Toward the development of an *in silico* human model for indoor environmental design

Some arguments for developing *in silico* model for fluid-initiated environmental design research in an enclosed space

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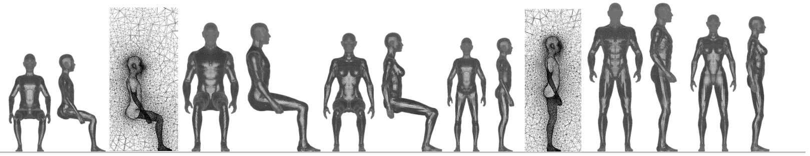
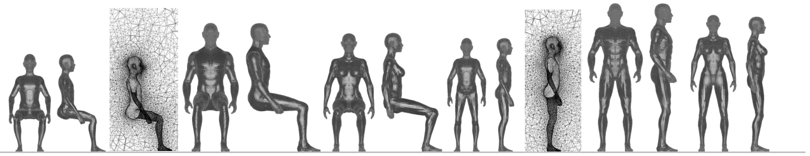


Toward the development of *in silico* models for inhalation exposure analysis

Some arguments for developing *in silico* Laboratory Animal models for Inhalation Exposure Analysis



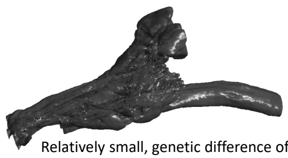
Upper Airway models for Surrogate Animals

Rat

Compact, genetic and environmental factors are completely controlled. Average life expectancy is around 1200 days, airway reactivity (high)

Rat (Sprague–Dawley)

Dog



Relatively small, genetic difference of individuals (small), fertility

Dog (Beagle)

Monkey

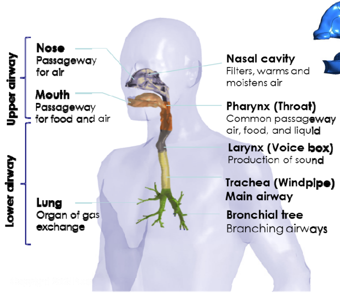
Temporomandibular joint, respiratory shape similar to human

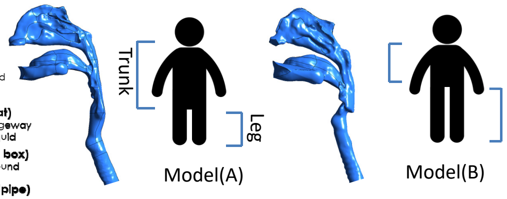
Monkey (Macaca fascicularis)

(Mitsumune, K. et al., 2016)

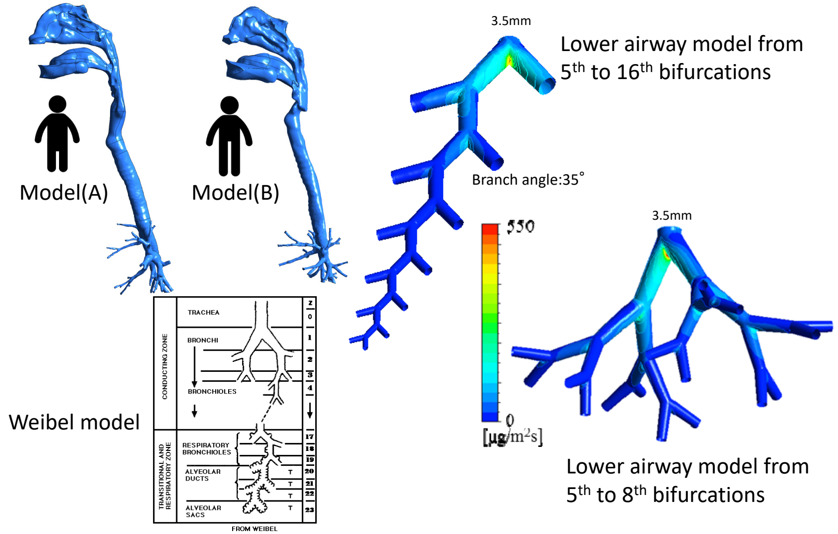
Upper Airway models for Humans

	Model (A) Japanese	Model (B) European
Body Height	1.7m	1.7m
BMI	21	21
Size (Height of Virtual Airway)	0.34568m	0.27381m
Inner Surface area (A)	0.057967m^2	0.044637m^2
Volume (V)	1.7336×10^{-4}m^3	1.2862×10^{-4}m^3
V/A	2.9908×10^{-3}m	2.8814×10^{-3}m





