Fluid-kinetic modelling for respiratory aerosols with variable size and temperature

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Outline of the talk

Introduction

Aerosol therapy

- Treat chronic pulmonary diseases (COPD)
- Difficulty of *in vivo* observation of drug delivery in the human airways
- Numerical simulations of the aerosol flow in the lung
- Accurate description of the deposition phenomenon (in part. its location)

Physical properties of the aerosol

- Very numerous particles
- Hygroscopic properties: water exchange with the bronchial (humid) air
- Strongly relying on thermal effects
- Size variation of the particles $\rightsquigarrow$ influence on deposition (quantity, characteristic times, location, ...)

State of the art

Aerosol description in the air

1. Two-phase models
   - Aerosol concentration in the air
   - Difficulty to determine the deposition areas
2. Agent-based models
   - Difficulty to track the trajectories of numerous particles
3. Kinetic models
   - Numerous particles in the aerosol with negligible volume compared to the airways

Taking into account the radius variation of the particles

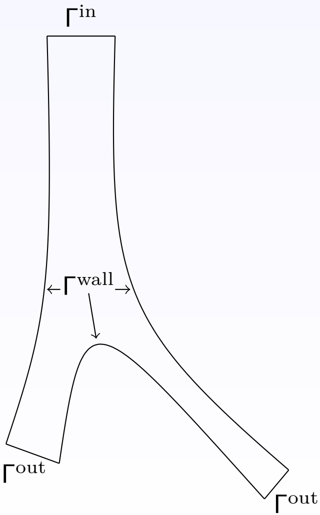
- Need to take into account thermal effects
- [Longest, Hindle, 2011]: ODE model for the droplet radius and temperature, as well as air temperature and vapour mass fraction
- Take into account spatial heterogeneity: PDE model

Outline of the talk

PDE modelling

- For the aerosol
  - variables: $t \geq 0$, $x \in \Omega$, $v \in \mathbb{R}^3$, $r > 0$, $T > 0$
  - distribution function $f(t, x, v, r, T)$
  - the particles remain spherical and do not interact with each other
- For the air
  - Newtonian and incompressible (air mass density ϱ_{air} constant)
  - velocity $u(t, x)$, pressure $p(t, x)$
  - water vapour mass fraction in the air $Y_{\mathrm{v,air}}(t, x)$
  - air temperature $T_{\mathrm{air}}(t, x)$

Simplified domain Ω



Kinetic model for the aerosol

Vlasov-type equation

$$\boxed{\partial_t f + v \cdot \nabla_x f + \mathrm{div}_v \Big[(\alpha(u - v) + g)f\Big] + \partial_r(af) + \partial_T(bf) = 0}$$

- g: gravitational field
- $\alpha(u - v)$: drag acceleration undergone by the aerosol from the air
- function a: radius growth evolution of the particles
- function b: temperature growth evolution of the particles

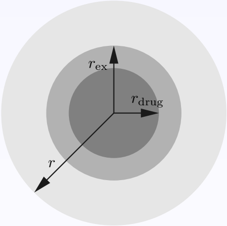
Boundary conditions :

- Deposition: $f(t, \cdot, v, r, T) = 0$ on Γ^{wall} if $v \cdot n \leq 0$
- Entrance distribution $f(t, \cdot, v, r, T) = f^{\mathrm{in}}$ on Γ^{in}

Description of the drag acceleration

Each droplet is comprised of active products (drug), excipient and water.

- r_{drug}: radius s. th. $\frac{4}{3}\pi r_{\mathrm{drug}}^3 \varrho_{\mathrm{drug}}$ is the drug mass inside the droplet
- r_{ex}: particle dry radius



The mass of the droplet is given by

$$m(r) = \frac{4}{3}\pi \left[r_{\mathrm{drug}}^3 \varrho_{\mathrm{drug}} + (r_{\mathrm{ex}}^3 - r_{\mathrm{drug}}^3)\varrho_{\mathrm{ex}} + (r^3 - r_{\mathrm{ex}}^3)\varrho_{\mathrm{w}} \right]$$

The drag force satisfies the Stokes law

$$\alpha(r) = \frac{6\pi\eta r}{m(r)}$$

where η is the (constant) air dynamic viscosity.

