Development of *In Silico* Human Model for Airborne Transmission Analysis in Indoor Environment

健康影響を可視化するin silico人体モデルの開発と環境設計への展開

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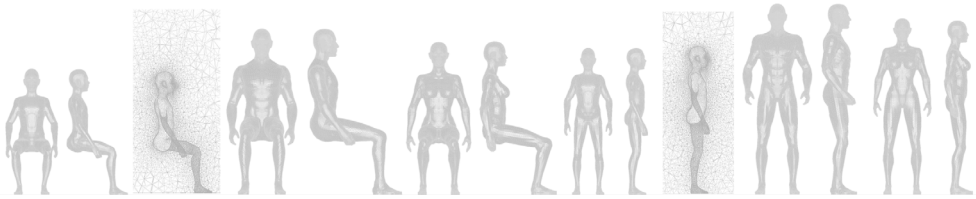
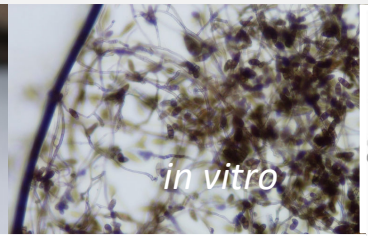
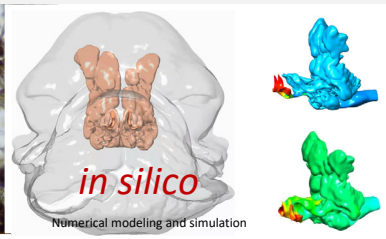
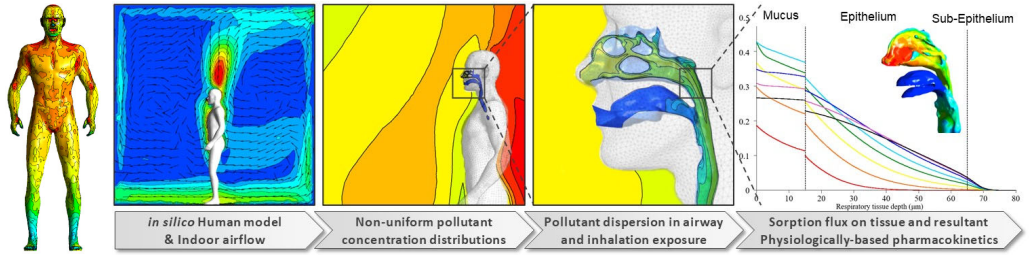


Toward *in silico* modeling-based replacement of *in vivo* and *in vitro* experiments

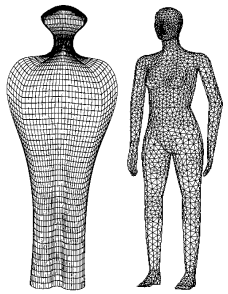




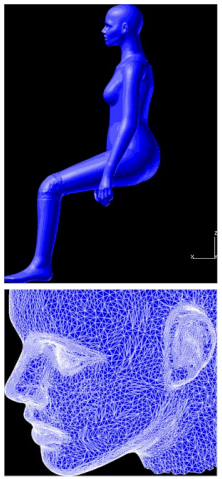


Development of ***in silico*** experiments that can complement *in vivo* and *in vitro* experiments for human volunteers or animal models

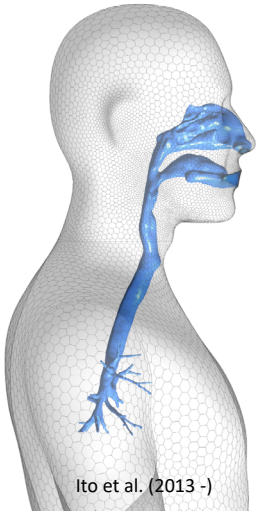
In silico human model development platform for Indoor Environmental Design



