1 Discretization

1.1 Discretizing governing equation with central difference approximation

Starting equation

$$\frac{D_{NO}}{r}\frac{d}{dr}\left(r\frac{dC_{NO}}{dr}\right)+R_{NO}=0 \tag{1}$$

Simplify

$$D_{NO}\frac{d^2C_{NO}}{dr^2}+\frac{D_{NO}}{r}\frac{dC_{NO}}{dr}=-R_{NO} \tag{2}$$

Compare to form

$$u''+P(r)u'=F(r) \tag{3}$$

$$u=C_{NO},\ P(r)=\frac{1}{r},\ F(r)=-\frac{R_{NO}}{D_{NO}} \tag{4}$$

Taylor expansion

$$u_{i+1}=u_i+u_i'\Delta r+\frac{1}{2}u_i''\Delta r^2,$$
$$u_{i-1}=u_i-u_i'\Delta r+\frac{1}{2}u_i''\Delta r^2$$

Central difference

$$u_i'=\frac{u_{i+1}-u_{i-1}}{2\Delta r},$$
$$u_i''=\frac{u_{i+1}-2u_i+u_{i-1}}{\Delta r^2}$$

Sub back into Eq. (3)

$$\frac{u_{i+1}-2u_i+u_{i-1}}{h^2}+P_i\frac{u_{i+1}-u_{i-1}}{2h}=F_i,\ h=\Delta r \tag{5}$$

where index i starts at 1.
Rearrange, let $a_i=\frac{h}{2}P_i$

$$(1-a_i)\,u_{i-1}+(-2)u_i+(1+a_i)\,u_{i+1}=h^2F_i \tag{6}$$

$$(-2)u_i=-(1-a_i)\,u_{i-1}-(1+a_i)\,u_{i+1}+h^2F_i \tag{7}$$

$$u_i=-\frac{1}{2}\left(-(1-a_i)\,u_{i-1}-(1+a_i)\,u_{i+1}+h^2F_i\right) \tag{8}$$

1.2 Discretization schemes for boundary condition

1.2.1 Use imaginary node and correction term

$$\frac{u_2-u_0}{2h}=0\rightarrow u_0=u_2 \tag{9}$$

$$\frac{u_{end+1}-u_{end-1}}{2h}=0\rightarrow u_{end+1}=u_{end-1} \tag{10}$$

Substitute into Eq. (3) when $i=1$

$$(-2)u_1=-2u_2+\frac{1}{2}h^2F_1 \tag{11}$$

Substitute into Eq. (3) when $i=end$

$$(-2)u_{end}=-(1-a_{end})\,u_{end-1}-(1+a_{end})\,u_{end+1}+h^2F_{end} \tag{12}$$

$$(-2)u_{end}=-2u_{end-1}+h^2F_{end} \tag{13}$$

1.2.2 Use second-order one-sided forward/backward approximation

From [1]:

$$\frac{-3u_1+4u_2-u_3}{2h}=0\rightarrow -3u_1+4u_2-u_3=0 \tag{14}$$

$$\frac{3u_{end}-4u_{end-1}+u_{end-2}}{2h}=0\rightarrow 3u_{end}-4u_{end-1}+u_{end-2}=0 \tag{15}$$

2 Solution algorithm

2.1 Gauss-Seidel

From [2]:

$$u_i^{k+1} = -\frac{1}{2}\left(-\left(1-a_i\right)u_{i-1}^{k+1} - \left(1+a_i\right)u_{i+1}^{k} + h^2 F_i\right) \tag{16}$$

2.2 Successive overrelaxation method

$$-\frac{2}{\omega}u_i^{k+1} = -\left(1-a_i\right)u_{i-1}^{k+1} - \left(1+a_i\right)u_{i+1}^{k} + h^2 F_i - \left(\frac{2}{\omega}-2\right)u_i^{k} \tag{17}$$

Alternative formula [3]:

$$\mathbf{u}^{k+1} = \left(\frac{1}{\omega}D + L\right)^{-1}\left\{\left[\left(\frac{1}{\omega}-1\right)D - U\right]\mathbf{u}^{k} + \mathbf{f}\right\} \tag{18}$$