Upper and Lower Airway models for Humans



Detail Geometry Data for *in silico* models

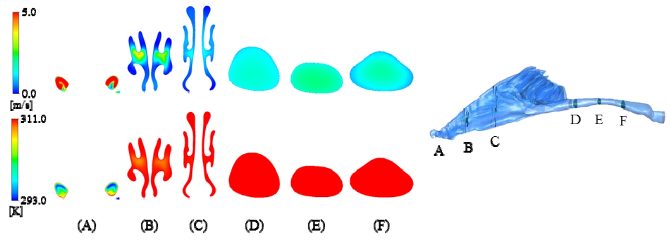
	Rat	Dog	Monkey	Model (A) Japanese	Model (B) European
Model geometry					
Total inner surface area	3.62×10^{-6} [m^2]	1.29×10^{-4} [m^2]	2.81×10^{-5} [m^2]	2.19×10^{-4} [m^2]	2.14×10^{-4} [m^2]
Total length	55.10 [mm]	1.45×10^{-1} [m]	1.05×10^{-1} [m]	2.39×10^{-1} [m]	1.95×10^{-1} [m]
Maxi. height	18.30 [mm]	7.16×10^{-2} [m]	4.32×10^{-2} [m]	1.46×10^{-1} [m]	1.34×10^{-1} [m]
Maxi. width	16.00 [mm]	4.97×10^{-2} [m]	2.8110^{-2} [m]	6.21×10^{-2} [m]	6.21×10^{-2} [m]
Area of naris/ Eq. diameter	3.72×10^{-7}[m^2] / 6.89×10^{-4} [m]	6.00×10^{-5}[m^2] / 8.74×10^{-3} [m]	5.48×10^{-6} [m^2]/ 2.64×10^{-3} [m]	8.00×10^{-5} [m^2]/ 1.00×10^{-2} [m]	8.00×10^{-5} [m^2]/ 1.00×10^{-2} [m]
Area of naris/ Eq. diameter	3.08×10^{-7} / 6.27×10^{-4} [m]	5.28×10^{-5} / 8.20×10^{-3} [m]	5.46×10^{-6} [m^2]/ 2.64×10^{-3} [m]	8.00×10^{-5} [m^2]/ 1.00×10^{-2} [m]	8.00×10^{-5} [m^2]/ 1.00×10^{-2} [m]

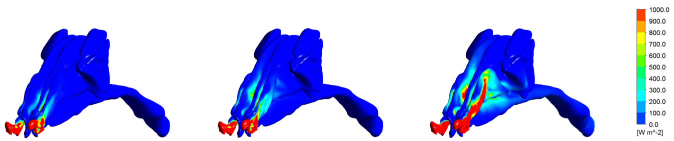
1.4% **34.7%** **8.8%** of Human model (A)

Numerical Boundary Conditions

	Rat	Dog	Monkey	Model (A) Japanese	Model (B) European
Model geometry					
Mesh (Unstructured, Tetra mesh)	5.34M	6.49M	7.03M	7.25M	3.81M
Outflow boundary [L/min]	0.275	3.5	2.0	7.5	7.5
Re number	186.1	396.9	485.3	652.9	660.5
Wall treatment	311K Velocity : no slip	311K Velocity : no slip	310.8K Velocity : no slip	309.8K Velocity : no slip	309.8K Velocity : no slip
Inflow boundary	Nasal opening : $U_{in}= k_{in}= \varepsilon_{in}$=Gradient zero				
Turb. model	Low Re Type k-ε model (Abe- Kondoh- Nagano Model, 3D Cal.)				

Rat

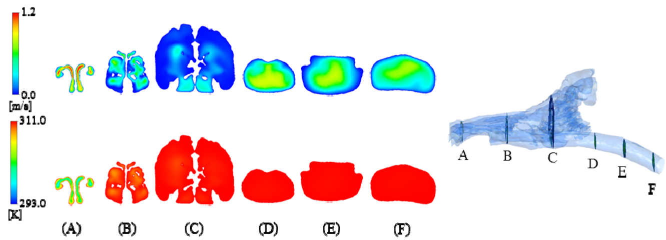


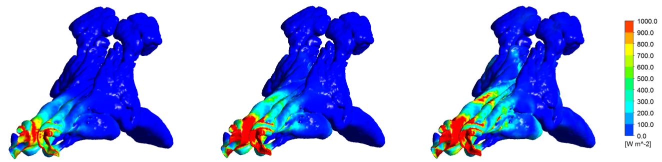


(1) Q_{in}=0.275 L/min (2) Q_{in}=0.55 L/min (3) Q_{in}=1.1 L/min

Convective heat transfer flux distributions on the upper airway surfaces of the rat

Dog

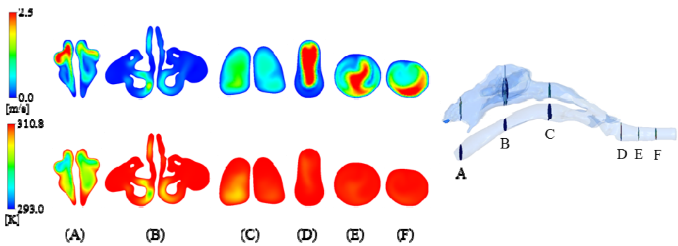


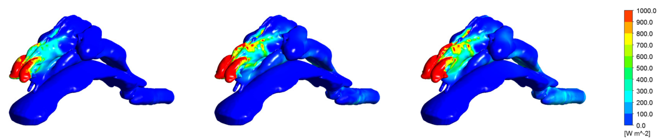


(1) Q_{in}=3.5 L/min (2) Q_{in}=7.0L/min (3) Q_{in}=10.5 L/min

Convective heat transfer flux distributions on the upper airway surfaces of the dog