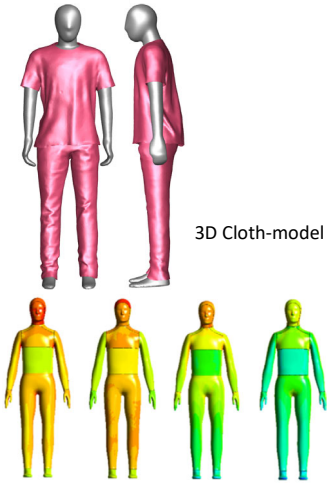
Kato and Murakami (1990)



D. Sorensen (2003)



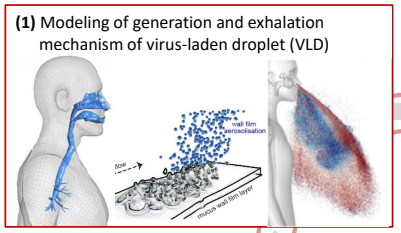
Ito et al. (2013 -)

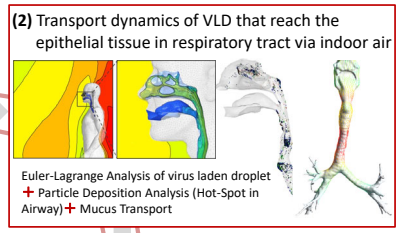


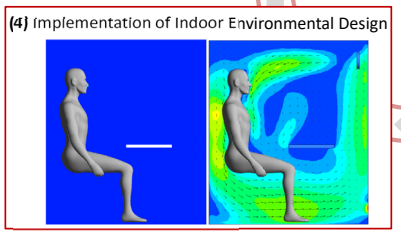
3D Cloth-model

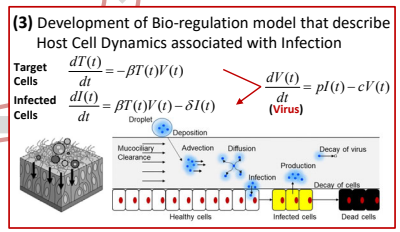
Fiala Thermo-regulation Model

Numerical Models required for Airborne Transmission Analysis









In Silico human for Inhalation Exposure and Airborne Airway Infection

[1] Chemical Compounds

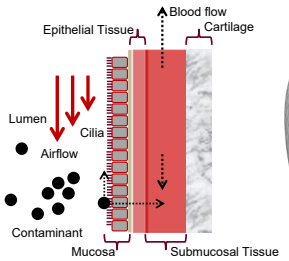
PBPK/TK (Physiologically Based Pharmaco/Toxico Kinetics) for Inhalation Exposure

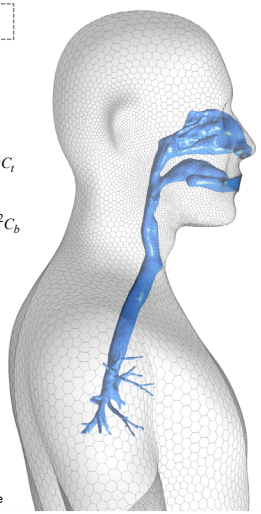
(Mucosa + Epithelium)

$$\frac{\partial C_t}{\partial t} = -\frac{(V_{\max 1C})C_t}{K_{m1} + C_t} - K_f C_t - K_b C_t + D_t \nabla^2 C_t$$

(Sub-mucosa)

$$\frac{\partial C_b}{\partial t} = -K_f C_b - K_b C_b - (Q_b / V_b) C_b + D_b \nabla^2 C_b$$





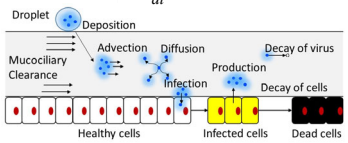
[2] Virus/Bacteria

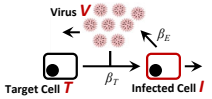
HCD (Host Cell Dynamics) for Airborne Airway Infection

