

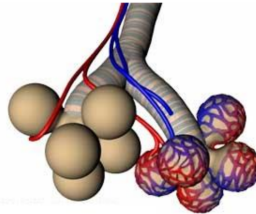
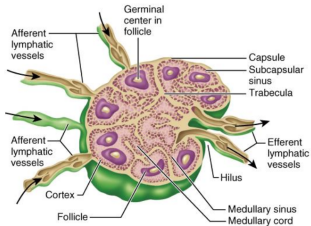
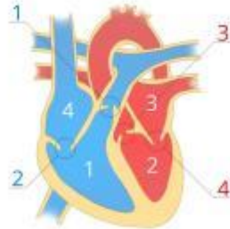
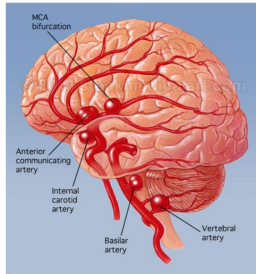
Multiscale modeling of the blood flow in the cardiovascular system

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Biological fluids flow



1D and 0D-like objects in physiology



Figure: Heart chambers, aneurysms, lymphatic nodes, alveoli

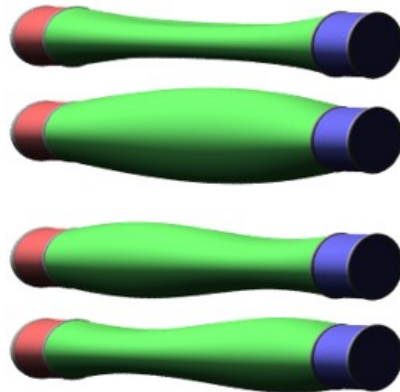


Figure: Arteries and veins, lymphatic vessels, bronchioles

- ① Large arteries (3D, dynamic)
 - Aorta
 - Carotid sinus
 - ...
- ② Large and medium vessels ($L \gg d$) (1D, dynamic)
 - ① Arteries
 - ② Superficial veins
 - ③ Deep veins
 - ④ Virtual effective vessels
- ③ Heart chambers, dumbbell shaped aneurysm (0D, dynamic)
- ④ Microcirculation (0D, static)

	1D	0D
Dynamic	✓	✓
Static	✗	✓

1D haemodynamics

$$(S, u) \quad \text{vs.} \quad (S, Q)$$

3D Navier-Stokes equations

$$\operatorname{div} \mathbf{u} = 0$$

$$\frac{\partial u_x}{\partial t} + \operatorname{div} (u_x \mathbf{u}) + \frac{1}{\rho} \frac{\partial P}{\partial x} - \nu \Delta u_x = 0$$

Assumptions:

$$u_x(t, x, y, z) = \bar{u}(t) \xi(x, y, z), \quad u_r(t, R, x) = \frac{\partial \eta}{\partial t}(t, x)$$

$$\xi(x, y, z) = \frac{\gamma + 2}{\gamma} \left(1 - \left(\frac{y^2 + z^2}{R^2(t, x)} \right)^{\gamma/2} \right), \quad y^2 + z^2 \leq R^2(t, x).$$

1D haemodynamics

$$u = \frac{1}{S} \int_{\Gamma_S} u_x ds, \quad Q|_{\Gamma_S} = \int_{\Gamma_S} u_x ds = Su$$

$$\frac{\partial S}{\partial t} + \frac{\partial Q}{\partial x} = 0$$

$$\frac{\partial Q}{\partial t} + \frac{\partial}{\partial x} \left(\alpha \frac{Q^2}{S} \right) + \frac{S}{\rho} \frac{\partial P}{\partial x} = K_r u,$$

$$K_r = -2\pi (\gamma + 2) \nu, \quad \alpha = \frac{1}{Su^2} \int_{\Gamma_S} u^2 ds = \frac{\gamma + 2}{\gamma + 1}$$

