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Supplemental Information

A Distribution-Moment Approximation for Coupled Dynamics of the Airway Wall and Airway Smooth Muscle

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A Distribution-Moment Approximation for Coupled Dynamics of the Airway Wall and Airway Smooth Muscle: Supporting material

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Supplemental Information

The piecewise functions $f_p(x)$, $g_p(x)$ and $g(x)$ are defined as

$$f_p\left(x\right) = \begin{cases} 0 & x < 0 \\ \dfrac{f_{p1} x}{h} & 0 \le x \le h \\ 0 & x > h \end{cases} \tag{1}$$

$$g_p\left(x\right) = \begin{cases} g_{p2} & x < 0 \\ \dfrac{g_{p1} x}{h} & 0 \le x \le h \\ \dfrac{\left(g_{p1} + g_{p3}\right) x}{h} & x > h \end{cases} \tag{2}$$

$$g\left(x\right) = \begin{cases} g_2 & x < 0 \\ \dfrac{g_1 x}{h} & 0 \le x \le h \\ \dfrac{\left(g_1 + g_3\right) x}{h} & x > h \end{cases} . \tag{3}$$

Additionally, $f_{p1} = 2k_3$, $g_{p1} = 2k_4$, $g1 = 2k_7$, $g_{p2} = 4\left(f_{p1} + g_{p1}\right)$, $g_2 = 20g_1$, $g_{p3} = 3g_{p1}$ and $g_3 = 3g_1$. The values of k_1 to k_7 as well as g_{p1} to g_{p3} and g_1 to g_3 are chosen to match experimental values (1).

The functions A_Λ to E_Λ for the Distribution Moment Approximation are constructed explicitly as follows. Given the reduced ODE form

$$\frac{d}{dt} M_{1\Lambda} + \Lambda v\left(t\right) M_{1(\Lambda-1)} + k_2 M_{1\Lambda} = A_\Lambda - B_\Lambda + C_\Lambda \tag{4}$$

the functions A_Λ-C_Λ are given by

$$A_\Lambda = \int_{-\infty}^{\infty} f_p\left(x\right) x^\Lambda n_{Mp} dx \tag{5}$$

$$B_\Lambda = \int_{-\infty}^{\infty} g_p\left(x\right) x^\Lambda n_{AMp} dx \tag{6}$$

$$C_\Lambda = k_1 \int_{-\infty}^{\infty} x^\Lambda n_{AM} dx \tag{7}$$

whereas the functions D_Λ and E_Λ of

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$$\frac{d}{dt}M_{2\Lambda}+\Lambda v\left(t\right)M_{2(\Lambda-1)}+k_1M_{2\Lambda}=D_\Lambda-E_\Lambda. \tag{8}$$

are given by

$$D_\Lambda=k_2\int_{-\infty}^{\infty}x^\Lambda n_{Amp}dx \tag{9}$$

$$E_\Lambda=\int_{-\infty}^{\infty}g\left(x\right)x^\Lambda n_{AM}dx. \tag{10}$$

We assume a Gaussian distribution for n_{AMp} of the form

$$n_{AMp}=\frac{M_{10}}{\sqrt{2\pi}q_1}e^{-\dfrac{\left(x-p_1\right)^2}{2q_1^2}} \tag{11}$$

for which

$$p_1=\frac{M_{11}}{M_{10}},q_1=\sqrt{\frac{M_{12}}{M_{10}}-\left(\frac{M_{11}}{M_{10}}\right)^2}. \tag{12}$$

Similarly n_{AM} is Gaussian with moments M_{20},M_{21},M_{22}.