(Target Cells) $\frac{dT(t)}{dt} = -\beta T(t) V(t)$

(Infected Cells) $\frac{dI(t)}{dt} = \beta T(t) V(t) - \delta I(t)$

(Virus) $\frac{dV(t)}{dt} = pI(t) - cV(t)$



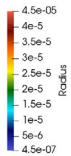


Droplet and Droplet Nuclei Dispersion

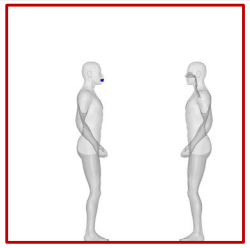
Time: 0.25 s

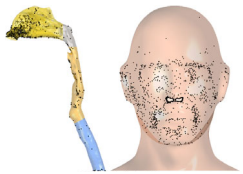
(Many Thanks, Prof Tsubokura, RIKEN)

$$\frac{d\vec{u}_p}{dt} = \frac{1}{\tau}\left(\vec{u} + \vec{u}' - \vec{u}_p\right) + \frac{(\rho_p - \rho)}{\rho_p} \cdot \vec{g} + \vec{F}_B + \vec{F}_S$$

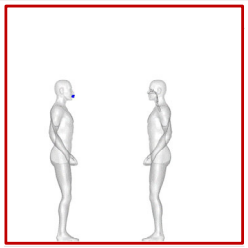


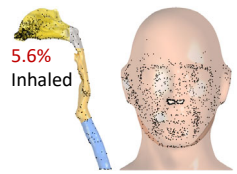
Droplet and Droplet Nuclei Dispersion



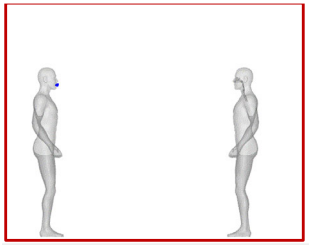


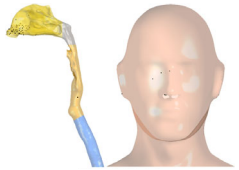
1m Physical distance
Steady inhalation of Targeted subject



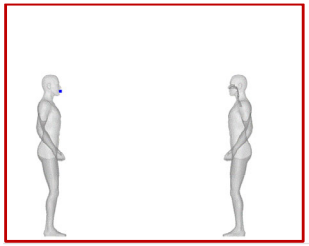


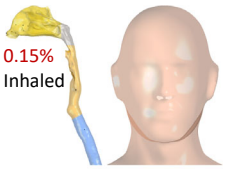
1m Physical distance
Transient inhalation of Targeted subject





2m Physical distance
Steady inhalation of TS

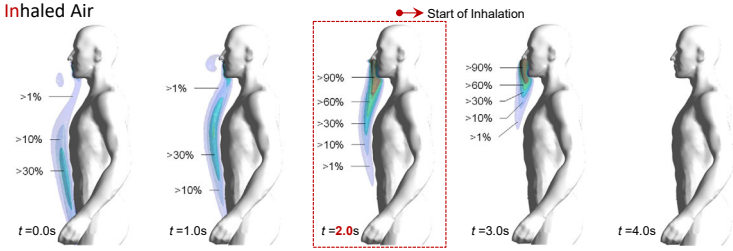


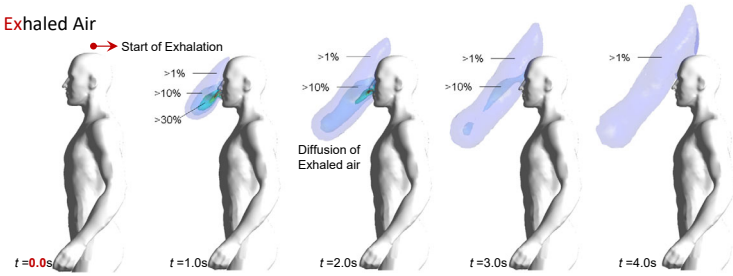


2m Physical distance
Transient inhalation of TS

Where and how much indoor air do we actually breathe?