3 Governing equation in individual compartment

3.1 Nitric oxide

RBC core $r_0 < r < r_1$

$$\frac{D_{NO}}{r}\frac{d}{dr}\left(r\frac{dC_{NO}}{dr}\right) - \lambda_{core}C_{NO} = 0$$

$$F_i = \frac{\lambda_{core}u_i}{D_{NO}}$$

CFL $r_1 < r < r_2$

$$\frac{D_{NO}}{r}\frac{d}{dr}\left(r\frac{dC_{NO}}{dr}\right) = 0$$

$$F_i = \frac{0}{D_{NO}}$$

EC $r_2 < r < r_3$

$$\frac{D_{NO}}{r}\frac{d}{dr}\left(r\frac{dC_{NO}}{dr}\right) + R_{NO} = 0$$

$$F_i = -\frac{R_{NO_{max}}}{D_{NO}}\frac{P_{O_2}}{P_{O_2}+K_{m,eNOS}}$$

VW $r_3 < r < r_4$

$$\frac{D_{NO}}{r}\frac{d}{dr}\left(r\frac{dC_{NO}}{dr}\right) - \lambda_{vw}C_{NO} = 0$$

$$F_i = \frac{\lambda_{vw}u_i}{D_{NO}}$$

T $r_4 < r < r_5$

$$\frac{D_{NO}}{r}\frac{d}{dr}\left(r\frac{dC_{NO}}{dr}\right) - \lambda_{t}C_{NO} = 0$$

$$F_i = \frac{\lambda_{t}u_i}{D_{NO}}$$

3.1.1 NO matrix

$$A = \begin{bmatrix}
-3 & 4 & -1 & \cdots & \cdots & \cdots & 0 \\
1-a_2 & -2 & 1+a_2 & 0 & \cdots & \cdots & \vdots \\
0 & 1-a_3 & -2 & 1+a_3 & \ddots & & \vdots \\
\vdots & \ddots & \ddots & \ddots & \ddots & & \vdots \\
\vdots & & \ddots & 1-a_{n-2} & -2 & 1+a_{n-2} & 0 \\
\vdots & \cdots & \cdots & 0 & 1-a_{n-1} & -2 & 1+a_{n-1} \\
0 & \cdots & \cdots & \cdots & 1 & -4 & 3
\end{bmatrix}, \tilde{\mathbf{u}} = \begin{bmatrix} u_1 \\ u_2 \\ u_3 \\ \vdots \\ u_i \\ \vdots \\ u_{n-1} \\ u_n \end{bmatrix}, F = \begin{bmatrix} 0 \\ h^2F_2 \\ h^2F_3 \\ \vdots \\ h^2F_i \\ \vdots \\ h^2F_{n-1} \\ 0 \end{bmatrix} \tag{19}$$

3.2 Oxygen

RBC core $r_0 < r < r_1$

$$P_{O_2} = 70$$

CFL $r_1 < r < r_2$

$$\alpha \frac{D_{O_2}}{r} \frac{d}{dr}\left(r \frac{dP_{O_2}}{dr}\right) = 0$$

$$G_i = \frac{0}{\alpha D_{O_2}}$$

EC $r_2 < r < r_3$

$$\alpha \frac{D_{O_2}}{r} \frac{d}{dr}\left(r \frac{dP_{O_2}}{dr}\right) - R_{NO} = 0$$

$$G_i = \frac{R_{NO_{max}}}{\alpha D_{O_2}} \frac{P_{O_2}}{P_{O_2} + K_{m,eNOS}}$$

VW $r_3 < r < r_4$

$$\alpha \frac{D_{O_2}}{r} \frac{d}{dr}\left(r \frac{dP_{O_2}}{dr}\right) - Q_{O_2\, max\, VW} \frac{P_{O_2}}{P_{O_2} + appK_m} = 0$$

$$appK_m = K_m\left(1 + \frac{C_{NO}}{C_{ref}}\right) \tag{20}$$

$$G_i = \frac{Q_{O_2\, max\, VW}}{\alpha D_{O_2}} \frac{P_{O_2}}{P_{O_2} + K_m\left(1 + \frac{u_i}{C_{ref}}\right)}$$