We also consider integrals of the form

$$J_\Lambda\left(\eta\right)=\frac{1}{\sqrt{2\pi}q_1}\int_{-\infty}^{\eta}x^\Lambda e^{-\dfrac{\left(x-p_1\right)^2}{2q_1^2}}dx \tag{13}$$

$$K_\Lambda\left(\eta\right)=\frac{1}{\sqrt{2\pi}q_2}\int_{-\infty}^{\eta}x^\Lambda e^{-\dfrac{\left(x-p_2\right)^2}{2q_2^2}}dx \tag{14}$$

If $y_i=\frac{(x-p_i)}{q_i}$ and $\tau_i=\frac{(\eta-p_i)}{q_i}$ for $i=1,2$, we may write $J_\Lambda\left(\eta\right)$ and $K_\Lambda\left(\eta\right)$ of the form

$$J_\Lambda\left(\tau_1\right)=\frac{1}{\sqrt{2\pi}}\int_{-\infty}^{\tau_1}\left(p_1+q_1y_1\right)^\Lambda e^{-\frac{y_1^2}{2}}dy_1 \tag{15}$$

$$K_\Lambda\left(\tau_2\right)=\frac{1}{\sqrt{2\pi}}\int_{-\infty}^{\tau_2}\left(p_2+q_2y_2\right)^\Lambda e^{-\frac{y_2^2}{2}}dy_2. \tag{16}$$

Expanding these integrals results in a series of integrals of the form

$$I_{1\Lambda}=\frac{1}{\sqrt{2\pi}}\int_{-\infty}^{\tau_1}y_1^\Lambda e^{-\frac{y_1^2}{2}}dy_1 \tag{17}$$

$$I_{2\Lambda}=\frac{1}{\sqrt{2\pi}}\int_{-\infty}^{\tau_2}y_2^\Lambda e^{-\frac{y_2^2}{2}}dy_2. \tag{18}$$

We define the error function as $I_{10}\left(\tau_1\right)$=$\phi_1\left(\tau_1\right)$=$\frac{1}{\sqrt{2\pi}}\int_{-\infty}^{\tau_1}e^{-\frac{y_1^2}{2}}dy_1$ and $I_{20}\left(\tau_2\right)$ =$\phi_2\left(\tau_2\right)$=$\frac{1}{\sqrt{2\pi}}\int_{-\infty}^{\tau_2}e^{-\frac{y_2^2}{2}}dy_2$. These lead to the following

$$J_0(\tau) = \phi_1(\tau) \tag{19}$$

$$K_0(\tau) = \phi_2(\tau) \tag{20}$$

$$J_1(\tau) = p_1\phi_1(\tau) - q_1\frac{e^{-\tau^2/2}}{\sqrt{2\pi}} \tag{21}$$

$$K_1(\tau) = p_2\phi_2(\tau) - q_2\frac{e^{-\tau^2/2}}{\sqrt{2\pi}} \tag{22}$$

$$J_2(\tau) = p_1^2\phi_1(\tau) - 2p_1q_1\frac{e^{-\tau^2/2}}{\sqrt{2\pi}} + q_1^2\left\{\phi_1(\tau) - \frac{\tau e^{-\tau^2/2}}{\sqrt{2\pi}}\right\} \tag{23}$$

$$K_2(\tau) = p_2^2\phi_2(\tau) - 2p_2q_2\frac{e^{-\tau^2/2}}{\sqrt{2\pi}} + q_2^2\left\{\phi_2(\tau) - \frac{\tau e^{-\tau^2/2}}{\sqrt{2\pi}}\right\} \tag{24}$$

$$J_3(\tau) = p_1^3\phi_1(\tau) - 3p_1^2q_1\frac{e^{-\tau^2/2}}{\sqrt{2\pi}} + 3p_1q_1^2\left\{\phi_1(\tau) - \frac{\tau e^{-\tau^2/2}}{\sqrt{2\pi}}\right\} - q_1^3\left(2+\tau^2\right)\frac{e^{-\tau^2/2}}{\sqrt{2\pi}} \tag{25}$$

$$K_3(\tau) = p_2^3\phi_2(\tau) - 3p_2^2q_2\frac{e^{-\tau^2/2}}{\sqrt{2\pi}} + 3p_2q_2^2\left\{\phi_2(\tau) - \frac{\tau e^{-\tau^2/2}}{\sqrt{2\pi}}\right\} - q_2^3\left(2+\tau^2\right)\frac{e^{-\tau^2/2}}{\sqrt{2\pi}} \tag{26}$$