Monkey

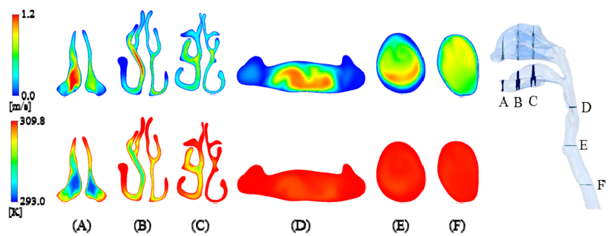


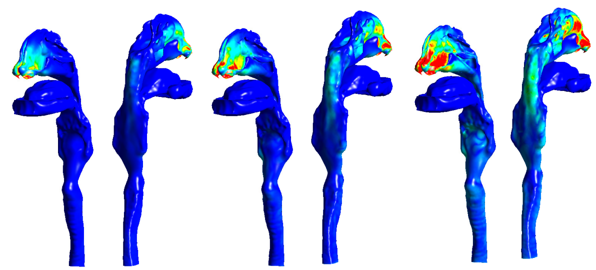


(1) Q_{in}=2.0 L/min (2) Q_{in}=4.0 L/min (3) Q_{in}=6.0 L/min

Convective heat transfer flux distributions on the upper airway surfaces of the monkey

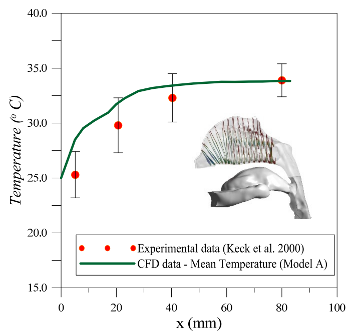
Human model (A)



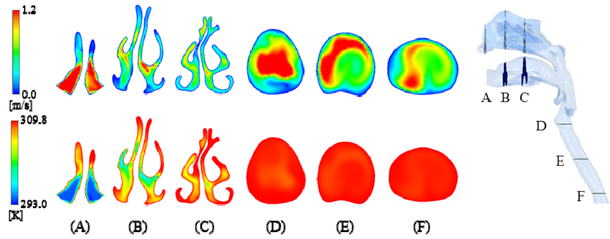


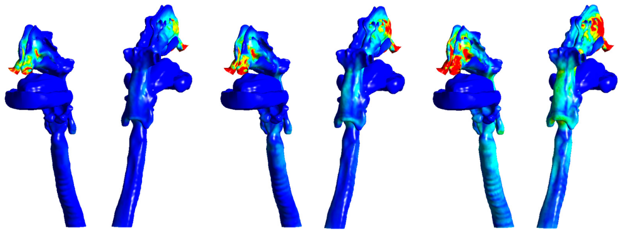
(1) Q_{in}=7.5 L/min (2) Q_{in}=15 L/min (3) Q_{in}=30 L/min

Temperature profiles across the nasal cavity in the case of Model A.



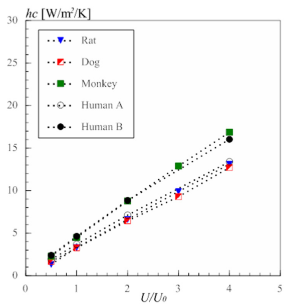
Human model (B)



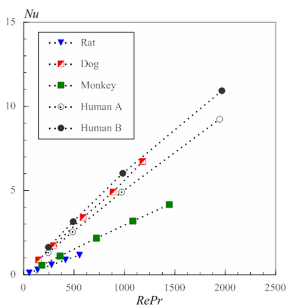


(1) Q_{in}=7.5 L/min (2) Q_{in}=15 L/min (3) Q_{in}=30 L/min

Nu versus product of *Re* and *Pr* for upper airways



Convective heat transfer coefficients (h_c) versus non-dimensional representative velocity in upper airway