1D haemodynamics

Substituting $Q = Su$:

$$\frac{\partial S}{\partial t} + \frac{\partial(Su)}{\partial x} = 0$$

$$\frac{\partial u}{\partial t} + \left(\alpha - \frac{1}{2}\right) \frac{\partial u^2}{\partial x} + (\alpha - 1) \frac{u^2}{S} \frac{\partial S}{\partial x} + \frac{1}{\rho} \frac{\partial P}{\partial x} = -2\pi(\gamma + 2) \nu \frac{u}{S}$$

$$P = F(S)$$

$$P = F(S) \longrightarrow S = \hat{F}(P)$$

$$\frac{\partial F}{\partial S} > 0 \longrightarrow \frac{\partial \hat{F}}{\partial P} > 0$$

$$\frac{\partial u}{\partial t} + \left(\alpha - \frac{1}{2} \right) \frac{\partial u^2}{\partial x} + \left(1 + (\alpha - 1) \frac{\rho u^2}{S} \frac{\partial \hat{F}}{\partial P} \right) \frac{1}{\rho} \frac{\partial P}{\partial x} = \psi(u, S)$$

$$\psi = -2\pi(\gamma + 2)\nu u S^{-1}$$

1D haemodynamics

$$F(S) = P_{ext} + \rho_w c_0^2 (e^{S/S_0-1} - 1)$$

$$\hat{F} = (1 + \ln(1 + \rho_w^{-1} c_0^{-2} P)) S_0$$

$$\frac{\partial u}{\partial t} + \left(\alpha - \frac{1}{2}\right) \frac{\partial u^2}{\partial x} + (1 + \varepsilon) \frac{1}{\rho} \frac{\partial P}{\partial x} = \psi,$$

$$\varepsilon = (\alpha - 1) \frac{\rho}{\rho_w} \frac{S_0}{S} \left(\frac{u}{c_0}\right)^2 \frac{1}{1 + \rho_w^{-1} c_0^{-2} P}.$$

1D haemodynamics

$$\varepsilon = (\alpha - 1) \frac{\rho}{\rho_w} \frac{S_0}{S} \left(\frac{u}{c_0} \right)^2 \frac{1}{1 + \rho_w^{-1} c_0^{-2} P}.$$

$$\gamma \geq 2 \longrightarrow 0 < \alpha = \frac{\gamma + 2}{\gamma + 1} \leq \frac{4}{3}$$

$$\rho < \rho_w$$

$$S > S_0$$

$$u < 0.5 \text{ m/s} \longrightarrow \varepsilon < 5 \cdot 10^{-3}$$

$$c_0 > 4 \text{ m/s}$$

1D haemodynamics

$$\frac{\partial u}{\partial t} + \frac{\partial}{\partial x} \left(\left(\alpha - \frac{1}{2} \right) u^2 + \frac{P}{\rho} \right) = \psi$$

- $\gamma = 9, \alpha = 1.1 \longrightarrow \varepsilon < 1.6 \cdot 10^{-3}$
- $\lim_{\alpha \rightarrow 1} \varepsilon = 0$

$$\frac{\partial u}{\partial t} + \frac{\partial}{\partial x} \left(\frac{u^2}{2} + \frac{P}{\rho} \right) = \psi$$

1D Blood flow in a single large vessel

$$\frac{\partial \mathbf{V}}{\partial t} + \frac{\partial \mathbf{F}(\mathbf{V})}{\partial x} = \mathbf{G}(t, x, \mathbf{V}), \quad \mathbf{V} = \begin{pmatrix} S \\ u \end{pmatrix}, \quad \mathbf{F} = \begin{pmatrix} Su \\ \frac{u^2}{2} + \frac{P(t, S)}{\rho} \end{pmatrix}$$

$\mathbf{G}$ — mass and momentum gain or loss (e.g. blood loss due to vascular damage, transfusion; friction force, inertial forces)

1D haemodynamics in a tube with elliptic cross-section

$$\xi_{ab}(y, z) = \frac{\gamma + 2}{\gamma} \left(1 - \left(\frac{y^2}{a^2} + \frac{z^2}{b^2} \right)^{\gamma/2} \right), \quad \frac{y^2}{a^2} + \frac{z^2}{b^2} \leq 1.$$

$$u(t, x, y, z) = \bar{u}(t) \xi_{ab}(x, y, z).$$

α remains the same!