Description of the radius growth evolution

Following [Longest, Hindle, 2011]

- Water mass flux N_{d} at the droplet surface

$$a(r, T, Y_{\mathrm{v,air}}(t,x)) = -\frac{N_{\mathrm{d}}(r, T, Y_{\mathrm{v,air}}(t,x))}{\varrho_{\mathrm{w}}}$$

- This flux N_{d} depends on r, T through the mass fraction $Y_{\mathrm{v,surf}}$ of water vapour at the droplet surface

$$N_{\mathrm{d}}(r, T, Y_{\mathrm{v,air}}(t,x)) = \varrho_{\mathrm{air}} \frac{\mathrm{Sh}\, D_{\mathrm{v}}\, C_m}{2r} \frac{Y_{\mathrm{v,surf}}(r,T) - Y_{\mathrm{v,air}}(t,x)}{1 - Y_{\mathrm{v,surf}}(r,T)},$$

- Highly nonlinear expression of $Y_{\mathrm{v,surf}}(r, T)$

$$Y_{\mathrm{v,surf}}(r,T) = \frac{S(r)K(r,T)P_{\mathrm{v,sat}}(T)}{\varrho_{\mathrm{d}}(r)R_{\mathrm{v}}T}$$

  - $S(r)$: water activity coefficient
  - $K(r, T)$: influence of the Kelvin effect on the droplet surface concentration of water vapor
  - $P_{\mathrm{v,sat}}(T)$: water vapour saturation pressure
  - $\varrho_{\mathrm{d}}(r)$: mass density of the particle

Description of the temperature growth evolution

Following [Longest, Hindle, 2011]

- Contributions of both the convective heat flux between the air and the droplets Q_{d} and the evaporating one $L_{\mathrm{v}} N_{\mathrm{d}}$, with L_{v} the latent heat of water vaporisation

$$b(r, T, Y_{\mathrm{v,air}}(t,x), T_{\mathrm{air}}(t,x)) = \frac{-3Q_{\mathrm{d}}(r, T, T_{\mathrm{air}}(t,x)) - 3L_{\mathrm{v}} N_{\mathrm{d}}(r, T, Y_{\mathrm{v,air}}(t,x))}{\varrho_{\mathrm{d}}(r) c_{P_{\mathrm{d}}} r}$$

- The convective flux Q_{d} is given by

$$Q_{\mathrm{d}}(r, T, T_{\mathrm{air}}(t,x)) = \frac{\mathrm{Nu}\, \kappa_{\mathrm{air}}\, C_T}{2r} (T - T_{\mathrm{air}}(t,x))$$

  - Nu: droplet Nusselt number
  - κ_{air}: thermal conductivity of the air as a gaseous mixture
  - C_T: Knudsen correlation

These terms ensure that $r \geq r_{\mathrm{ex}}$ and $T \geq T_{\min}$.

PDE model for the air (1)

- Incompressible Navier-Stokes equations

$$\boxed{\begin{cases} \varrho_{\mathrm{air}}\Big[\partial_t u + (u \cdot \nabla_x u)\Big] - \eta \Delta_x u + \nabla_x p = F \\ \mathrm{div}_x\, u = 0 \end{cases}}$$

- Aerosol retroaction F on the air

$$F(t,x) = - \iiint\limits_{\mathbb{R}^3 \times \mathbb{R}_+ \times \mathbb{R}} m(r)\alpha(r)(u(t,x) - v) f(t,x,v,r,T)\, \mathrm{d}v\, \mathrm{d}r\, \mathrm{d}T$$

- Dirichlet boundary conditions on u on Γ^{in}
- Homogeneous Dirichlet boundary conditions on u on Γ^{wall}
- Free flow boundary conditions on the stress tensor on Γ^{out}

PDE model for the air (2)

- Advection-diffusion equation for $Y_{\mathrm{v,air}}$

$$\boxed{\varrho_{\mathrm{air}}\left[\partial_t Y_{\mathrm{v,air}} + (u \cdot \nabla_x) Y_{\mathrm{v,air}}\right] - \mathrm{div}_x\left(D_{\mathrm{v}} \nabla_x Y_{\mathrm{v,air}}\right) = S_Y}$$

