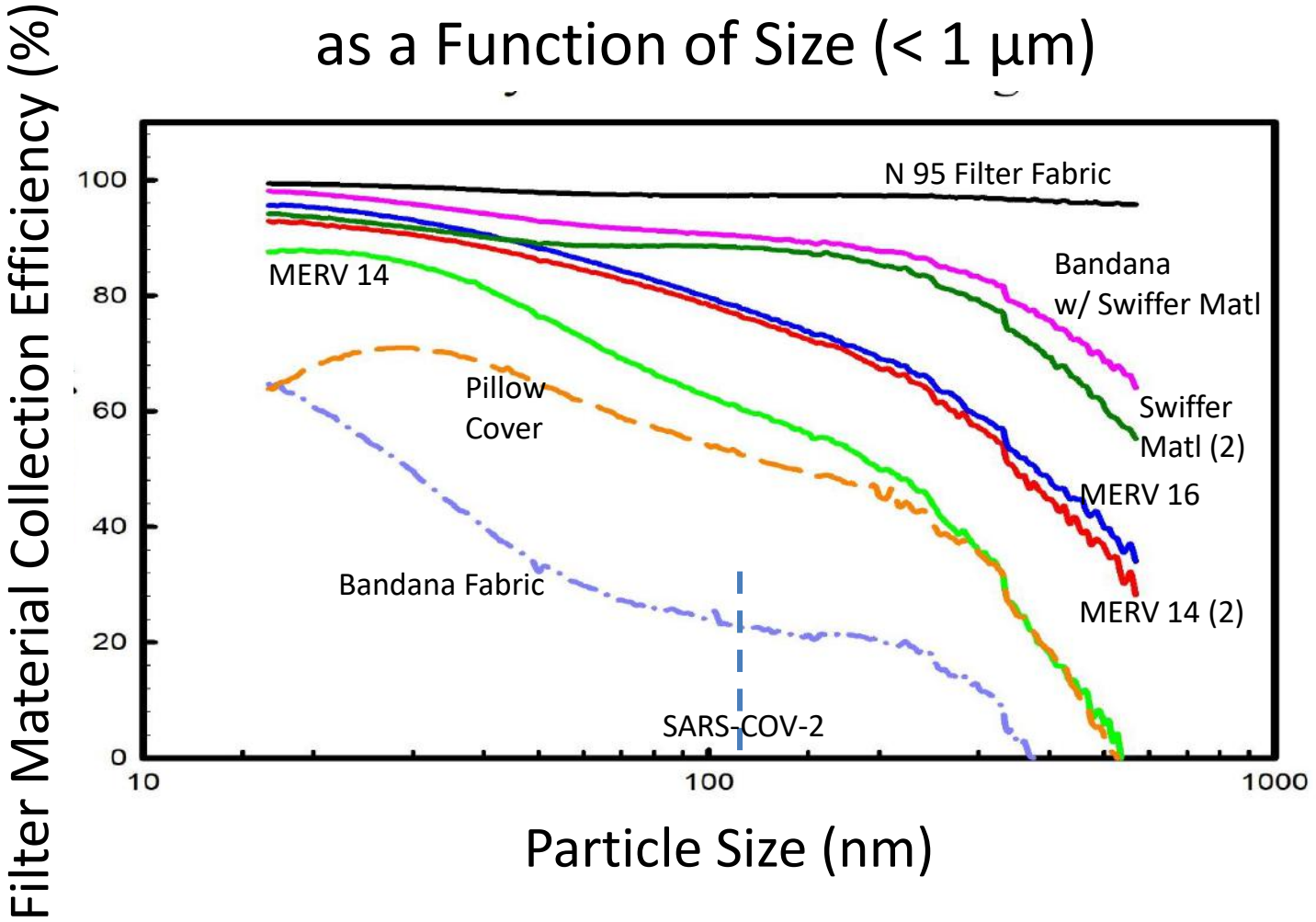


# Test Station Comparison



