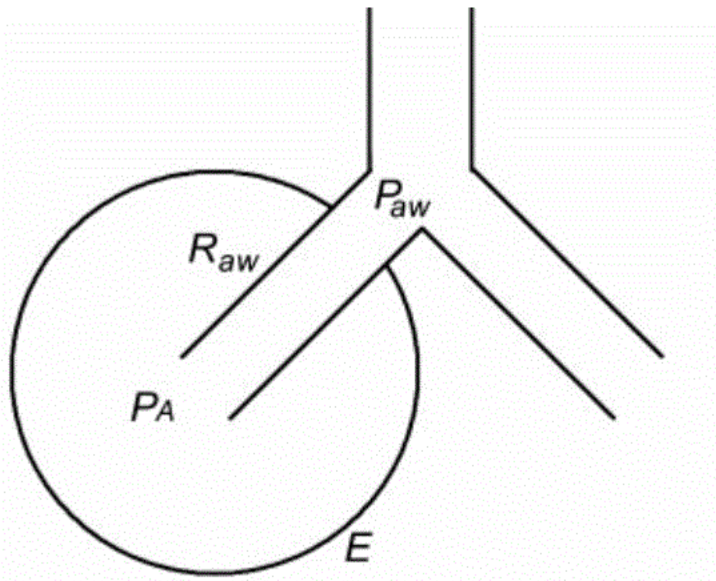
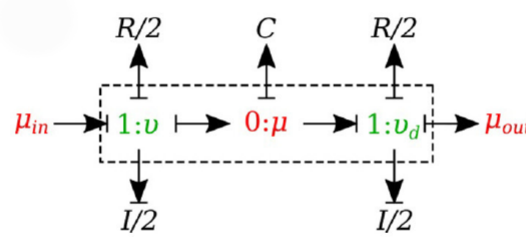
Airway BG attempt

BG constituent relations

We model a peripheral airway embedded in surrounding parenchyma with airflow being driven by the difference between airway entrance pressure and alveolar pressure. In BGs, we model the terminal locations using RCR Windkessel elements. The region of parenchyma served by the airway has elastance (E) and the airway is surrounded by the parenchyma it serves. We use the pp-type model as developed by Safaei et al 2018



(a)



(b)

Figure 1: Figure (a) shows the system being modelled, taken from Anafi and Wilson 2001. Figure (b) represents the pp-type model developed by Safaei et al 2018

The governing equations for this model are

$$u = u_v + (v - v_d)R_v \tag{1}$$

$$\frac{du_v}{dt} = \frac{v - v_d}{C} \tag{2}$$

$$\frac{dv}{dt} = \frac{u_{in} - u - v\frac{R}{2}}{\frac{I}{2}} \tag{3}$$

$$\frac{dv_d}{dt} = \frac{u - u_{out} - v_d\frac{R}{2}}{\frac{I}{2}} \tag{4}$$

$$R_v = \frac{f}{C} \tag{5}$$

$$R_{aw} = \frac{12\mu L}{\pi r^4} \tag{6}$$

$$C = \frac{2\pi r^3 L}{hE} \tag{7}$$

$$I = \frac{\rho L}{\pi r^2} \tag{8}$$

R-element: Energy u can be dissipated by a resistor R in proportion to the flow v via $u = vR$. In respiratory mechanics we choose the R-element to represent viscous resistance in opposition to airflow via

Modified Poiseuille equation.

C-element: Energy, u can be stored statically by a capacitor C without any loss. Here C represents the airway wall compliance, and we assume the airway to be homogeneous linear elastic material with compliance C.

I -element: Dynamic energy storage is used to model the mass-inertial effects in the airway and can be defined for straight cylindrical vessels.