- Dirichlet boundary conditions on $Y_{\mathrm{v,air}}$ on Γ^{in} (fresh air) and Γ^{wall} (humid air)
- Neumann boundary conditions on $Y_{\mathrm{v,air}}$ on Γ^{out}
- Source term S_Y: water mass exchanges between the bronchial air and the aerosol

$$S_Y(t,x) = \varrho_{\mathrm{w}} \iiint_{\mathbb{R}^3 \times \mathbb{R}_+^* \times \mathbb{R}_+^*} 4\pi r^2 N_{\mathrm{d}}(r, T, Y_{\mathrm{v,air}}(t,x))\, f(t,x,v,r,T)\, \mathrm{d}v\, \mathrm{d}r\, \mathrm{d}T$$

Ensures the physical conservation of the water vapour mass!

PDE model for the air (3)

- Advection-diffusion equation for T_{air}

$$\boxed{\varrho_{\mathrm{air}} c_{P_{\mathrm{air}}} [\partial_t T_{\mathrm{air}} + (u \cdot \nabla_x) T_{\mathrm{air}}] - \kappa_{\mathrm{air}} \Delta_x T_{\mathrm{air}} = S_T}$$

- Dirichlet boundary conditions on T_{air} on Γ^{in} (room temperature) and Γ^{wall} (body temperature)
- Neumann boundary conditions on T_{air} on Γ^{out}
- Source term S_T: heat transfer between the air and the aerosol through the water vapour

$$S_T(t,x) = \iiint_{\mathbb{R}^3 \times \mathbb{R}_+^* \times \mathbb{R}_+^*} 4\pi r^2 Q_{\mathrm{d}}(r, T, T_{\mathrm{air}}(t,x)) \, f(t,x,v,r,T) \, \mathrm{d}v \, \mathrm{d}r \, \mathrm{d}T$$

Ensures the physical conservation of the thermal energy associated to water transfers!

Outline of the talk

Numerical method (1)

- 2D computations, use of `FreeFem++`

Time marching scheme uncoupling the fluid and aerosol equations

1. Solve the fluid equations with explicit source terms (using the aerosols quantities)
2. Solve the kinetic equation with updated fluid quantities

1. Standard weak formulations and function spaces for the fluid equations
   - $\mathbb{P}_2$ functions for u, $\mathbb{P}_1$ functions for p, $Y_{\mathrm{v,air}}$, T_{air}
   - Convective terms treated with the characteristics method (`convect` command)
   - Neglect the retroaction of the particles on the fluid ($F = 0$)
2. Particle method for the Vlasov equation
   - Discretization of the distribution function f as a weighted sum of Dirac masses in x, v, r, T variables
   - N_{num} numerical particles, each having representativity ω

$$f(t,x,v,r,T) \simeq \omega \sum_{p=1}^{N_{\mathrm{num}}} \delta_{x_p(t)} \otimes \delta_{v_p(t)} \otimes \delta_{r_p(t)} \otimes \delta_{T_p(t)}(x,v,r,T)$$

Numerical method (2)

The particle coordinates satisfy the differential system

$$\begin{cases} \dot{x}_p(t) = v_p(t) \\ \dot{v}_p(t) = \alpha(r_p(t))\Big(u\big(t, x_p(t)\big) - v_p(t)\Big) + (1 - \frac{\varrho_{\mathrm{air}}}{\varrho_{\mathrm{d}}})g \\ \dot{r}_p(t) = a\Big(r_p(t), T_p(t), Y_{\mathrm{v,air}}\big(t, x_p(t)\big)\Big) \\ \dot{T}_p(t) = b\Big(r_p(t), T_p(t), Y_{\mathrm{v,air}}\big(t, x_p(t)\big), T_{\mathrm{air}}\big(t, x_p(t)\big)\Big) \end{cases}$$

- High precision for the ODE on r_p: use of a RK4 scheme
- Semi-implicit Euler scheme for v_p and T_p
- Position x_p updated using the new velocity v_p
- Allows to update the fluid source terms S_Y and S_T

Numerical method (3)