Considering B_Λ, D_Λ and the Gaussian assumed for n_{AMp} we obtain

$$\begin{aligned} B_\Lambda = {} & \frac{M_{10}}{\sqrt{2\pi}q_1h}\left[\int_{-\infty}^{0} g_{p2}x^\Lambda e^{-\frac{(x-p_1)^2}{2q_1^2}}dx + \int_0^1 g_{p1}x^{\Lambda+1}e^{-\frac{(x-p_1)^2}{2q1^2}}dx\right] \\ & + \frac{M_{10}}{\sqrt{2\pi}q_1h}\left[\int_1^{\infty}\left(g_{p1}+g_{p3}\right)x^{\Lambda+1}e^{-\frac{(x-p_1)^2}{2q_1^2}}dx\right] \end{aligned} \tag{27}$$

$$\begin{aligned} D_\Lambda = {} & \frac{k_2M_{10}}{\sqrt{2\pi}q_1h}\left[\int_{-\infty}^{0} x^\Lambda e^{-\frac{(x-p_1)^2}{2q_1^2}}dx + \int_0^1 x^\Lambda e^{-\frac{(x-p_1)^2}{2q_1^2}}dx\right] \\ & + \frac{k_2M_{10}}{\sqrt{2\pi}q_1h}\left[\int_1^{\infty} x^\Lambda e^{-\frac{(x-p_1)^2}{2q_1^2}}dx\right] \end{aligned} \tag{28}$$

Similarly by considering the Gaussian for n_{AM} we obtain the expressions for C_Λ and E_Λ

$$\begin{aligned} C_\Lambda = {} & \frac{k_1M_{20}}{\sqrt{2\pi}q_2h}\left[\int_{-\infty}^{0} x^\Lambda e^{-\frac{(x-p_2)^2}{2q_2^2}}dx + \int_0^1 x^\Lambda e^{-\frac{(x-p_2)^2}{2q_2^2}}dx\right] \\ & + \frac{k_1M_{20}}{\sqrt{2\pi}q_2h}\left[\int_1^{\infty} x^\Lambda e^{-\frac{(x-p_2)^2}{2q_2^2}}dx\right] \end{aligned} \tag{29}$$

$$E_\Lambda = \frac{M_{20}}{\sqrt{2\pi}q_2 h}\left[\int_{-\infty}^{0} g_2 x^\Lambda e^{-\frac{(x-p_2)^2}{2q_2^2}} + \int_0^1 g_1 x^{\Lambda+1} e^{-\frac{(x-p_2)^2}{2q_2^2}} dx\right] + \frac{M_{20}}{\sqrt{2\pi}q_2 h}\left[\int_1^\infty (g_1+g_3)\, x^{\Lambda+1} e^{-\frac{(x-p_2)^2}{2q_2^2}}\right] \tag{30}$$

Finally in order to compute a form for A_Λ we consider the conservation condition $[n_M]$+$[n_{AM}]$+$[n_{Mp}]$+$[n_{AMp}]$=1 and obtain,

$$\frac{d}{dt}\left([n_M]+[n_{Mp}]\right) = -k_1\left([n_M]+[n_{AM}]\right) + k_2\left([n_{Mp}]+[n_{AMp}]\right) \tag{31}$$