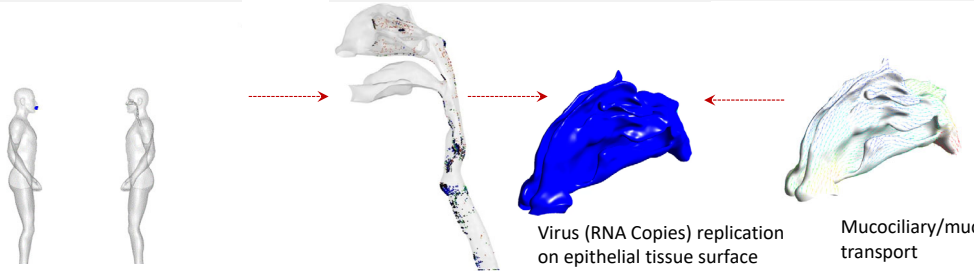
Contribution ratio of inhaled and exhaled air





(***Indoor Air***, 2022)

Regional deposition of airborne SARS-CoV-2-laden droplets in the upper airway and its effects determined using host cell dynamics

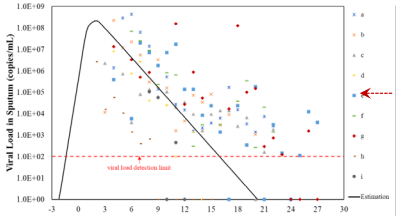


Virus (RNA Copies) replication on epithelial tissue surface

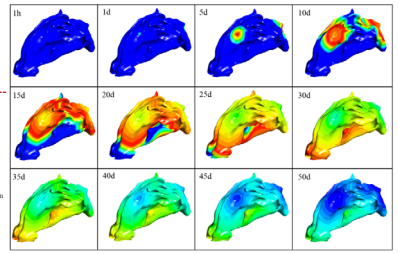
Mucociliary/mucus transport

$$\frac{dT(t)}{dt} = -\beta T(t)V(t)$$
$$\frac{dI(t)}{dt} = \beta T(t)V(t) - \delta I(t)$$
$$\frac{\partial \overline{V}}{\partial t} + \frac{\partial \overline{U}_j \overline{V}}{\partial x_j} = D_m \frac{\partial^2 \overline{V}}{\partial x_j^2} + \frac{p'}{V_{mucus}} I_j - cV$$

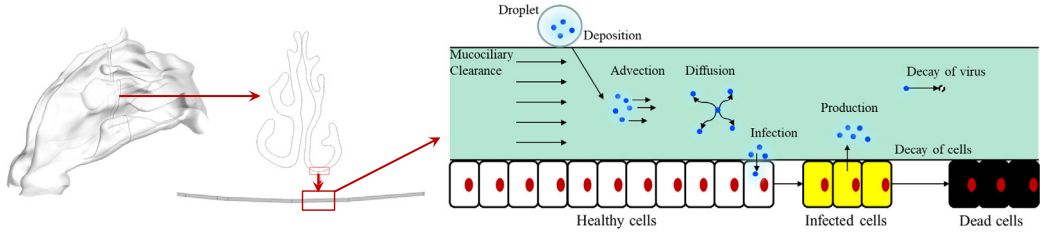
Bioregulation – Host Cell Dynamics
(Host cells, Pathogen, Adaptive Immune System)



Resultant viral replication



Host Cell Dynamics Model
Coupling of target-cell limited model and convection-diffusion model



Mucus Flow: $S_m = \rho(\nabla \cdot \vec{u})$

Source term was added to the continuity equation for the mucus domain

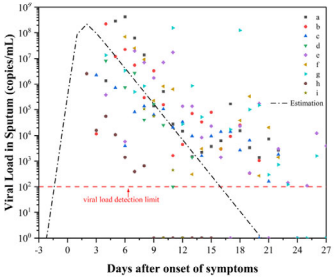
Virus load/concentration [RNA copies/ml]

Susceptible target cells [cells]

Infected cells [cells]