Nu versus product of *Re* and *Pr* for upper airways

$$h_c = \frac{Q_c}{(T_w - T_{air})}$$

$$Nu = \frac{h_c D_T}{\lambda}$$

$$\mathrm{Re} = \frac{u D_T}{\nu}$$

$$\mathrm{Pr} = \frac{\nu}{\alpha}$$

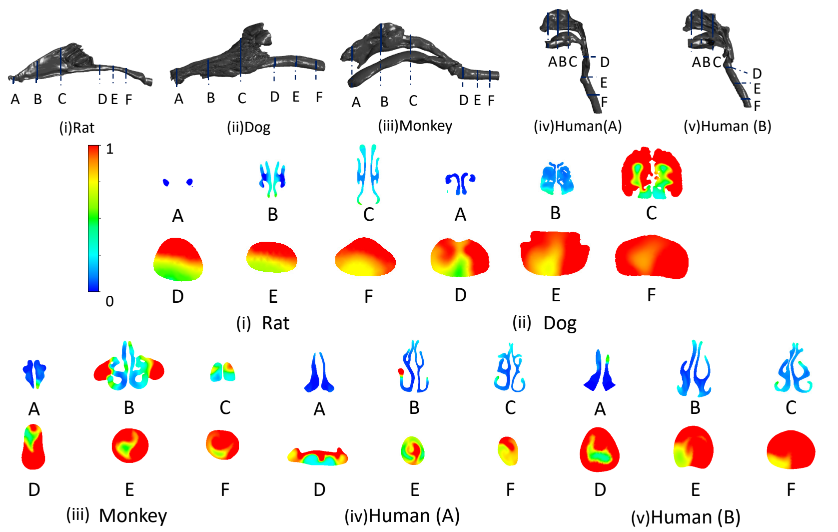
Correlation of *Nu* versus product of *Re* and *Pr*

Target airway model	Correlation function	Range of Re
Rat	$Nu = 0.0021(\mathrm{Re}\cdot \mathrm{Pr})^{0.9973}$	$75 < \mathrm{Re} < 750$
Dog	$Nu = 0.0069(\mathrm{Re}\cdot \mathrm{Pr})^{0.9707}$	$200 < \mathrm{Re} < 1600$
Monkey	$Nu = 0.0039(\mathrm{Re}\cdot \mathrm{Pr})^{0.9612}$	$250 < \mathrm{Re} < 2000$
Human model A	$Nu = 0.0075(\mathrm{Re}\cdot \mathrm{Pr})^{0.9414}$	$330 < \mathrm{Re} < 2600$
Human model B	$Nu = 0.0107(\mathrm{Re}\cdot \mathrm{Pr})^{0.9965}$	$330 < \mathrm{Re} < 2600$

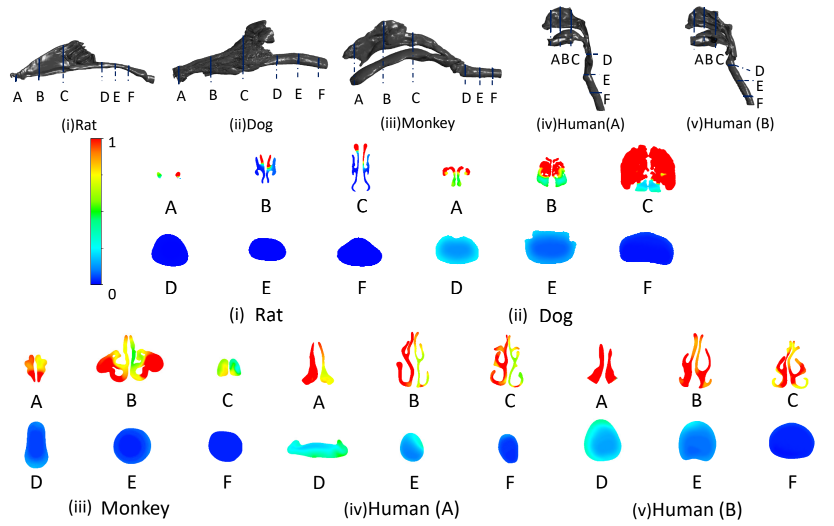
$$\mathrm{Nu} = 0.023\ (\mathrm{RePr})^{0.854}$$

(Nuckols et al., *J Biomech Eng* 105(1), 24-30, 1983)

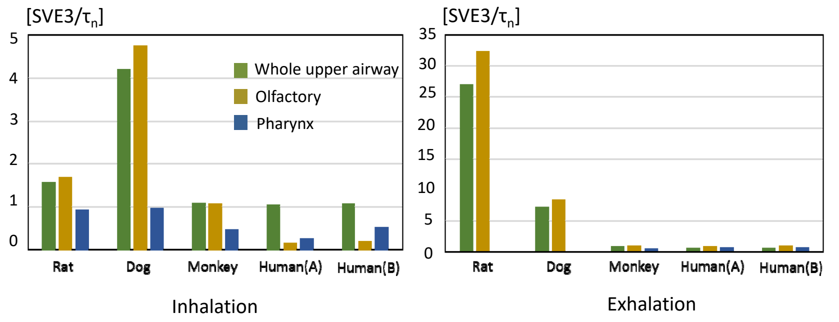
Vent. Efficiency in Respiratory Tracts (Inhalation)



Vent. Efficiency in Respiratory Tracts (Exhalation)