If we then make the substitution of c=$[n_M]+[n_{AM}]$ (equivalently $\int_0^1 n_M(x,t)\,dx$+M_{20} in the DM system) we are then able to calculate $[n_{Mp}]$=$1-c-M_{10}$ (required by the expression of A_Λ), as well as $[n_M]$=$1-M_{20}-M_{10}-[n_{Mp}]$. The resulting expression for A_Λ is then given by

$$A_\Lambda = \frac{f_{p_1}(1-c)}{(\Lambda+2)h} - f_{p_1}\frac{M_{10}}{\sqrt{2\pi}q_1}\int_0^1 x^{\Lambda+1} e^{-\frac{(x-p_1)^2}{2q_1^2}} dx. \tag{32}$$

Expressing $\frac{M_{10}}{\sqrt{2\pi}q_1}\int_0^1 x^{\Lambda+1} e^{-\frac{(x-p_1)^2}{2q_1^2}} dx$ using Eq (13) leads to

$$A_\Lambda = \frac{f_{p_1}(1-c)}{(\Lambda+2)h} - f_{p_1}\left(J_{\Lambda+1}(1) - J_{\Lambda+1}(0)\right) M_{10} \tag{33}$$

Finally the coupled system of ODEs is now given as

$$\frac{dM_{10}}{dt} = A_0 - B_0 + C_0 - k_2 M_{10} \tag{34}$$
$$\frac{dM_{11}}{dt} = A_1 - B_1 + C_1 - k_2 M_{11} - v(t)\, M_{10} \tag{35}$$
$$\frac{dM_{12}}{dt} = A_2 - B_2 + C_2 - k_2 M_{12} - 2v(t)\, M_{11} \tag{36}$$
$$\frac{dM_{20}}{dt} = D_0 - E_0 - k_1 M_{20} \tag{37}$$
$$\frac{dM_{21}}{dt} = D_1 - E_1 - k_1 M_{21} - v(t)\, M_{20} \tag{38}$$
$$\frac{dM_{22}}{dt} = D_2 - E_2 - k_1 M_{22} - 2v(t)\, M_{21} \tag{39}$$
$$\frac{dc}{dt} = -k_1 c + (1-c)\, k_2 \tag{40}$$
$$\frac{dr}{dt} = \rho\left(R\left(P_{tm}\right) - r\right) \tag{41}$$

The transmural pressure P_{tm} for the DM system is then given by

$$P_{tm} = P_0 - \frac{\lambda F_{ASM}}{r} \tag{42}$$

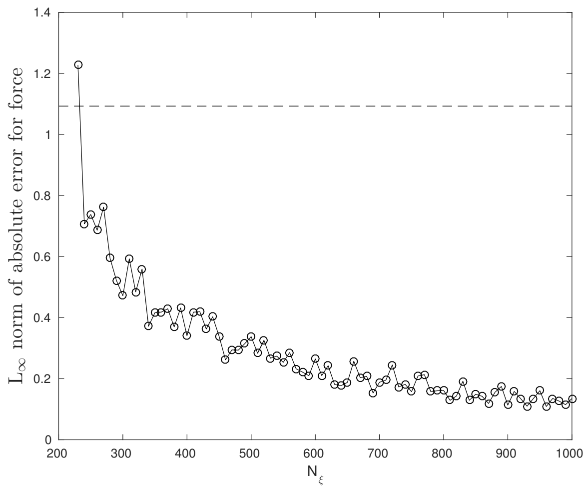

Figure 1: L_∞ norm of the absolute error between the force produced by the MoC at each point and the MoC evaluated at "gold standard" of $N_\xi = 2000$ ODEs. The number of ODEs are reduced until the error is approximately equal to the norm of the absolute error between the DM approximation and the MoC at gold standard. The dashed line indicates the level of error from the 7 ODE DM approximation. Here $\alpha_0 = 20$, $P_{min} = 20$, $f = 0.2$.

where F_{ASM} is given by $F_{ASM}\,(t) = \int_{-\infty}^{\infty} x\,[n_{AM}(x,t) + n_{AMp}(x,t)]\,dx$ and written as $F_{ASM} = \lambda\,[M_{10} + M_{20}]$ for the DM. P_0 is the pressure through the airway and the parameters $\rho = 1s^{-1}$ and $\gamma_0 = 25$. Crossbridge model parameter are from (2), specifically: $k_2 = 0.1s^{-1}$, $f_{p1} = 0.88s^{-1}$, $g_{p1} = 0.22s^{-1}$, $g_1 = 0.01s^{-1}$ and $k_1 = 0.1s^{-1}$ for $0 < t < 5s$ and $0.06s^{-1},$ for $t > 5s$. For this work, $h = 1$.