Deposition or exiting the domain

- Computation of the distance of the particle to Γ^{wall} or Γ^{out} $\rightsquigarrow$ deposition on the wall or exiting the domain through the outlet
- If the distance to the boundary is smaller than r_p, also deposition or exit

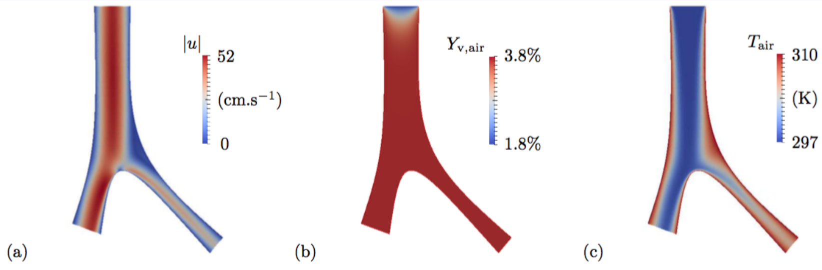
Time subcycling for the particles

- Prevent the aerosol particles to go across various cells during one single fluid time step
- Important in particular because of the stiff ODE on the temperature

Outline of the talk

Numerical data (1)

- Domain: trachea and first bifurcation in the human airways
- 3D-2D correction: $D_0 = 1.80$ cm, $\ell_0 = 7.52$ cm
- Entrance velocity: Poiseuille law, order of magnitude 1 m.s^{-1}
- $T_{\mathrm{air}}|_{t=0} = 37°\mathrm{C}$, $T_{\mathrm{air}}^{\mathrm{in}} = 24°\mathrm{C}$, $T_{\mathrm{wall}} = 37°\mathrm{C}$
- Initial and boundary values of $Y_{\mathrm{v,air}}$ computed from the relative humidities in the airways
- Stationary state for the fluid



Numerical data (2)

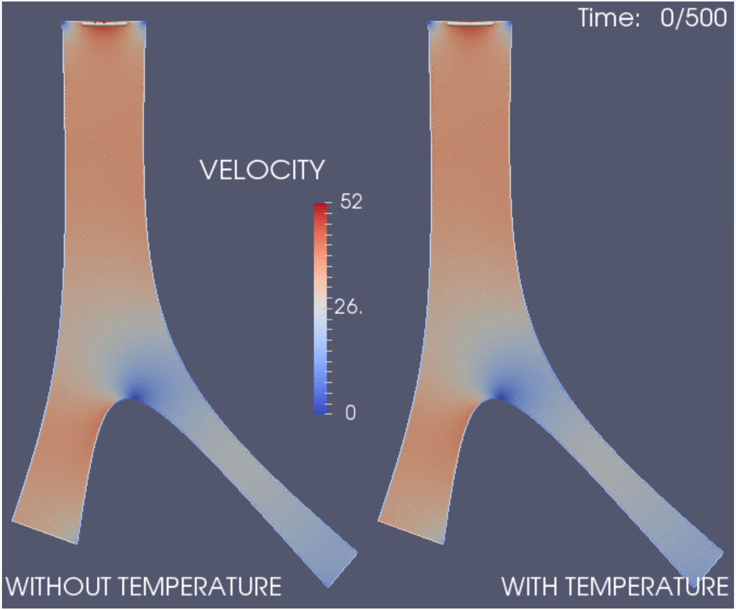
- 5 injections of 100 numerical particles, with $\omega = 10^4$
- Periodic releases between $t = 0$ and $t = 0.25$ s, final time $t = 1$ s
- Initial radii $r_p(0) = 2.25\ 10^{-5}$ cm (no excipient)
- Initial temperatures equal to the entrance air temperature
- Initial positions uniform in $[-D_0/4, D_0/4] \rightsquigarrow$ maximizes the deposition
- Averaged computations over 10 initial randomly chosen particle distributions