T $r_4 < r < r_5$

$$\alpha \frac{D_{O_2}}{r} \frac{d}{dr}\left(r \frac{dP_{O_2}}{dr}\right) - Q_{O_2\, max\, T} \frac{P_{O_2}}{P_{O_2} + appK_m} = 0$$

$$appK_m = K_m\left(1 + \frac{C_{NO}}{C_{ref}}\right) \tag{21}$$

$$G_i = \frac{Q_{O_2\, max\, T}}{\alpha D_{O_2}} \frac{P_{O_2}}{P_{O_2} + K_m\left(1 + \frac{u_i}{C_{ref}}\right)}$$

3.2.1 O_2 matrix

$$A = \begin{bmatrix} 1 & 0 & 0 & \cdots & \cdots & \cdots & 0 \\ 1 - a_{r_1+1} & -2 & 1 + a_{r_1+1} & 0 & \cdots & \cdots & 0 \\ 0 & 1 - a_{r_1+2} & -2 & 1 + a_{r_1+2} & \ddots & & \vdots \\ \vdots & \ddots & \ddots & \ddots & \ddots & & \vdots \\ \vdots & & \ddots & 1 - a_{n-2} & -2 & 1 + a_{n-2} & 0 \\ \vdots & \cdots & \cdots & 0 & 1 - a_{n-1} & -2 & 1 + a_{n-1} \\ 0 & \cdots & \cdots & \cdots & 1 & -4 & 3 \end{bmatrix}, \tilde{\mathbf{v}} = \begin{bmatrix} v_{r_1} \\ v_{r_1+1} \\ \vdots \\ v_i \\ \vdots \\ v_{n-1} \\ v_n \end{bmatrix}, B = \begin{bmatrix} 70 \\ h^2 G_{r_1+1} \\ \vdots \\ h^2 G_i \\ \vdots \\ h^2 G_{n-1} \\ 0 \end{bmatrix} \tag{22}$$

4 Velocity profile

4.1 Axisymmetric

$$\frac{\dot{\gamma}}{\frac{P_g R_1}{4\mu_{\infty m}}} = \frac{\mu_{\infty m}}{\mu_\infty}[r - \alpha(1+q)\sqrt{r} + \alpha^2 + (\sqrt{r} - \alpha)C_r] \tag{23}$$

$$-\frac{dV}{dR} = \frac{P_g R_1 \mu_{\infty m}}{4\mu_{\infty m}\mu_\infty}[r - \alpha(1+q)\sqrt{r} + \alpha^2 + (\sqrt{r} - \alpha)C_r] \tag{24}$$

where

$$\begin{aligned} \alpha &= \frac{\sqrt{\tau_0} + \sqrt{\mu_\infty \Lambda}}{\sqrt{\lambda \tau_w}} \\ q &= \frac{\sqrt{\tau_0} - \sqrt{\mu_\infty \Lambda}}{\sqrt{\tau_0} + \sqrt{\mu_\infty \Lambda}} \\ C_r &= \sqrt{r - 2\alpha q\sqrt{r} + \alpha^2} \end{aligned} \tag{25}$$

where

$$\begin{aligned} \mu_\infty &= \frac{\mu_p}{(1 - \frac{1}{2}k_\infty H)^2} \\ \Lambda &= \gamma_c \left(\frac{1 - \frac{1}{2}k_0 H}{1 - \frac{1}{2}k_\infty H}\right)^2 \\ \tau_0 &= \mu_p \gamma_c \frac{\left[\frac{1}{2}H(k_0 - k_\infty)\right]^2}{\left(1 - \frac{1}{2}k_\infty H\right)^4} \end{aligned} \tag{26}$$

where

$$\begin{aligned} k_0 &= \exp\{3.874 + H[-10.41 + H(13.8 - 6.738H)]\} \\ k_0 &= 0.275363 + \frac{2.0}{0.100158 + H} \\ k_\infty &= \exp\{1.3435 + H[-2.803 + H(2.711 - 0.6479H)]\} \\ \gamma_c &= \exp\{-6.1508 + H[27.923 + H(-25.6 + 3.697H)]\} \end{aligned} \tag{27}$$

5 Physiological parameters

Table 1: Systemic parameters and NCFL widths [4]