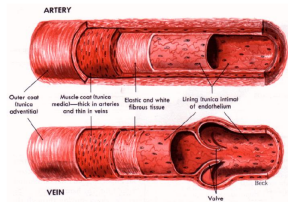
$$K_r = -\pi\nu(\gamma + 2) \frac{a^2 + b^2}{ab}.$$

Remaining aspects

- ① Elasticity of the vessel's wall
- ② Boundary conditions at the junctions of the vessels
 - ① Mass conservation
 - ② Compatibility conditions along outgoing characteristics
 - ③ Some other flow conditions (Bernoulli theorem, Hagen-Poiseuille pressure drop, pressure continuity)

Elasticity of the vessel's wall

1) Vessel wall elasticity

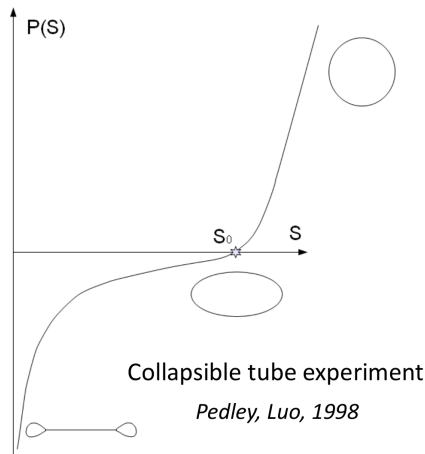


Analytic approximation

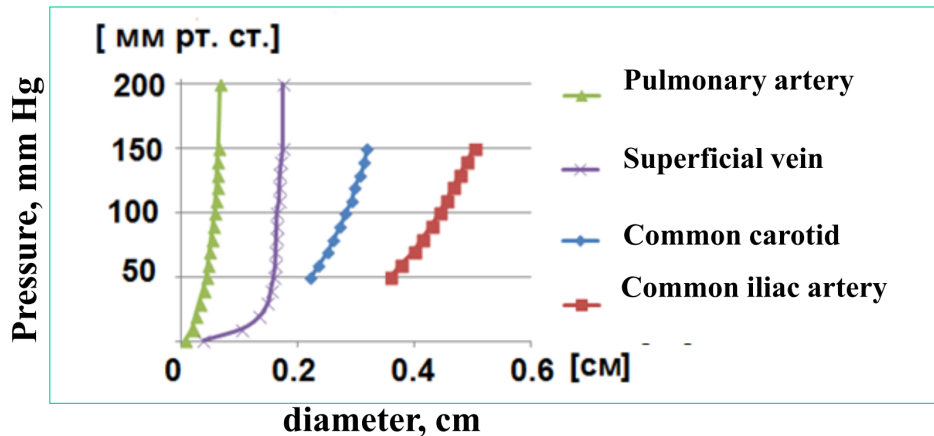
$$P(S) = P^{ext}(t, x) + \rho c^2 f(S)$$

$$f(S) = \begin{cases} \exp(S/S_0 - 1) - 1, & S > S_0 \\ \ln(S/S_0), & S \leq S_0 \end{cases}$$

Kholodov, 2001



Elasticity of the vessel's wall: clinical data



Elasticity of the vessel's wall: review and comparison

Quarteroni, Formaggia

$$f(S) \sim \sqrt{\chi} - 1$$

$$P(S) = P^{ext}(t, x) + \rho c^2 f(S)$$

Olufsen, Peskin

$$f(S) \sim 1 - 1/\sqrt{\chi}$$

$$\chi = S/S_0$$

Favorskii, Mukhin

$$f(S) \sim \chi$$

Toro, Mueller

$$f(S) \sim (\chi)^m - (\chi)^n, m > 0, n \in (-2, 0)$$

Pedley, Luo

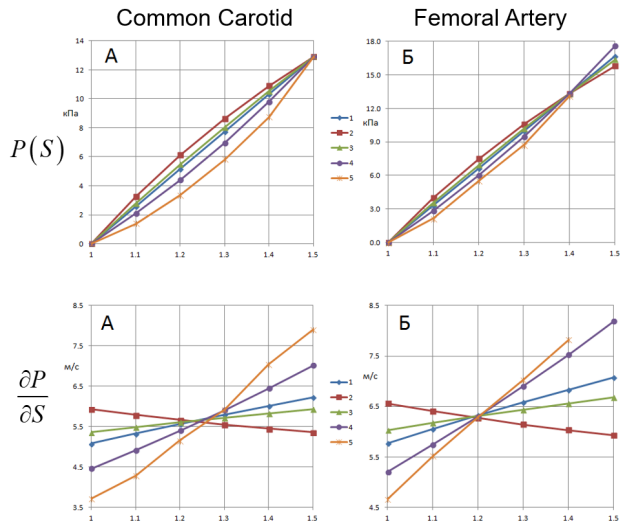
$$f(S) \sim \begin{cases} \chi - 1, \chi > 1 \\ 1 - (\chi)^{-\frac{3}{2}}, \chi \leq 1 \end{cases}$$