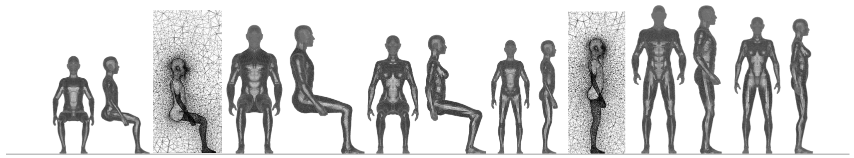
Volume-Averaged Age of Air



Nominal time constant (Basic inhalation air flow rate)

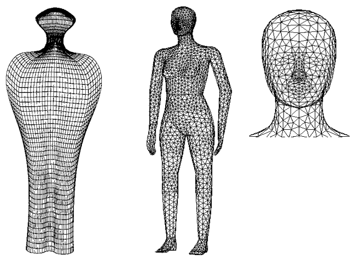
Human (A)	Human (B)	Monkey	Dog	Rat
1.155[s]	0.9[s]	3.860×10^{-1}[s]	8.595×10^{-1}[s]	8.768×10^{-2}[s]

Some arguments for developing *in silico* Human model for Inhalation Exposure Analysis

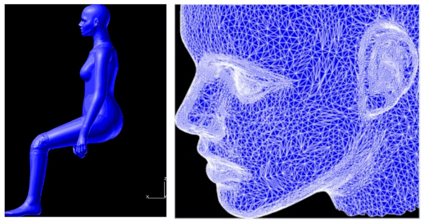


Human Model for CFD

- Micro-Climate analysis around human body
  - Numerical Thermal Manikin, Computer Simulated Person, Virtual Manikin
  - www.cfd-benchmarks.com (Aalborg Univ.)



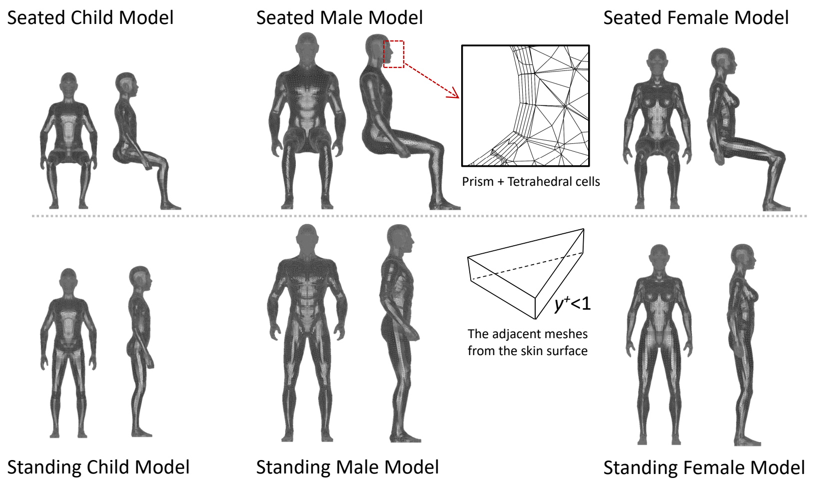
Kato, Murakami (1990)



D. Sorensen (2003)

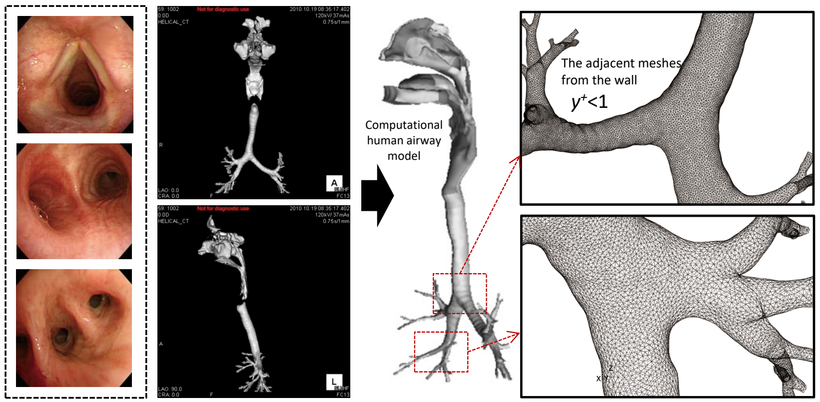
Virtual Manikin

www.phe-kyudai.jp



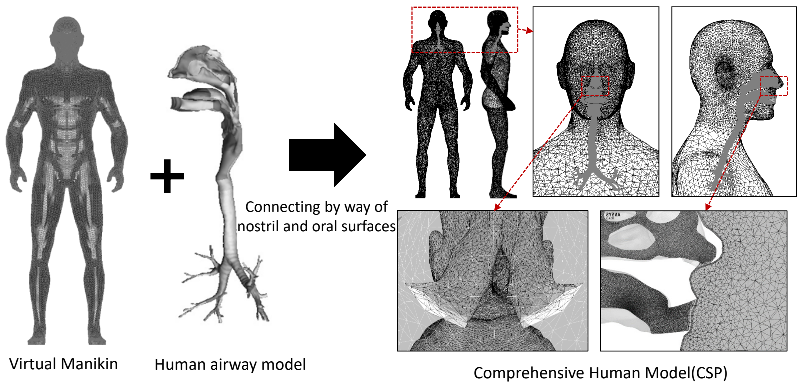
Virtual Airway model for CFD

- From Nasal cavity to Bronchi based on CT data (DICOM format)