			NCFL (%)	
Aggregating conditions	Hct (%)	Diameter (μm)	Outer	Inner
Non	44.0 ± 1.6	52.5 ± 4.7	14.4 ± 2.1	11.1 ± 1.1
Normal	42.8 ± 1.7	50.0 ± 4.7	21.3 ± 3.4	13.5 ± 1.2
Hyper	42.2 ± 1.6	51.8 ± 4.4	23.6 ± 2.7	15.3 ± 1.7

5.1 CFL widths from mass conservation

Hematocrit measures proportion of volume of red blood cells (RBC) to total blood volume (RBC and plasma) [5]. Cell volume fraction or tube hematocrit H_t is calculated as:

$$H_t = \frac{N_c V_{eff}}{V_t} \tag{28}$$

where N_c is the number of RBCs in the tube volume $V_t = \pi R^2 L$, R is the tube radius, and L is the tube length [6].

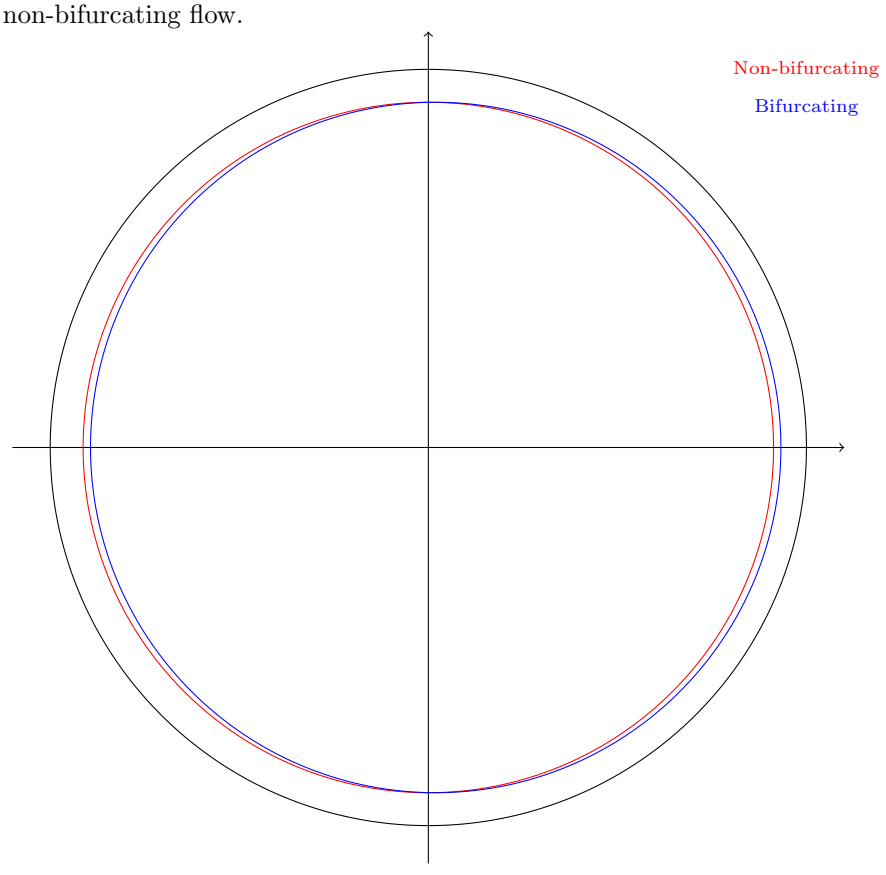
An empirical relation between H_t and H_d is given by:

$$\frac{H_t}{H_d} = H_d + (1 - H_d)\left(1 + 1.7e^{-0.35D} - 0.6e^{-0.01D}\right) \tag{29}$$

where D is the tube diameter in micrometers, and discharge hematocrit H_d is equal to systemic hematocrit [7].

Since systemic hematocrit in both cases (non-bifurcating and bifurcating flow) is the same, H_t is the same according to Eq. 29. Since V_t is the same due to constant vessel diameter, N_c assumed (?) to be the same, V_{eff} must be the same (Eq. 28).

Ignoring gravity effect and assuming symmetry, we need to find a egg / ellipse shaped graph with the same area as the circle in non-bifurcating flow.



Assumptions: Define normal CFL width as mean of inner and outer CFL width.

$$NCFL_{normal} = \frac{NCFL_{inner} + NCFL_{outer}}{2} \tag{30}$$

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