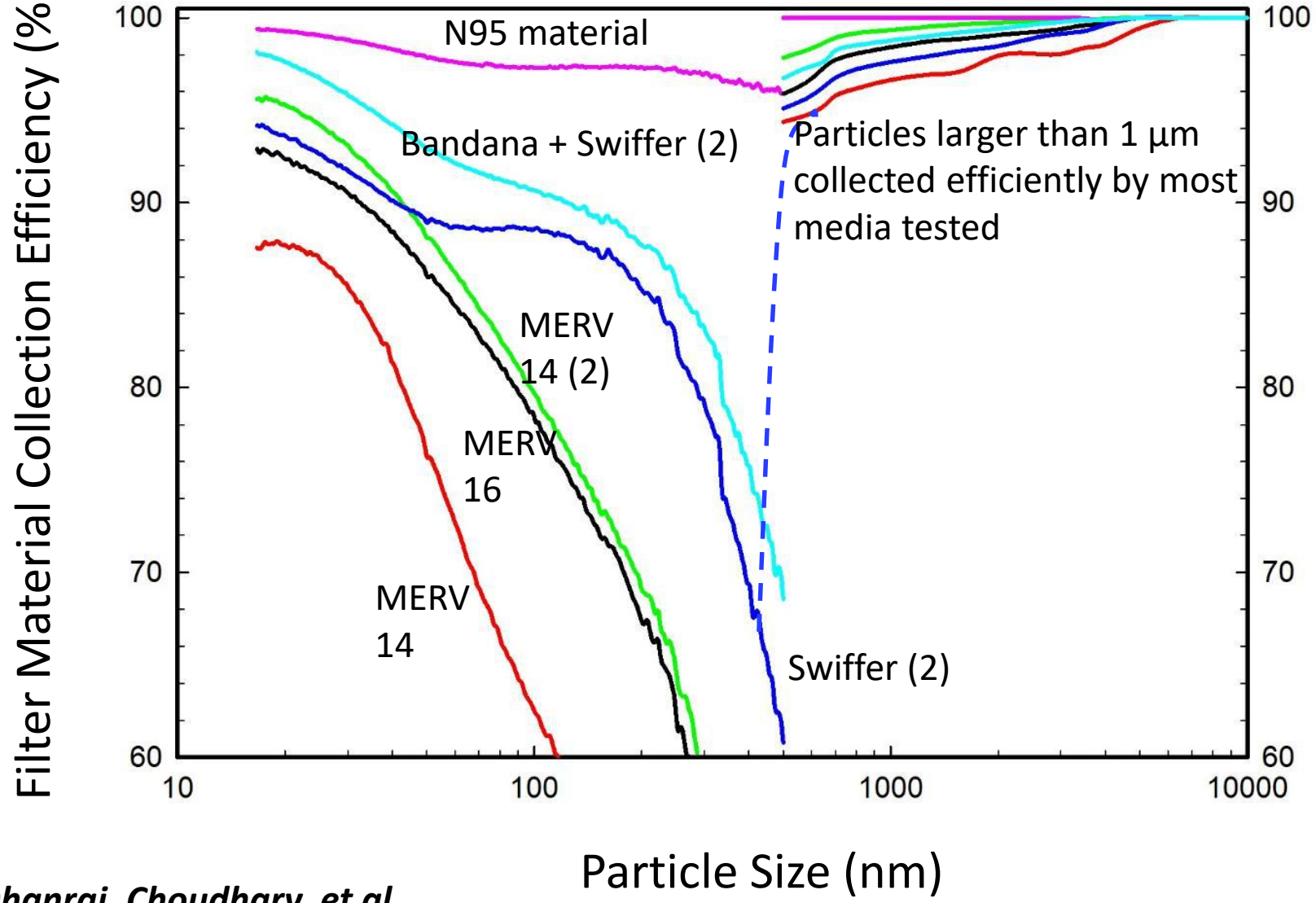
# Test Station #1 (AAQRL lab – full size distribution)