Kholodov

$$f(S) = \begin{cases} \exp(\chi - 1) - 1, \chi > 1 \\ \ln(\chi), \chi \leq 1 \end{cases}$$

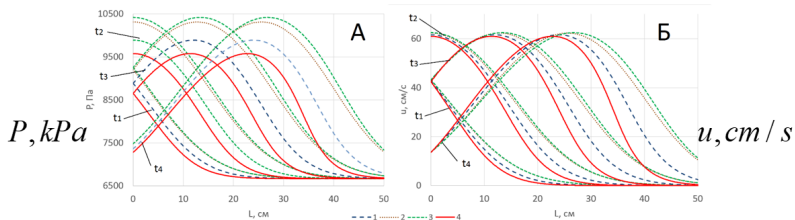
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Elasticity of the vessel's wall: review and comparison

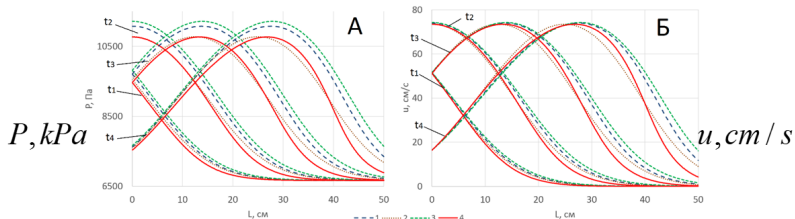


Elasticity of the vessel's wall: review and comparison

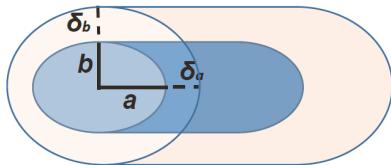
Common Carotid



Femoral Artery



Elasticity of the elliptic tube



Strains along the major and minor axes δ_a and δ_b are¹

$$\delta_a = \frac{C_a a^4}{D} P, \quad \delta_b = \frac{C_b a^4}{D} P$$

D — bending stiffness, $k = \sqrt{1 - \frac{b^2}{a^2}}$ — eccentricity

¹Avery R.T., Tidrick G.A. Elliptical Vacuum Chamber Stress and Deflections, IEEE Transactions on Nuclear Science 1969, 16(3), 952–953.

Elasticity of the elliptic tube

$$C_a = K_1 \left(\frac{b^2}{2a^2} + \frac{b}{2ka} \arcsin k \right) - \frac{1 - 3k^2 + 2k^4}{16} + \frac{b}{16ka} \arcsin k,$$

$$C_b = \frac{K_1}{2} + \frac{3k^2 - 1}{16} + \frac{b^2 (8K_1 + 1 + 3k^3)}{32ka^2} \ln \frac{1 + k}{1 - k},$$

Elasticity of the elliptic tube

$$S = \pi(a + \delta_a)(b + \delta_b) = \pi a \left(b + (a + b) \frac{C_a a^3}{D} P + \frac{C_a C_b a^7}{D^2} P^2 \right) = \hat{F}(P, a, b)$$

$$P = \frac{-B + \sqrt{B^2 - 4AC}}{2A} = F(S, a, b)$$

$$A = \pi \frac{C_a C_b a^8}{D^2} > 0, B = \pi (a + b) \frac{C_a a^4}{D} > 0, C = \pi ab - S$$

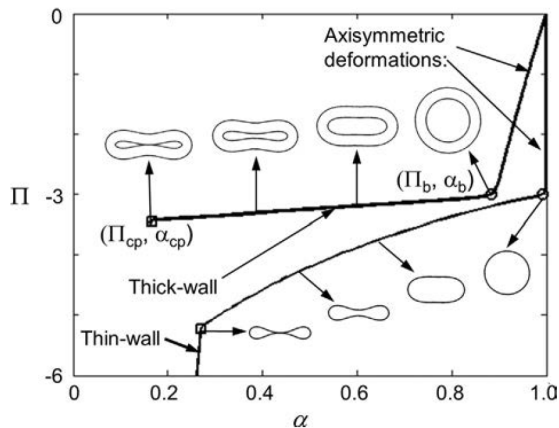
$$P > 0 \text{ for } S > \pi ab \text{ and } P < 0 \text{ for } \pi ab - (a + b)^2 \frac{C_a}{4C_b} < S < \pi ab.$$