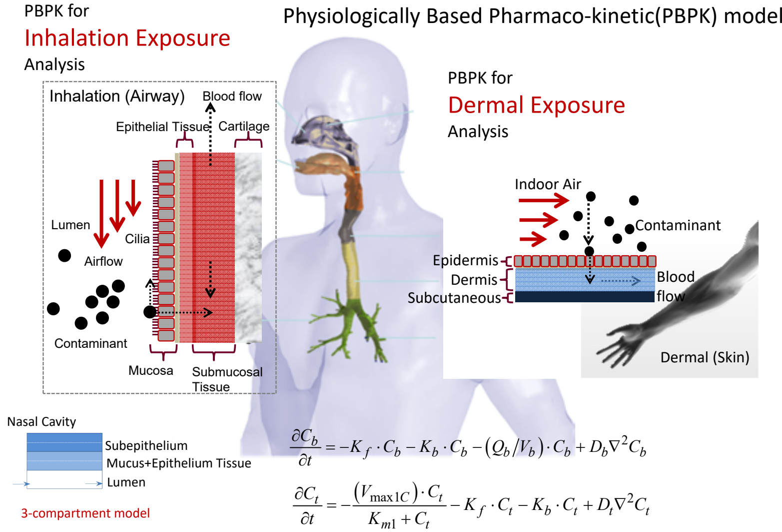


Computer Simulated Person

- Grid design of comprehensive human body incorporating human body geometry and respiratory tract



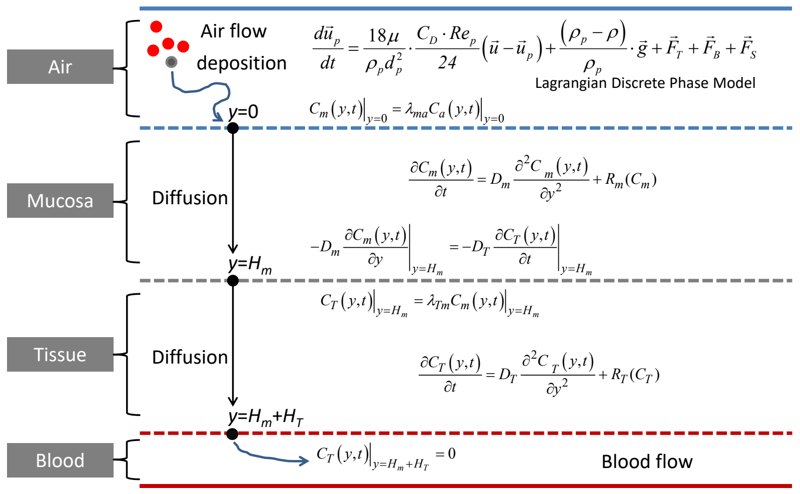
Inhalation and Dermal Exposure Assessment



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

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

Governing Equations of AMTB model



$$\frac{d\vec{u}_p}{dt} = \frac{18\mu}{\rho_p d_p^2} \cdot \frac{C_D \cdot Re_p}{24} (\vec{u} - \vec{u}_p) + \frac{(\rho_p - \rho)}{\rho_p} \cdot \vec{g} + \vec{F}_T + \vec{F}_B + \vec{F}_S$$

$$C_m(y,t)\big|_{y=0} = \lambda_{ma} C_a(y,t)\big|_{y=0}$$

$$\frac{\partial C_m(y,t)}{\partial t} = D_m \frac{\partial^2 C_m(y,t)}{\partial y^2} + R_m(C_m)$$

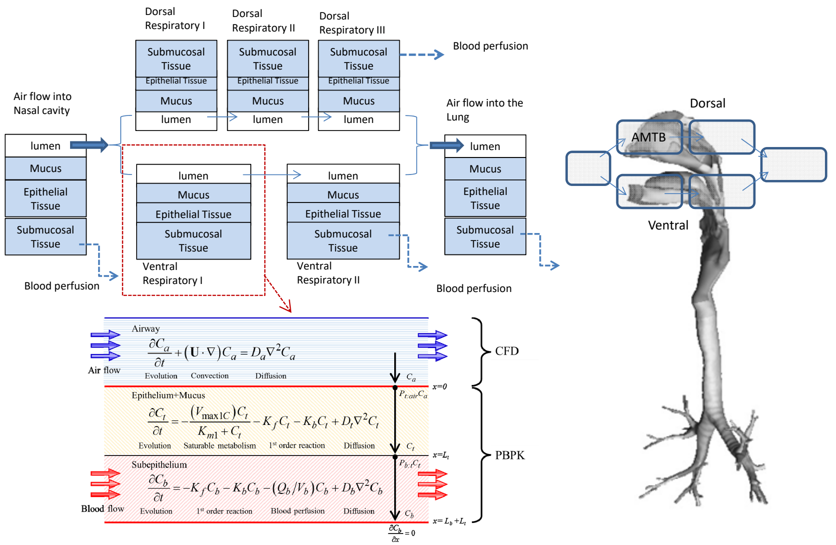
$$-D_m \frac{\partial C_m(y,t)}{\partial y}\bigg|_{y=H_m} = -D_T \frac{\partial C_T(y,t)}{\partial t}\bigg|_{y=H_m}$$