## Various Filter Media Particle Removal Efficiency as a Function of Size (< 1 µm)




***Dhanraj, Choudhary, et al.***

# VARIOUS FILTER MEDIA COLLECTION EFFICIENCY AS A FUNCTION OF PARTICLE SIZE

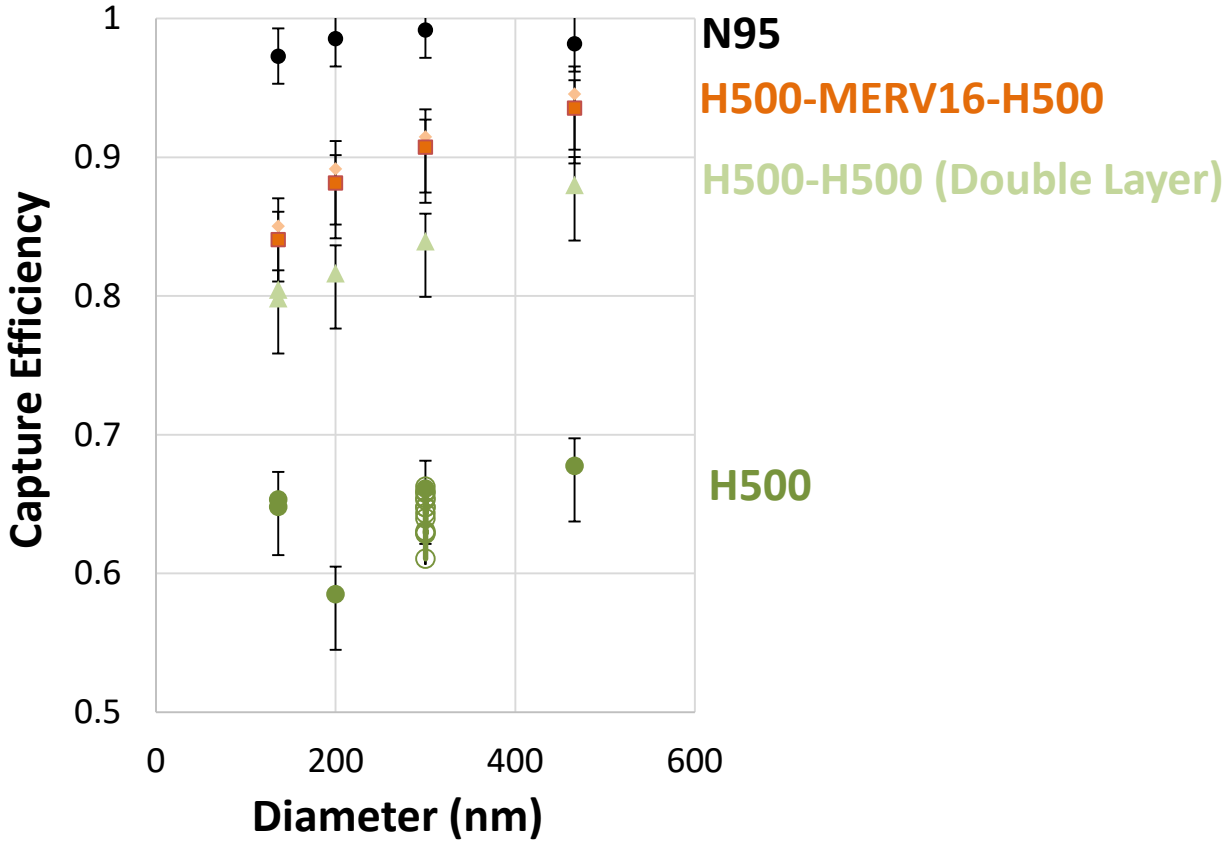


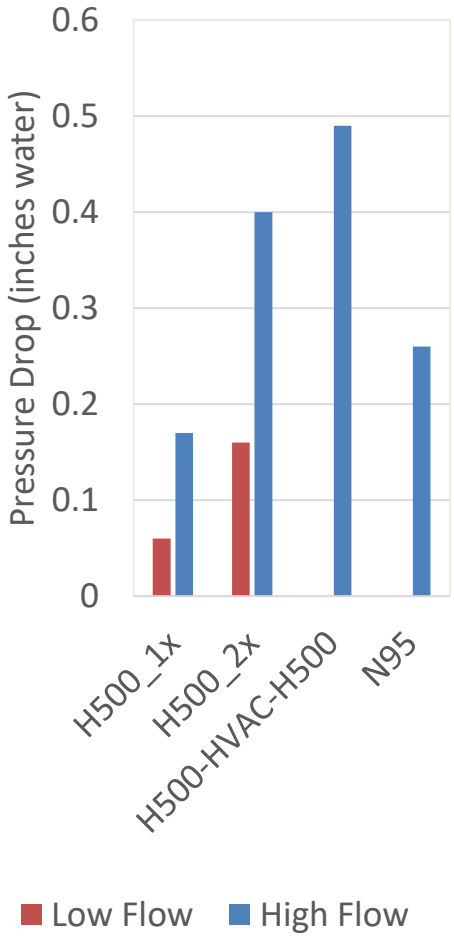