Elasticity of the elliptic tube

$$\varepsilon = (\alpha - 1) \frac{\rho u^2}{S} \frac{\partial \hat{F}}{\partial P}$$

Circular cross-section	Elliptic cross-section
$\frac{\partial \hat{F}}{\partial P} = \frac{\rho_w^{-1} c_0^{-2} S_0}{1 + \rho_w^{-1} c_0^{-2} P}$	$\frac{\partial \hat{F}}{\partial P} = \pi \frac{C_a a^4}{D} \left(a + b + \frac{C_b a^4}{D} P \right)$

Elasticity of the elliptic tube ²



²P. Kozlovsky, U. Zaretsky, A. Jaffa, D. Elad. General tube law for collapsible thin and thickwall tubes. Journal of Biomechanics, 2014, 10.1016/j.jbiomech.2014.04.033

$$u < \sqrt{\frac{S}{\rho} \frac{\partial P}{\partial S}}$$

Circular cross-section	Elliptic cross-section
$\frac{\partial P}{\partial S} = \frac{\rho_w c_0^2}{S_0} e^{\frac{S}{S_0} - 1}$	$\frac{\partial P}{\partial S} = \frac{D}{2\pi a^4} \sqrt{C_a C_b \left(\frac{(a+b)^2}{4} \frac{C_a}{C_b} - ab \right) + \frac{S}{S_0}}$

Boundary conditions

2) Mass conservation

$$\sum_{k=k_1, \dots, k_{M_l}} \varepsilon_k^l u_k(t, \tilde{x}_k) S_k(t, \tilde{x}_k) = 0, \quad \tilde{x}_k = 0, L_k, \varepsilon_k^l = \pm 1$$

3) Compatibility condition along outgoing characteristic

$$\mathbf{w}_{ki} \cdot \left(\frac{\partial \mathbf{V}_k}{\partial t} + \lambda_{ki} \frac{\partial \mathbf{V}_k}{\partial x} \right) = \mathbf{0}, \quad i = 1 \text{ or } 2$$

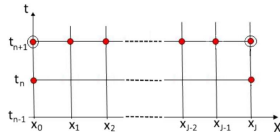
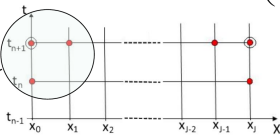
λ_{ki} - eigenvalues, $\mathbf{w}_{ki}$ - eigenvectors of $\mathbf{J} = \frac{\partial \mathbf{F}}{\partial \mathbf{V}}$

$$\lambda_{ki} = u_k + (-1)^i \sqrt{\frac{S_k}{\rho} \frac{\partial p_k}{\partial S}} \quad \mathbf{w}_{ki} = \left\{ \sqrt{\frac{1}{\rho S_k} \frac{\partial p_k}{\partial S}}, (-1)^i \right\}$$

$$|u_k| < \sqrt{\frac{S_k}{\rho} \frac{\partial p_k}{\partial S}} \quad k = k_1, k_2, \dots, k_{M_l}, \quad \tilde{x}_k = 0, L_k, \varepsilon_k^l = \pm 1$$

Boundary conditions

$$\mathbf{w}_{ki} \cdot \left(\frac{\partial \mathbf{V}_k}{\partial t} + \lambda_{ki} \frac{\partial \mathbf{V}_k}{\partial x} \right) = \mathbf{0}, i = 1 \text{ or } 2$$