Validation

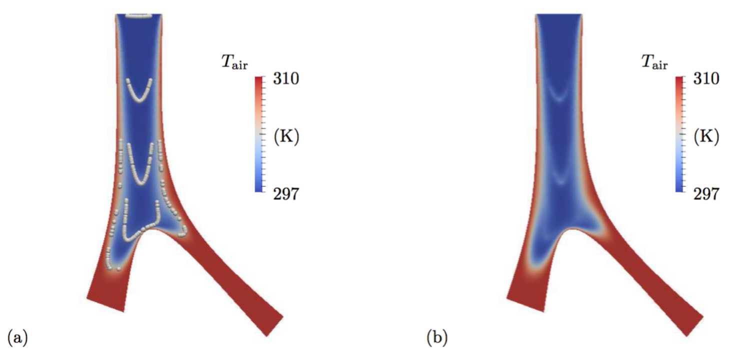
- Mass conservation in the water vapour exchange between air and aerosol
- Thermal energy balance

Comparison of different models

- Full model (A)
- No variation of T_{air}, T (B)
- No variation of T_{air}, T nor $Y_{\mathrm{v,air}}$, r (C)


Time: 0/500
VELOCITY
52
26.
0
WITHOUT TEMPERATURE
WITH TEMPERATURE

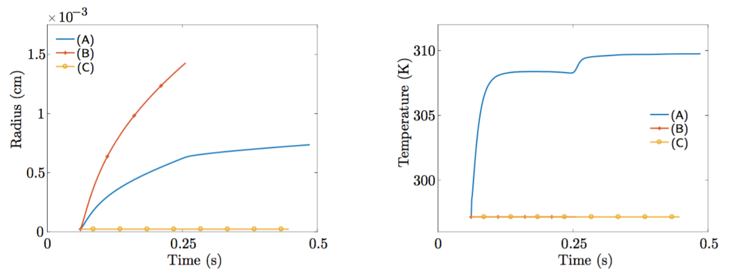
Local influence of the particles on the air temperature



- Local air temperature increasing at the location of the particles
- Comes from the water vapour mass exchange between the humidified air and the droplets

Radius and temperature evolution of a particular droplet

- Droplet going out through the left branch in the full model
- Comparison between the different models (A), (B), (C)

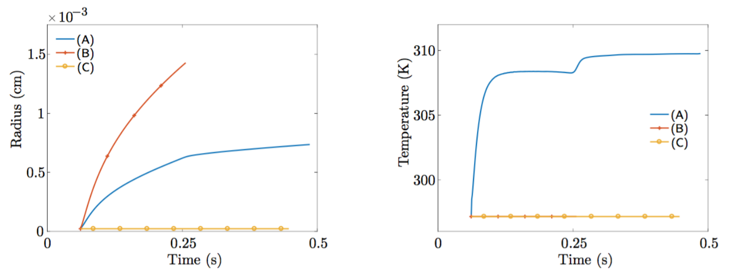


Radius evolution

- Except for the first release, the aerosol evolves in a cooled air
- Larger size growth with model (B) than with (A)
- In model (A), part of the radius variation has a temperature effect
- $\rightsquigarrow$ More deposition with model (B), and shorter mean deposition time

Radius and temperature evolution of a particular droplet

- Droplet going out through the left branch in the full model
- Comparison between the different models (A), (B), (C)



Temperature evolution

- Only in model (A)
- Temperature jump when the particles go into the branches of the bifurcation (smaller diameter)
- Stronger wall effect in the branches $\rightsquigarrow$ higher temperature increase