***Dhanraj, Choudhary, et al.***

# Can a combination of materials perform like an N95 mask?

H500 = Halyard H500 material used in medical gowns

MERV16 = HVAC-type filter material



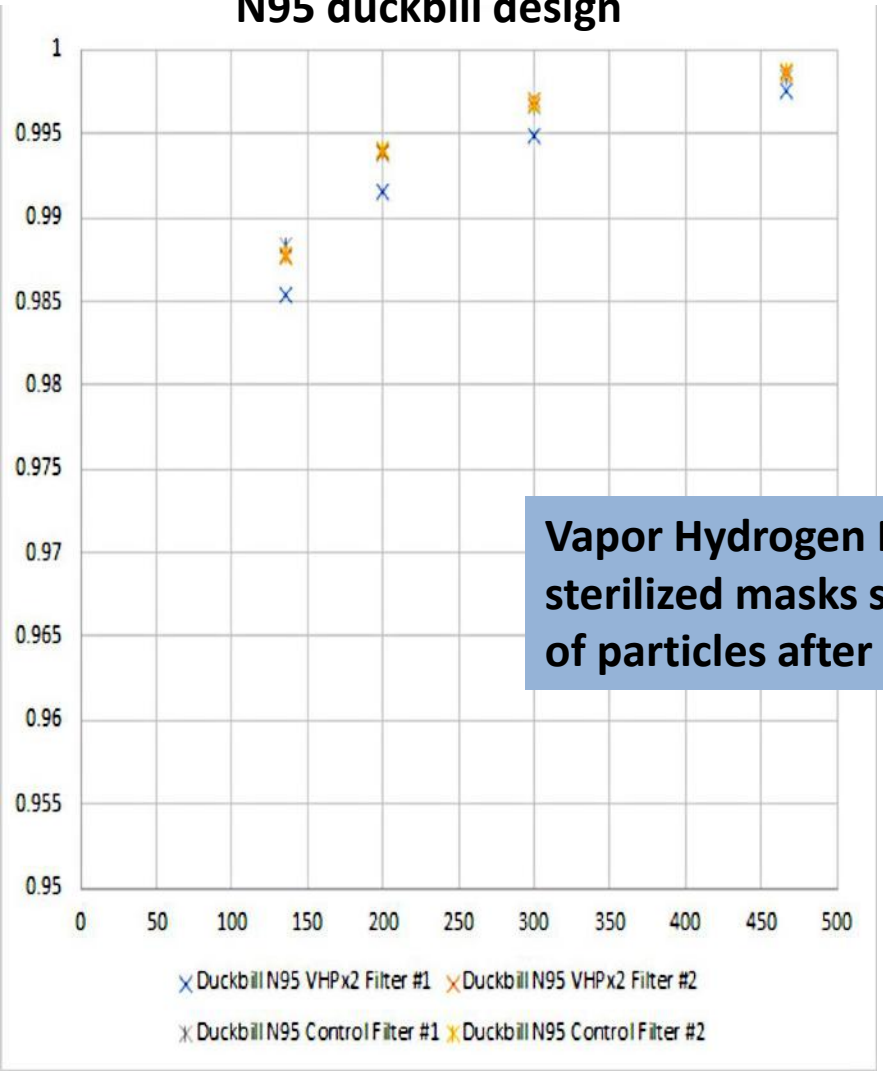




*Dang, Kumfer, et al.*

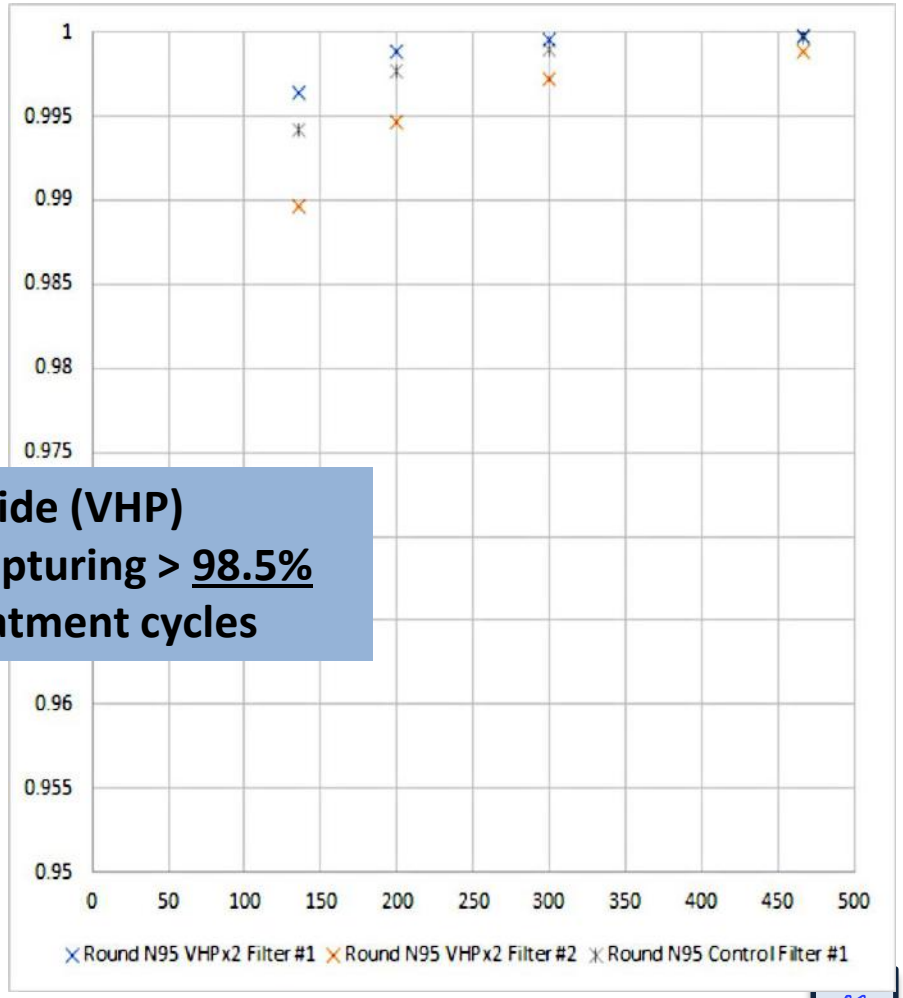
# Testing Station #2 (CASE shared lab facility)