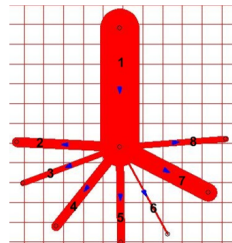
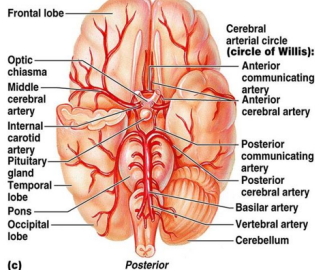
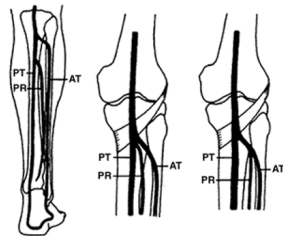
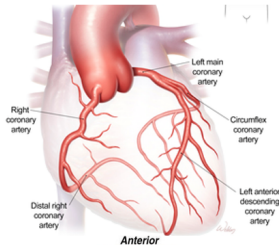
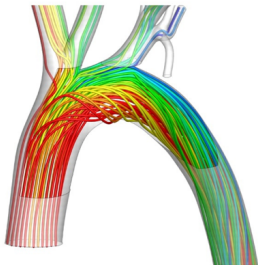
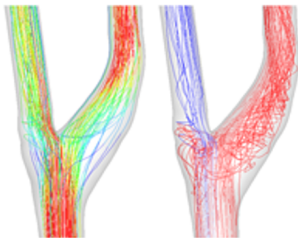
$$u_k(t_{n+1}, \tilde{x}_k) = \alpha_k^n S_k(t_{n+1}, \tilde{x}_k) + \beta_k^n$$

$$\alpha_k^n = \sqrt{\frac{1}{\rho S_k^{n+1}} \frac{\partial p_k}{\partial S}} = w_0^n$$

$$\beta_k^n = \frac{w_0^n (\sigma S_1^{n+1} - S_0^n) + u_0^n - \sigma u_1^{n+1}}{1 - \sigma}$$

$$k = k_1, k_2, \dots, k_{M_l}, \tilde{x}_k = 0, L_k, \varepsilon_k^l = \pm 1 \quad \sigma = \frac{\lambda \tau}{h}$$

Boundary conditions



Boundary conditions

4.1) Bernoulli theorem

Momentum at the junction: steady flow, neglect friction

$$\cancel{\frac{\partial u}{\partial t}} + \frac{\partial}{\partial x} \left(\frac{u^2}{2} + \frac{p}{\rho} \right) = \cancel{f_{fr}(S, u)} \longrightarrow \frac{\partial}{\partial x} \left(\frac{u^2}{2} + \frac{p}{\rho} \right) = 0$$

4.2) Hagen-Poiseuille pressure drop condition

High vorticity, non-stationary flow,
complex geometry, $Re \gg 1$

$\longrightarrow$ ~~3.1)~~

4.3) Pressure continuity condition

Medium/small vessels,

$$u_{k_l} \approx u_{k_m}, Re \approx 1$$

$$4.1) \longrightarrow \frac{\partial}{\partial x} \left(\cancel{\frac{u^2}{2}} + \frac{p}{\rho} \right) = 0$$

Boundary conditions

4.1) Bernoulli theorem

$$\frac{u_k^2(t, \tilde{x}_k)}{2} + \frac{p_k(S(t, \tilde{x}_k))}{\rho} = I^l, \quad k = k_1, k_2, \dots, k_{M_l}$$

4.2) Hagen-Poiseuille pressure drop condition

$$p_k(S_k(t, \tilde{x}_k)) - p_{node}^l = \varepsilon_k R_k^l S_k(t, \tilde{x}_k) u_k(t, \tilde{x}_k)$$

Ventricles to aorta/pulmonary artery connections

4.3) Pressure continuity condition

$$p_k(S_k(t, \tilde{x}_k)) = p_{node}^l$$

Veins to auricles connections

$$k = k_1, k_2, \dots, k_{M_l}, \tilde{x}_k = 0, L_k, \varepsilon_k^l = \pm 1$$

Boundary conditions

$$\mathbf{Q}(\mathbf{S}) = \mathbf{A}\mathbf{S}^H + \mathbf{B}\mathbf{S} + \mathbf{R}\mathbf{P}(\mathbf{S}) + \mathbf{D} = \mathbf{0}$$

$$\mathbf{S} = \left\{ S_{k_m} \right\}_{m=1}^{M_l}, \mathbf{S}^H = \left\{ S_{k_m}^2 \right\}_{m=1}^{M_l}, \mathbf{P}(\mathbf{S}) = \left\{ p_{k_m}(S_{k_m}) \right\}_{m=1}^{M_l}$$