Numerical efficiency

In order to compare the efficiency of the DM to the MoC, we considered the number of ODEs required to be solved by each method. For the DM method, this is fixed: 7 ODEs. For the MoC approach, one must choose the spatial discretization; specifically, the N_ξ points over the spatial domain. We consider $N_\xi = 2000$ as our "gold standard" solution. The key idea is that one might also reduce the computational cost by reducing N_ξ, though doing so introduces additional error. Thus our approach to quantifying the numerical efficiency is to determine the value of N_ξ at which DM achieves the same error (relative to the gold standard). In particular, we determined the maximum absolute error in the force produced between the MoC at $N_\xi = 2000$ (gold standard) and the DM approximation. The number of ODEs for the MoC was then systematically reduced and at each point, the maximum absolute error between this and the MoC at gold standard was found. The number of ODEs for which the error in the MoC is approximately equal to the error between the DM and gold standard MoC, was then considered equivalent to the DM approximation. This process is represented in Fig 1. For these parameter values, the MoC requires $\approx 690 = 3N_\xi$ ODEs compared with 7 ODEs required by the DM approximation to obtain the same relative error. These parameter values were chosen as they represent a reasonable mid-range value in the main panel of Figure 4 of the main article. Other points in parameter space were similarly explored for numerical efficiency and displayed similar improvements in DM vs MoC. Thus using this approach, the DM method is approximately 100 times more efficient numerically than an equivalent MoC scheme.

Order	$R_i(cm)$	$r_{imax}(cm)$	$P_1(cmH_2O)$	n_1	n_2
1	0.0058	0.0296	0.1603	1	7
2	0.0065	0.0318	0.1768	1	7
3	0.0073	0.0337	0.1985	1	7.185
4	0.0083	0.0358	0.2319	1	7.778
5	0.0096	0.0384	0.2767	1	8
6	0.0113	0.0414	0.3283	1	8
7	0.0132	0.0445	0.4020	1	8
8	0.0156	0.0484	0.4803	1	8.148
9	0.0185	0.0539	0.5680	1	8.741
10	0.0222	0.0608	0.6669	1	9.333
11	0.0269	0.0692	0.7746	1	9.926
12	0.0326	0.0793	0.8976	1	10
13	0.0395	0.0913	1.0242	1	10
14	0.0475	0.1052	1.1569	1	10
15	0.0569	0.1203	1.3357	1	10
16	0.0686	0.1374	1.5605	1	10
17	0.084	0.1585	1.7763	0.952	10
18	0.1026	0.183	1.9933	0.893	10
19	0.1244	0.2108	2.2320	0.833	10
20	0.1537	0.2463	2.5690	0.774	10
21	0.1908	0.2885	3.0320	0.715	10
22	0.2315	0.3307	3.5675	0.656	10
23	0.2791	0.3763	4.2393	0.6	10
24	0.341	0.4319	6.5936	0.6	10
25	0.4261	0.4982	15.1759	0.578	10
26	0.5375	0.5819	34.1380	0.519	10
27	0.6694	0.6995	40.0637	0.5	10
28	0.8157	0.8686	40.0637	0.5	10

Table 1: Table showing parameter values used from (3). Additionally in order to maintain continuity at $P_{tm} = 0$ we have $P_2 = \dfrac{P_1 n_2 \left(R_i^2 - r_{imax}^2\right)}{n_1 R_i^2}$.

References

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