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

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

Central difference

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

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 $a_i = \frac{h}{2}P_i$

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

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

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

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 $i = end$

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

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

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

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

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 $r_3 < r < r_4$

$$\begin{gathered} \alpha \frac{D_{O_2}}{r} \frac{d}{dr} \left(r \frac{dP_{O_2}}{dr} \right) - Q_{O_2\, max\, VW} \frac{P_{O_2}}{P_{O_2} + appK_m} = 0 \\ appK_m = K_m \left(1 + \frac{C_{NO}}{C_{ref}} \right) \\ G_i = \frac{Q_{O_2\, max\, VW}}{\alpha D_{O_2}} \frac{P_{O_2}}{P_{O_2} + K_m \left(1 + \frac{u_i}{C_{ref}} \right)} \end{gathered} \tag{20}$$

T $r_4 < r < r_5$

$$\begin{gathered} \alpha \frac{D_{O_2}}{r} \frac{d}{dr} \left(r \frac{dP_{O_2}}{dr} \right) - Q_{O_2\, max\, T} \frac{P_{O_2}}{P_{O_2} + appK_m} = 0 \\ appK_m = K_m \left(1 + \frac{C_{NO}}{C_{ref}} \right) \\ G_i = \frac{Q_{O_2\, max\, T}}{\alpha D_{O_2}} \frac{P_{O_2}}{P_{O_2} + K_m \left(1 + \frac{u_i}{C_{ref}} \right)} \end{gathered} \tag{21}$$

3.2.1 $\mathbf{O_2}$ 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 Parameter manipulation

I_e is the second invariant of the rate of deformation tensor.

Velocity gradients:

$$\mathbf{L}_{ij} = \frac{\partial \mathbf{v}}{\partial \mathbf{x}} = \begin{bmatrix} \frac{\partial u}{\partial x} & \frac{\partial u}{\partial y} & \frac{\partial u}{\partial z} \\ \frac{\partial v}{\partial x} & \frac{\partial v}{\partial y} & \frac{\partial v}{\partial z} \\ \frac{\partial w}{\partial x} & \frac{\partial w}{\partial y} & \frac{\partial w}{\partial z} \end{bmatrix} = \begin{bmatrix} 0 & 0 & 0 \\ \frac{\partial v}{\partial x} & 0 & \frac{\partial v}{\partial z} \\ 0 & 0 & 0 \end{bmatrix} \tag{23}$$

as $u = 0, w = 0, \frac{\partial v}{\partial y} = 0$.

Rate of deformation tensor:

$$\mathbf{D}_{ij} = \frac{1}{2}(\mathbf{L}_{ij} + \mathbf{L}_{ij}^T) = \frac{1}{2}\left(\begin{bmatrix} 0 & 0 & 0 \\ \frac{\partial v}{\partial x} & 0 & \frac{\partial v}{\partial z} \\ 0 & 0 & 0 \end{bmatrix} + \begin{bmatrix} 0 & \frac{\partial v}{\partial x} & 0 \\ 0 & 0 & 0 \\ 0 & \frac{\partial v}{\partial z} & 0 \end{bmatrix} \right) = \frac{1}{2} \begin{bmatrix} 0 & \frac{\partial v}{\partial x} & 0 \\ \frac{\partial v}{\partial x} & 0 & \frac{\partial v}{\partial z} \\ 0 & \frac{\partial v}{\partial z} & 0 \end{bmatrix} \tag{24}$$

Second invariant of the rate of deformation tensor

$$\begin{aligned} I_e &= \frac{1}{2}[(\operatorname{Tr} \mathbf{D}_{ij})^2 - \operatorname{Tr}(\mathbf{D}_{ij}^2)] \\ &= D_{11}D_{22} + D_{22}D_{33} + D_{11}D_{33} - D_{12}D_{21} - D_{23}32 - D_{13}31 \\ &= 0 + 0 + 0 - \frac{1}{4}\left(\frac{\partial v}{\partial x}\right)^2 - \frac{1}{4}\left(\frac{\partial v}{\partial z}\right)^2 - 0 \\ &= -\frac{1}{4}\left[\left(\frac{\partial v}{\partial x}\right)^2 + \left(\frac{\partial v}{\partial z}\right)^2\right] \end{aligned} \tag{25}$$

Conversion from Cartesian derivatives to cylindrical derivatives [4]

$$\begin{aligned} I_e &= -\frac{1}{4}\left[\left(\frac{\partial v}{\partial x}\right)^2 + \left(\frac{\partial v}{\partial z}\right)^2\right] \\ &= -\frac{1}{4}\left[(\cos^2\theta + \sin^2\theta)\left(\frac{\partial v}{\partial r}\right)^2\right] \\ &= -\frac{1}{4}\left(\frac{\partial v}{\partial r}\right)^2 \\ &= -\frac{1}{4}\dot{\gamma}^2 \end{aligned} \tag{26}$$