Outline of the talk

Conclusion and prospects

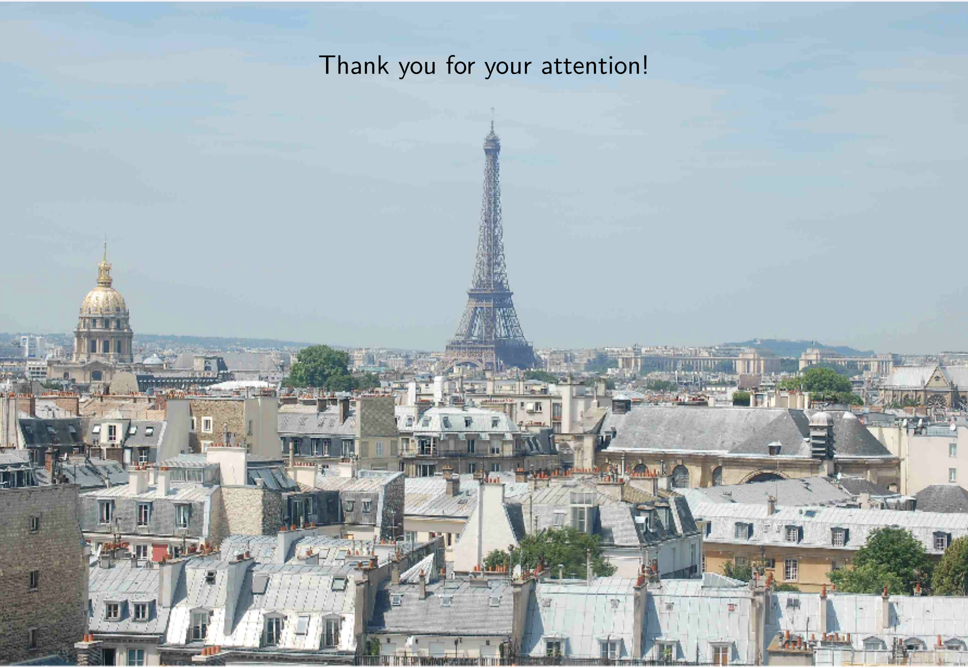
Conclusion

- Fluid-kinetic model for respiratory aerosols, taking into account size variation of the droplets
- Importance of taking into account both humidity and temperature (for the droplets and the air) to properly describe the hygroscopic effects on aerosols

Prospects

- Taking into account excipients (different hygroscopic properties)
- Other geometrical domains
- Expiration (problem for boundary conditions)
- 3D computations (PhD of David Michel)

Thank you for your attention!



Physical conservation of the water vapour mass exchange

Assume that $u = 0$, $\nabla_x Y_{\mathrm{v,air}} \cdot n = 0$ and $f = 0$ on on $\partial\Omega$. Then we have

$$\frac{\mathrm{d}}{\mathrm{d}t}\left[\int_\Omega \left(\varrho_{\mathrm{air}} Y_{\mathrm{v,air}}(t,x) + \iiint_{\mathbb{R}^3\times\mathbb{R}_+^*\times\mathbb{R}_+^*} m(r) f(t,x,v,r,T)\,\mathrm{d}v\,\mathrm{d}r\,\mathrm{d}T\right)\mathrm{d}x\right] = 0.$$

Proof.

- Multiply the Vlasov equation by $m(r)$, integrate w. r. t. x, v, r, T, and eliminate the conservative terms through integrations by parts
- Integrate equation for $Y_{\mathrm{v,air}}$ on Ω, use the definitions of the terms a and S_Y

$\square$

Physical conservation of thermal energy associated to water transfers

Assume that $u = 0$, $\nabla_x Y_{\mathrm{v,air}} \cdot n = 0$ and $f = 0$ on on $\partial\Omega$. Then we have

$$\frac{\mathrm{d}}{\mathrm{d}t}\left[\int_{\Omega}\left(\varrho_{\mathrm{air}} c_{P_{\mathrm{air}}} T_{\mathrm{air}}(t,x) + \iiint_{\mathbb{R}^3\times\mathbb{R}_+^*\times\mathbb{R}_+^*} m(r) c_{P_{\mathrm{d}}} T\, f(t,x,v,r,T)\,\mathrm{d}v\,\mathrm{d}r\,\mathrm{d}T\right)\mathrm{d}x\right]$$

$$= -\int_{\Omega}\iiint_{\mathbb{R}^3\times\mathbb{R}_+^*\times\mathbb{R}_+^*} 4\pi r^2 (L_{\mathrm{v}} + c_{P_{\mathrm{d}}} T) N_{\mathrm{d}}(r, T, Y_{\mathrm{v,air}}(t,x))\, f(t,x,v,r,T)\,\mathrm{d}v\,\mathrm{d}r\,\mathrm{d}T\,\mathrm{d}x.$$

Proof.

- Integrate equation for T_{air} over Ω
- Multiply the Vlasov equation by $m(r) c_{P_{\mathrm{d}}} T$, integrate w. r. t. x, v, r, T
- Sum both equalities, the term involving Q_{d} vanishes
- It remains two terms involving N_{d}:
  - one with L_{v} to take the change of physical state into account
  - one with the added thermal energy in the aerosol due to the mass exchange.

$\square$