## Do sterilized N95 masks still filter as well as a new mask?

### N95 duckbill design



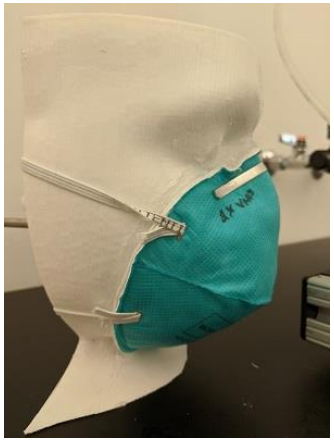

### N95 round design

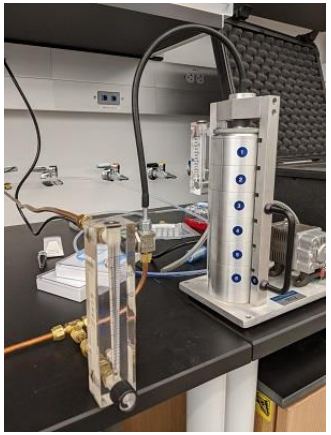



**Vapor Hydrogen Peroxide (VHP) sterilized masks still capturing > 98.5% of particles after 2 treatment cycles**

*Dang, Kumfer, et al.*

# Do Fibers release from masks that have been sterilized?

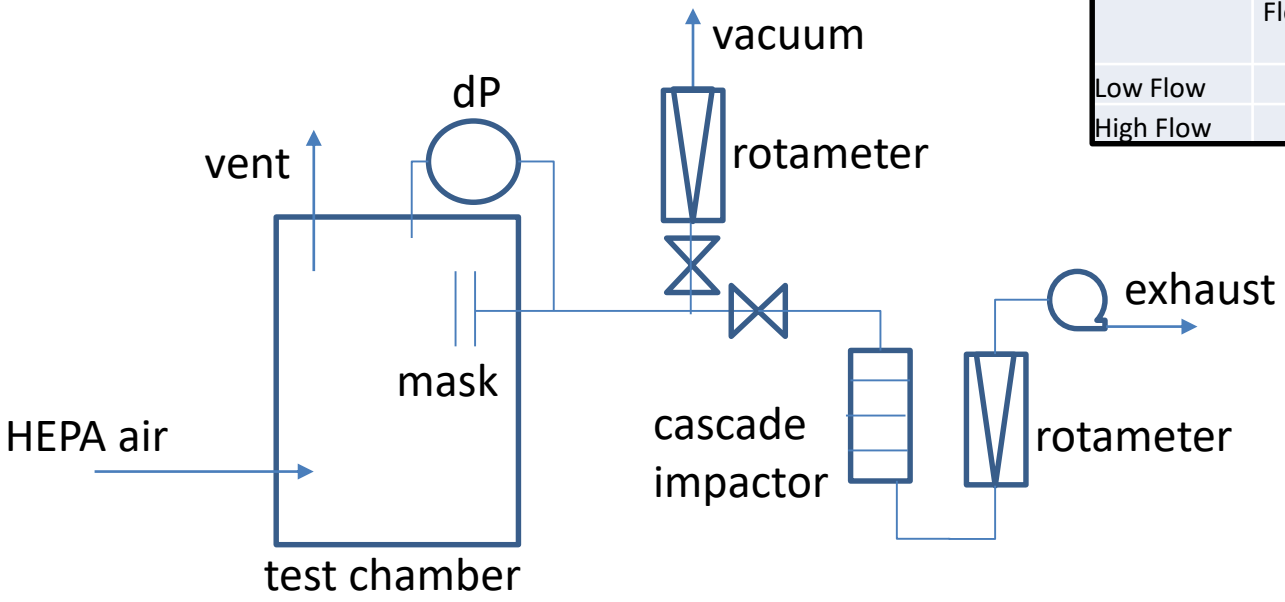




Mask:
Blue N95
previously fit tested
2x VHP treated

Test Conditions

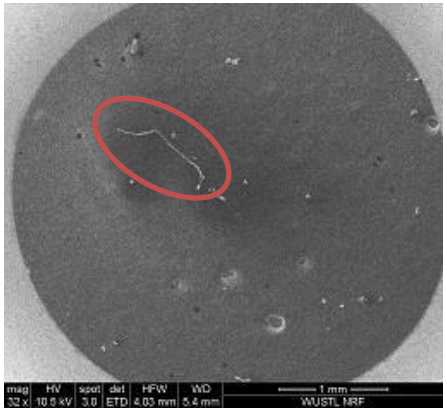
| | Flow Rate (LPM) | Sampler Flow Rate (LPM) | Total Mask Flow Rate (LPM) | dP (in H2O) |
|---|---|---|---|---|
| Low Flow | 32.8 | 2.2 | 35.0 | 2.0 |
| High Flow | 62.6 | 1.6 | 64.2 | 12.5 |



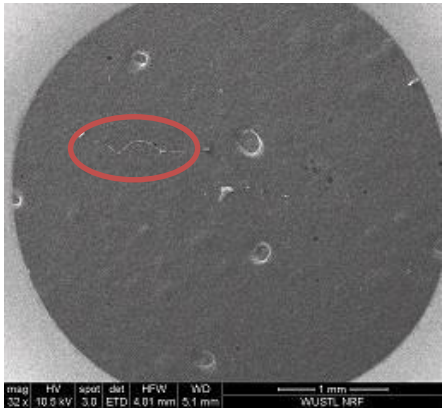
# Do Fibers release from masks that have been sterilized?