4.2 Axisymmetric

$$\frac{\dot{\gamma}}{\frac{P_g R_1}{4\mu_{\infty m}}} = \frac{\mu_{\infty m}}{\mu_\infty}[r - \alpha(1+q)\sqrt{r} + \alpha^2 + (\sqrt{r} - \alpha)C_r] \tag{27}$$

$$-\frac{dV}{dR} = \frac{P_g R_1 \mu_{\infty m}}{4\mu_{\infty m}\mu_\infty}[r - \alpha(1+q)\sqrt{r} + \alpha^2 + (\sqrt{r} - \alpha)C_r] \tag{28}$$

where

$$\begin{aligned} \alpha &= \frac{\sqrt{\tau_0} + \sqrt{\mu_\infty \Lambda}}{\sqrt{\lambda \tau_w}} \\ q &= \frac{\sqrt{\tau_0} - \sqrt{\mu_\infty \Lambda}}{\sqrt{\tau_0} + \sqrt{\mu_\infty \Lambda}} \\ C_r &= \sqrt{r - 2\alpha q\sqrt{r} + \alpha^2} \end{aligned} \tag{29}$$

where

$$\begin{aligned} \mu_\infty &= \frac{\mu_p}{(1 - \frac{1}{2}k_\infty H)^2} \\ \Lambda &= \gamma_c \left(\frac{1 - \frac{1}{2}k_0 H}{1 - \frac{1}{2}k_\infty H}\right)^2 \\ \tau_0 &= \mu_p \gamma_c \frac{\left[\frac{1}{2}H(k_0 - k_\infty)\right]^2}{\left(1 - \frac{1}{2}k_\infty H\right)^4} \end{aligned} \tag{30}$$

where

$$\begin{aligned} k_0 &= 0.275363 + \frac{2.0}{0.100158 + H} \\ k_\infty &= \exp\{1.3435 + H[-2.803 + H(2.711 - 0.6479H)]\} \\ \gamma_c &= \exp\{-6.1508 + H[27.923 + H(-25.6 + 3.697H)]\} \end{aligned} \tag{31}$$

5 Physiological parameters

Table 1: Systemic parameters and NCFL widths [5]

			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) [6]. Cell volume fraction or tube hematocrit H_t is calculated as:

$$H_t = \frac{N_c V_{eff}}{V_t} \tag{32}$$

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 [7].

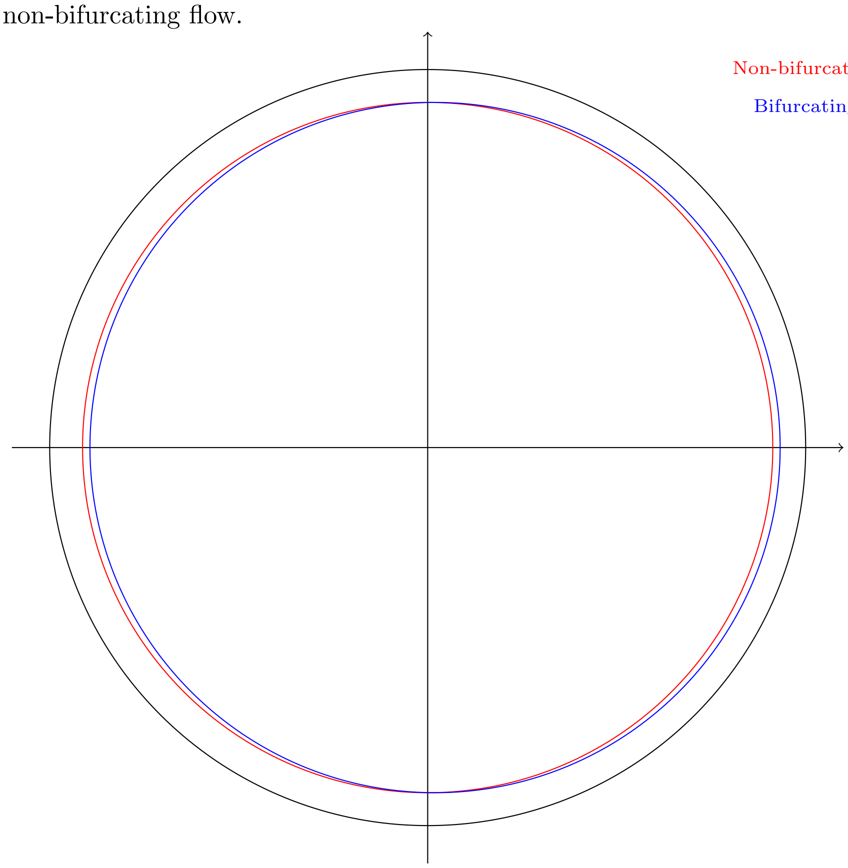
An empirical relation between H_t and H_d is given by:

$$\frac{H_t}{H_d} = H_d + (1 - H_d)\left(1 + 1.7e^{-0.35D} - 0.6e^{-0.01D}\right) \tag{33}$$

where D is the tube diameter in micrometers, and discharge hematocrit H_d is equal to systemic hematocrit [8].

Since systemic hematocrit in both cases (non-bifurcating and bifurcating flow) is the same, H_t is the same according to Eq. 33. 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. 32).

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.

$$NCFL_{normal} = \frac{NCFL_{inner} + NCFL_{outer}}{2} \tag{34}$$

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