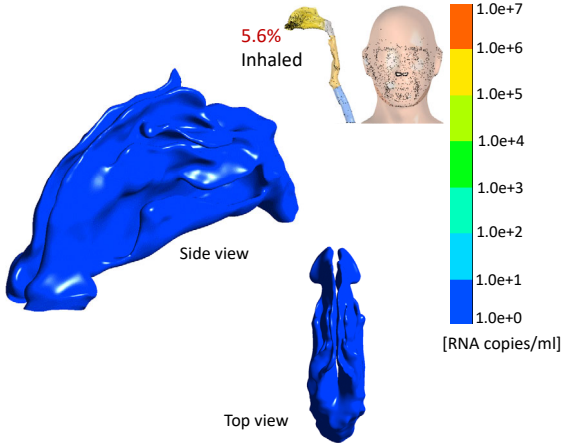
$$\begin{cases} \dfrac{\partial V}{\partial t} + \dfrac{\partial U_i V}{\partial x_i} = D_m \dfrac{\partial^2 V}{\partial x_i^2} + \dfrac{p'}{V_{mucus}} I - cV & (1) \\ \dfrac{\partial T}{\partial t} = -\beta TV & (2) \\ \dfrac{\partial I}{\partial t} = \beta TV - \delta I & (3) \end{cases}$$

β : infection rate [1/(RNA copies/ml)/day]

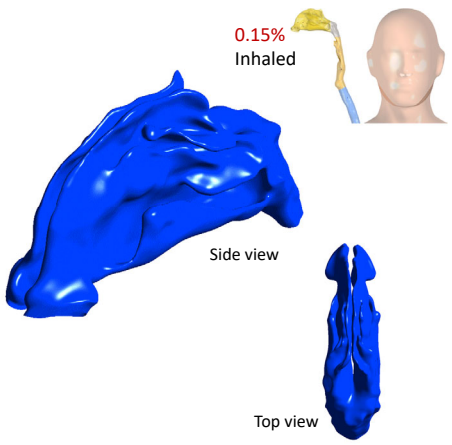


Visualization of SARS-CoV-2 Diffusion in the Nasal Cavity–Nasopharynx model

Viral replication [RNA copies/mL]
[1m physical distance, 20 days]

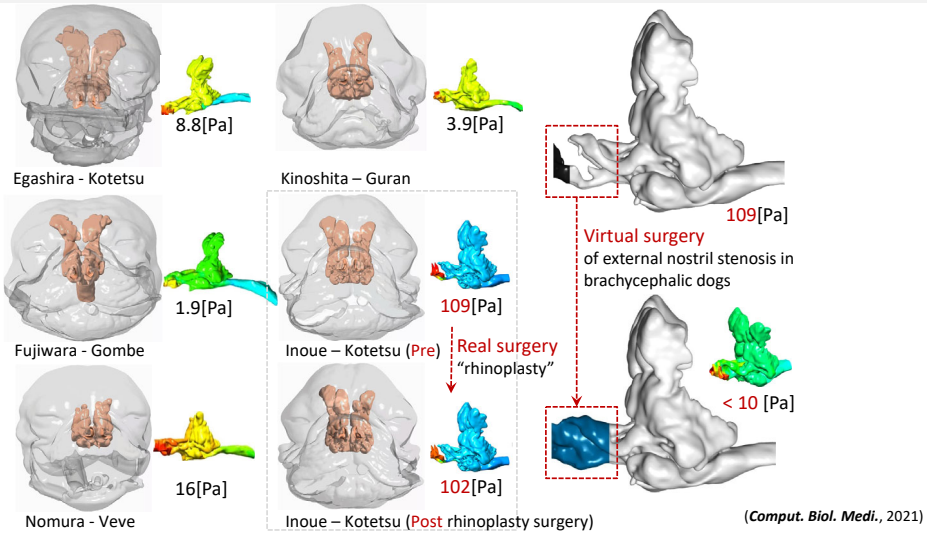


Viral replication [RNA copies/mL]
[2m physical distance, 20 days]



Application/evolvement of *in silico* modeling of animals

Pressure loss calculation in upper airway of French Bulldog and Virtual Surgery



(***Comput. Biol. Medi.***, 2021)

What can we do for "*in vivo*" animal models?

In Silico Human Model based Indoor Environmental Design

- Multi-stage optimization of local environmental quality by in silico human model as a sensor for HVAC control