## SEM Images

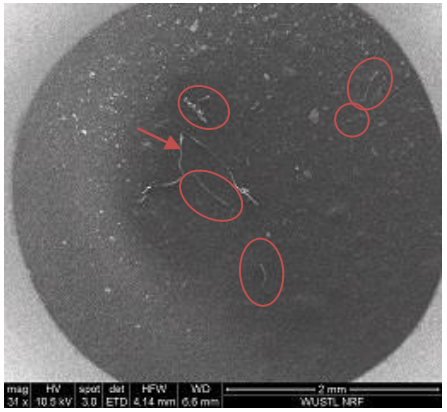
Stage 1, 35 LPM Mask Flow



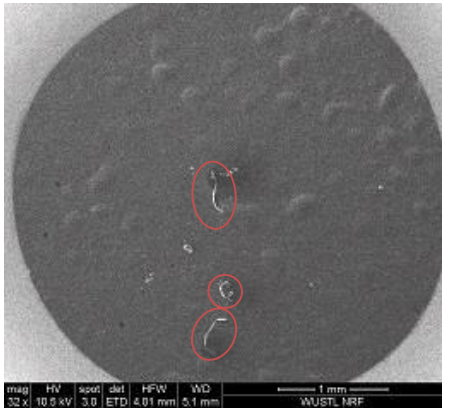
Stage 1, 64 LPM Mask Flow

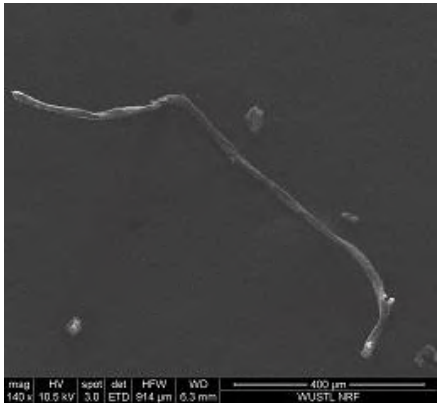


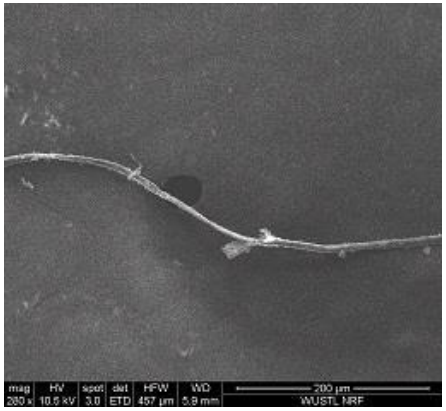
Stage 2, 35 LPM Mask Flow

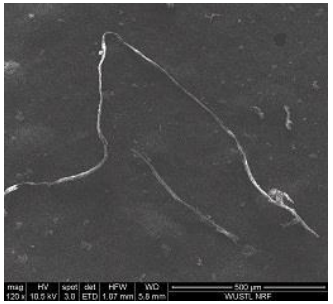


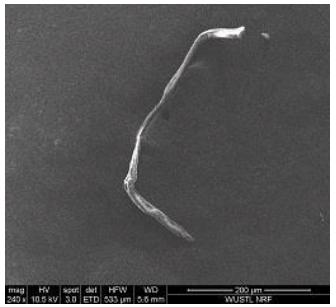
Stage 2, 64 LPM Mask Flow











11 fibers collecting over 20 minutes of total sampling time

***Kumfer, Shetty, et al.***

# Agitator

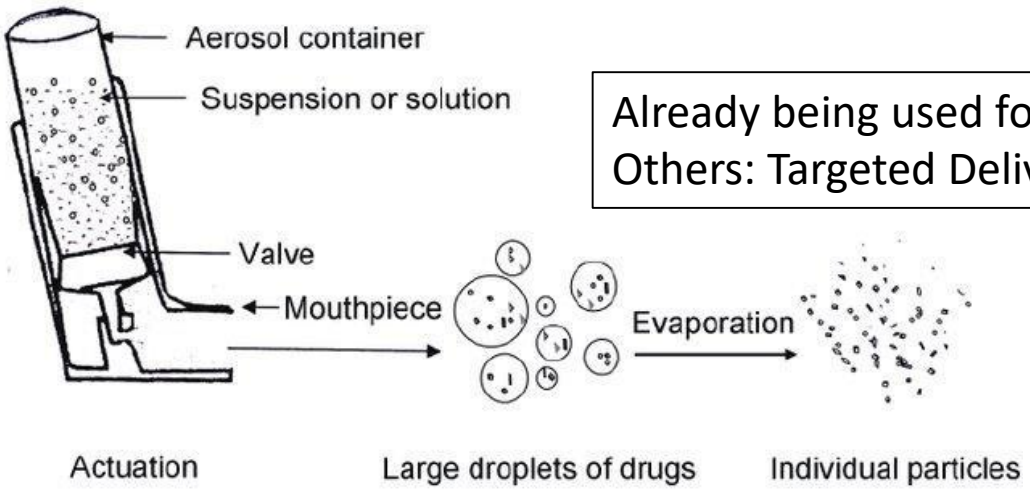
Slowly rotates and brushes against mask

With agitation:
20 fibers (**double**) collected over same sample time

More testing underway…….

# Aerosolized Delivery of Antivirals

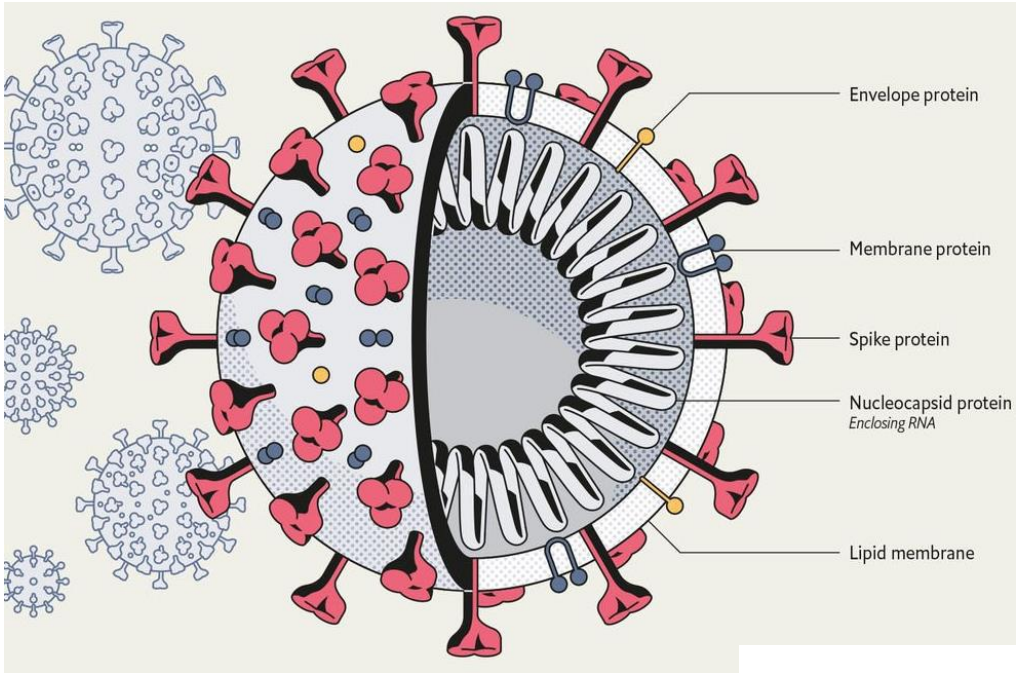
Hao Zhou and Pratim Biswas




Already being used for respiratory disease treatment: Asthma
Others: Targeted Delivery for Diabetes, Variety of Vaccines