$$C_T(y,t)\big|_{y=H_m} = \lambda_{Tm} C_m(y,t)\big|_{y=H_m}$$

$$\frac{\partial C_T(y,t)}{\partial t} = D_T \frac{\partial^2 C_T(y,t)}{\partial y^2} + R_T(C_T)$$

$$C_T(y,t)\big|_{y=H_m+H_T} = 0$$

PBPK model (Respiratory Tract)

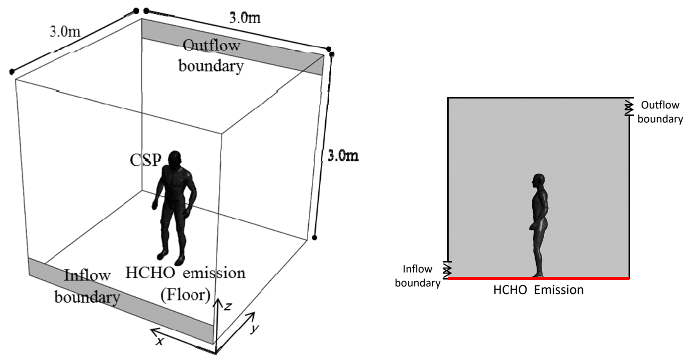


$$\frac{\partial C_a}{\partial t} + (\mathbf{U} \cdot \nabla) C_a = D_a \nabla^2 C_a$$

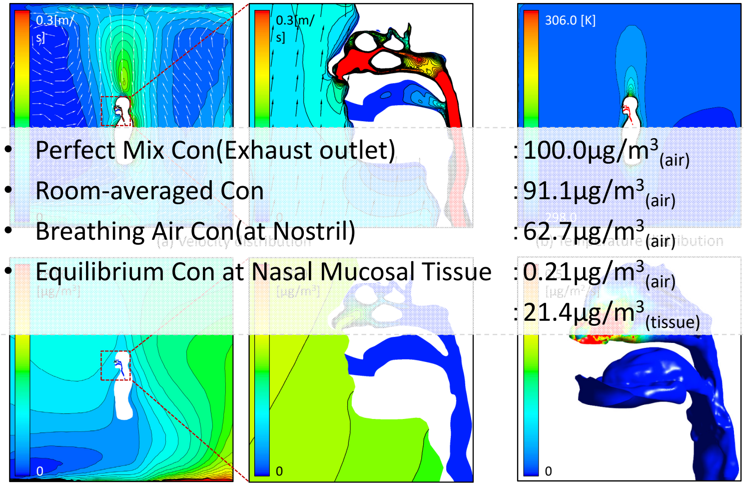
$$\frac{\partial C_t}{\partial t} = -\frac{(V_{\max 1C}) C_t}{K_{m1} + C_t} - K_f C_t - K_b C_t + D_t \nabla^2 C_t$$

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

Case Study for Inhalation Exposure (Steady State)



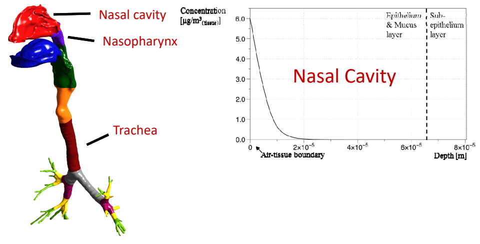
Representative Results

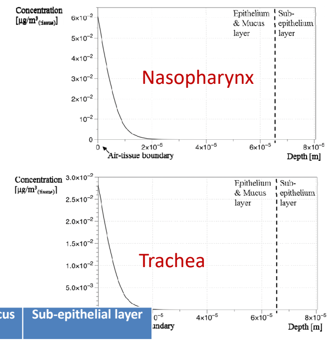


- Perfect Mix Con(Exhaust outlet) : 100.0μg/m^3$_{(air)}$
- Room-averaged Con : 91.1μg/m^3$_{(air)}$
- Breathing Air Con(at Nostril) : 62.7μg/m^3$_{(air)}$
- Equilibrium Con at Nasal Mucosal Tissue : 0.21μg/m^3$_{(air)}$: 21.4μg/m^3$_{(tissue)}$