Airway Dynamics

The equilibria for radii of the airway lumen can be found following the modified form of Lambert et al 1982 as described in Politi et al,2010. Here the airway radius is modeled as a function of transmural pressure u_{tm}, where first order dynamics apply.

$$R\left(u_{tm}\right)=\begin{cases}\sqrt{R_i^2\left(1-P_{tm}/P_1\right)^{-nA}} & P_{tm}\leq 0\\ \sqrt{r_{imax}^2-\left(r_{imax}^2-R_i^2\right)\left(1-P_{tm}/P_2\right)^{-nB}} & P_{tm}>0\end{cases} \tag{9}$$

where

$$u_{tm}\left(r_i\right)=u_{in}-\frac{f_a R_{ref}}{r_i}+\tau \tag{10}$$

and $P_1, P_2, R_i,$ *and* r_{imax} are all airway specific parameters taken from Politi et al,2010. We model the time dependent radii via the 1st order kinetic equation

$$\frac{dr}{dt}=p\left(R(u_{tm})-r\right). \tag{11}$$

Parenchymal tethering stress (τ) contributes to the transmural pressure via the form proposed by Lai-Fook (1979) where

$$\tau=u_{out}+u_{out}\left(1.4x+2.1x^2\right) \tag{12}$$

where x represents the parenchymal distortion and is given by

$$x=1-(r_i/v^{\frac{1}{3}}) \tag{13}$$

where

$$v=\frac{0.2*V_{TLC}+(u_{out}/E)}{V_{TLC}} \tag{14}$$

denotes the nondimensionalized acinar volume at total lung capacity (TLC). We follow the work of Anafi and Wilson 2001 and model the pressure at the top of the airway (P_{aw}) as

$$u_{in}=\bar{u}+\left|u_{in}\right| sin(\omega t). \tag{15}$$

Assuming R_{aw} and E remain approximately constant, the Acinar pressure P_A is approximately sinusodial with phase lag α,

$$u_{out}=\bar{u}+\left|u_{out}\right| sin\left(\omega t-\alpha\right) \tag{16}$$

where

$$\left|u_{out}\right|=\left|u_{in}\right|\frac{E}{\sqrt{E^2+\left(\omega R_{aw}\right)^2}} \tag{17}$$

and $\alpha=arctan\left[\frac{\omega R_{aw}}{E}\right]$.

We also include the kinetic model for the 4 state ODE actin-myosin muscle contraction model as developed by Hai and Murphy,1988

$$\begin{aligned}\frac{dM}{dt}&=-K_1(c)M+K_2(c)M_p+K_7AM\\ \frac{dM_p}{dt}&=K_4AM_p+K_1(c)M-\left(K_2(c)+K_3\right)M_p\\ \frac{dAM_p}{dt}&=K_3M_p+K_6AM-\left(K_4+K_5\right)AM_p\\ \frac{dAM}{dt}&=K_5AM_p-\left(K_7+K_6\right)AM\end{aligned}$$

where M, M_p represents unphosphorylated, phosphorylated myosin and AM, $AM_p$are the actin-myosin bound unphophorylated and phosphorylated population respectively. This is subject to the constraint $M + M_p + AM_p + AM = 1$. ASM force (f_a) is applied to the airway via

$$f_a = \kappa * (AM_p + AM) \tag{18}$$

where κ represents a scaling factor.

References

[Lambert et al 1982] Lambert, RODNEY K., THEODORE A. Wilson, ROBERT E. Hyatt, and JOSEPH R. Rodarte. "A computational model for expiratory flow." Journal of applied physiology 52, no. 1 (1982): 44-56.

[Hai and Murphy, 1988] Hai, Chi-Ming, and Richard A. Murphy. "Cross-bridge phosphorylation and regulation of latch state in smooth muscle." American Journal of Physiology-Cell Physiology 254, no. 1 (1988): C99-C106.

[Politi et al, 2010] Politi, Antonio Z., Graham M. Donovan, Merryn H. Tawhai, Michael J. Sanderson, Anne-Marie Lauzon, Jason HT Bates, and James Sneyd. "A multiscale, spatially distributed model of asthmatic airway hyper-responsiveness." Journal of theoretical biology 266, no. 4 (2010): 614-624.

[Lai-Fook (1979)] Lai-Fook, STEPHEN J. "A continuum mechanics analysis of pulmonary vascular interdependence in isolated dog lobes." Journal of applied physiology 46, no. 3 (1979): 419-429.

[Safaei et al 2018] Safaei, Soroush, Pablo J. Blanco, Lucas O. Müller, Leif R. Hellevik, and Peter J. Hunter. "Bond graph model of cerebral circulation: toward clinically feasible systemic blood flow simulations." Frontiers in physiology 9 (2018): 148.

[Anafi and Wilson 2001] Anafi, Ron C., and Theodore A. Wilson. "Airway stability and heterogeneity in the constricted lung." Journal of Applied Physiology 91, no. 3 (2001): 1185-1192.