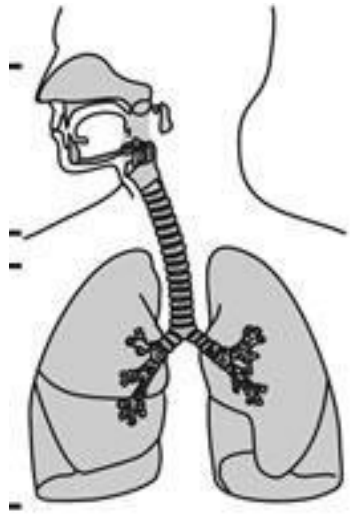
**Electrospray Enabled Aerosol Studies**

- Controlled studies on self assembly in droplets
  - Understand assembly of nucleocapside protein
- Explore innovative delivery methods
  - Denature proteins with appropriate agents
  - Target proteins in cells, prevent reassembly

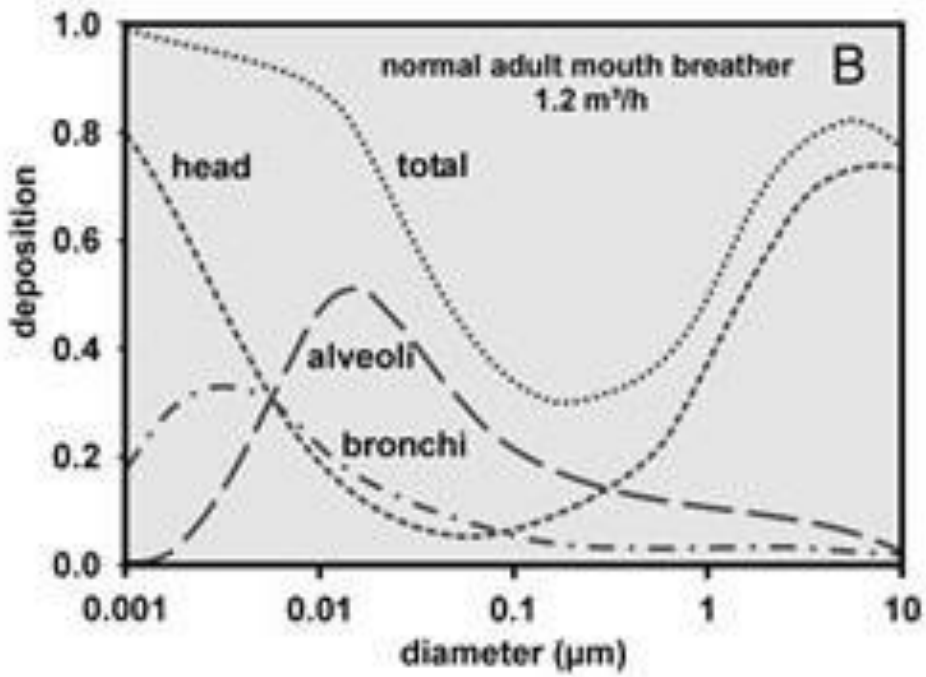



*Antiviral should prevent this RNA replication (assembly of Nucleocapsid Protein)
*Promote aggregation – but in a random manner so that the virus is not infective
*Deliver antiviral agent at targeted location