(c) Formaldehyde concentration distribution (d) Formaldehyde adsorption flux distribution

Tissue Dosimetry in Respiratory Tract

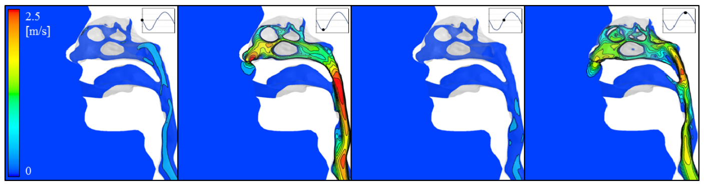




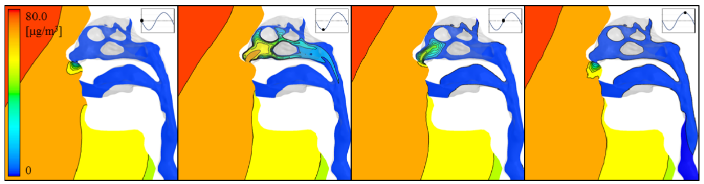
Dose of inhaled formaldehyde (HCHO) and contributions of each reaction term in tissue [μg/m^3$_{(tissue)}$/s].

	Epithelium + Mucus layer	Sub-epithelial layer	Epithelium + Mucus layer	Sub-epithelial layer
	Saturable metabolic clearance $\frac{(V_{max1C})\cdot C_t}{K_{m1}+C_t}$	1st order Reaction $(K_f+K_b)\cdot C_t$	1st order Reaction $(K_f+K_b)\cdot C_b$	Blood Perfusion $(Q_b/V_b)\cdot C_b$
Nasal cavity	17.05	3.15×10^{-3}	0	0
Nasopharynx	0.17	3.16×10^{-5}	0	0
Larynx	1.21×10^{-1}	2.23×10^{-5}	0	0
Oropharynx	9.62×10^{-2}	1.78×10^{-5}	0	0
Trachea	8.01×10^{-2}	1.48×10^{-5}	0	0

Transient Simulation

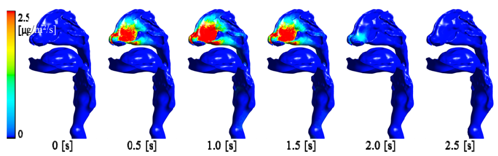


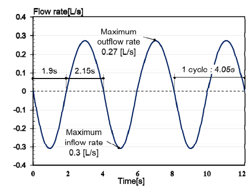
Time series of analysis result of velocity distributions inside airway (0 ~ 3sec)

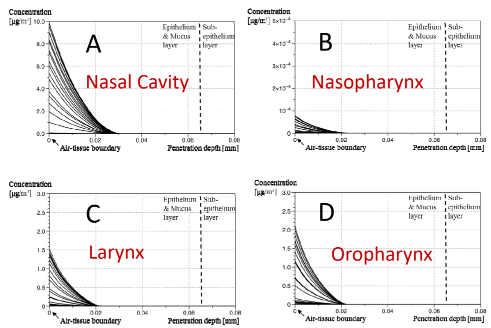


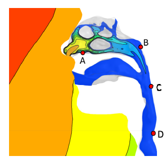
Time series of analysis result of HCHO con distributions inside virtual airway (0 ~ 3sec)

Time series of HCHO con. profile inside the airway tissue









More detail…

K Ito*: Toward the development of an *in silico* human model for indoor environmental design, ***Proc. Jpn. Acad., Ser. B,*** Vol. 92, No.7, 2016, 185-203 (DOI: 10.2183/pjab.92.185)

NL Phuong, M Yamashita, SJ Yoo, K Ito*: Prediction of convective heat transfer coefficient of human upper and lower airway surfaces in steady and unsteady breathing conditions, ***Building and Environ***, 100, 2016, 172-185

K Ito*, K Mitsumune, K Kuga, NL Phuong, K Tani, K Inthavong: Prediction of convective heat transfer coefficients for the upper respiratory tracts of rat, dog, monkey, and humans, ***Indoor and Built Environ***, 2016, In press (DOI: 0.1177/1420326X16662111)

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K Kuga, K Ito*, SJ Yoo, W Chen, P Wang, Z Liao, J Fowles, D Shusterman, K Kumagai: First- and second-hand smoke exposure assessment from e-cigarettes using integrated numerical analysis of CFD and a computer-simulated person with a respiratory tract model, ***Indoor and Built Environ***, 2017, In press (DOI: 10.1177/1420326X17694476)

SJ Yoo* and K Ito: Numerical Prediction of Tissue Dosimetry in Respiratory Tract using Computer Simulated Person integrated with physiologically based pharmacokinetic-computational fluid dynamics Hybrid Analysis, ***Indoor and Built Environ***, 2017, In press (DOI: 10.1177/1420326X17694475)