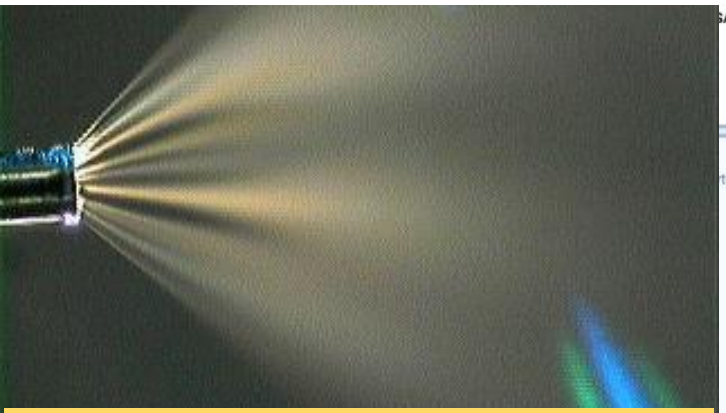
*From: The New Yorker*



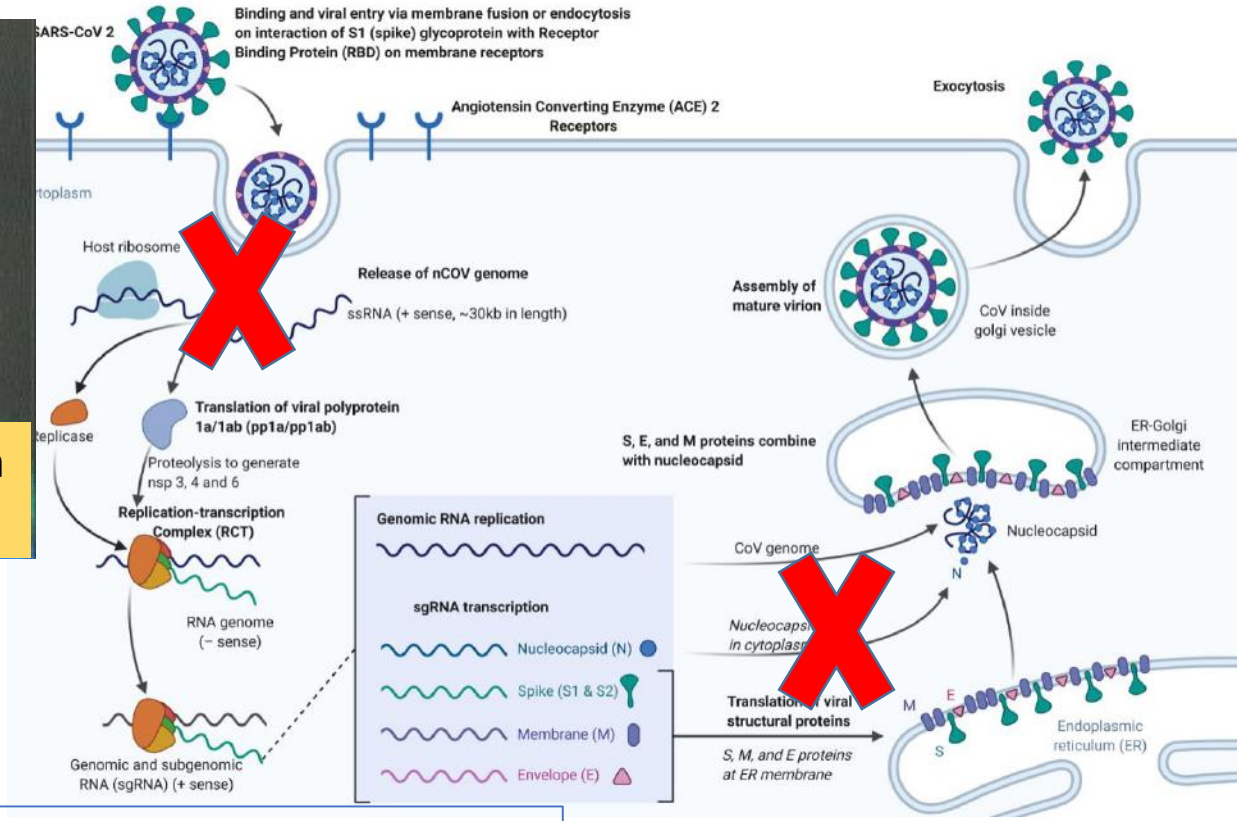
From Geiser and Kreyling,



# Can Aerosol Systems be an effective method to deliver antiviral medication?



Electrospray Drug Delivery System (Hao and Biswas, 2020)




From R.B. Singh (Casella et al, 2020)

Strategy:

- Delivery to associate with SARS-COV-2 virus (same location)
- Denature assembled nucleocapsid protein
- Do not allow re-assrembly or replication

Hypothesis:

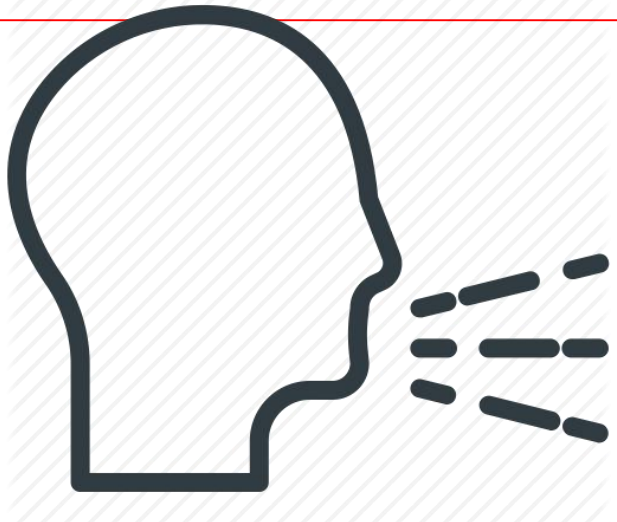
Aerosolized Delivery Plausible Methodology that will enable

Collaborators:
Rohit Pappu (BME)
Abhinav Diwan (Cardiology)
Kartik Mani (Cardiology, VA)

SARS-COV-2 is a tough nanoparticle: Common-cold coronaviruses tend to infect only the upper respiratory tract (mainly the nose and throat). *SARS*-CoV-2 is more readily transmitted and infective in the lower portions of the lung; it is a mutant hybrid of all the human coronaviruses that came before it.

Finally, you may have heard this already, but hopefully understand WHY ?

1) Stay isolated and physically distanced (how far ?)
2) Wash your hands often – minimize FOMITE transmission
3) If you go out to public places, please wear some kind of FACE MASK (even homemade)
4) Save the high quality face masks (N95) for HCW and HCPs
5) Support basic science and engineering research – vaccine and antiviral development



Washington University in St. Louis

Eece.wustl.edu
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center for aerosol science and engineering

# CASE Researchers Tackling COVID-19

**Pratim Biswas:** Airborne Transmission of SARS-COV-2

**Rajan Chakrabarty:** Models to predict spread of the coronavirus in populations

**Richard Axelbaum:** Guidance to front line health care physicians on masks

**Brent Williams:** Facemask Filter Testing in the Laboratory

**Pratim Biswas & Rajan Chakrabarty :** Delivery of Antiviral Drugs for Treatment of COVID-19

***THANK YOU FOR ATTENDING***