4.1) Bernoulli theorem

$$\begin{aligned} A_{mm} &= \delta \alpha_{k_m}, A_{mn} = 0, m \neq n & \delta &= \sum_{m=1}^{M_l} \frac{\varepsilon_{k_m}}{\alpha_{k_m}} \\ B_{mm} &= \frac{\beta_{k_m}}{2\alpha_{k_m}} \left(\delta - \frac{\varepsilon_{k_m}}{2\alpha_{k_m}} \right), B_{mn} = -\varepsilon_{k_n} \beta_{k_n}, m \neq n \\ R_{mm} &= 2 \left(\delta - \frac{1}{\alpha_{k_m}} \right), R_{mn} = -\frac{2}{\alpha_{k_n}}, m \neq n & D_m &= \beta_{k_m}^2 \left(\delta - \frac{\varepsilon_{k_m}}{\alpha_{k_m}} \right) \\ & & & m, n = 1, \dots, M_l \end{aligned}$$

Boundary conditions

$$\mathbf{Q}(\mathbf{S}) = \mathbf{A}\mathbf{S}^{\mathbf{II}} + \mathbf{B}\mathbf{S} + \mathbf{R}\mathbf{P}(S) + \mathbf{D} = \mathbf{0}$$

4.2) Hagen-Poiseuille pressure drop condition

$$A_{mm} = \Delta \varepsilon_{k_m} \alpha_{k_m}, A_{mn} = 0, m \neq n$$

$$\Delta = \sum_{i=1}^{M_l} \prod_{\substack{j=1 \\ j \neq i}}^{M_l} R_{kj}^l$$

$$B_{mm} = \Delta \varepsilon_{k_m} \beta_{k_m}, B_{mn} = 0, m \neq n$$

$$R_{mm} = - \sum_{\substack{n=1 \\ n \neq m}}^{M_l} \prod_{\substack{p=1 \\ p \neq m \\ p \neq n}}^{M_l} R_{kp}^l, R_{mn} = \prod_{\substack{p=1 \\ p \neq m \\ p \neq n}}^{M_l} R_{kp}^l, m \neq n \quad D_m = 0$$

$$m, n = 1, \dots, M_l$$

Boundary conditions

$$\mathbf{Q}(\mathbf{S}) = \mathbf{A}\mathbf{S}^{II} + \mathbf{B}\mathbf{S} + \mathbf{R}\mathbf{P}(S) + \mathbf{D} = \mathbf{0}$$

4.3) Pressure continuity

$$S_{k_m} = \tilde{p}_{k_m}(p_{node}^l) = \begin{cases} S_{k_0} \left(1 + \ln \left(1 + \frac{p_{node}^l}{\rho c^2} \right) \right), & p_{node}^l > \rho c^2 (e - 1) \\ S_{k_0} \exp \left(\frac{p_{node}^l}{\rho c^2} \right), & p_{node}^l < \rho c^2 (e - 1) \end{cases}$$

$$\sum_{k=k_1, \dots, k_{M_l}} \varepsilon_k^l \left(\alpha_k \tilde{p}_k^2(p_{node}^l) + \beta_k \tilde{p}_k(p_{node}^l) \right) = 0$$

$$m, n = 1, \dots, M_l$$

Boundary conditions

$$\mathbf{Q}(\mathbf{S}) = \mathbf{A}\mathbf{S}'' + \mathbf{B}\mathbf{S} + \mathbf{R}\mathbf{P}(S) + \mathbf{D} = \mathbf{0}$$

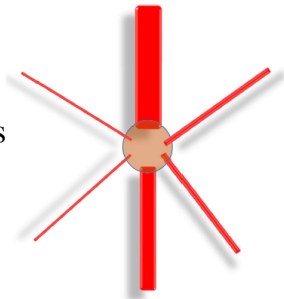
$$\mathbf{S}^{r+1} = \mathbf{S}^r - \mathbf{J}^{-1}(\mathbf{S}^r) \mathbf{Q}(\mathbf{S}^r), \mathbf{J}(\mathbf{S}) = \left\{ \frac{\partial Q_m}{\partial S_n} \right\}$$

✓ Computational complexity

$$O\left((2M_l + 1)^3\right) \rightarrow O\left(M_l^3\right) \approx 10 \text{ times}$$

✓ Convergence improved

✓ Stable for complex junctions



	1D	0D
Dynamic	✓	✓
Static	✗	✓

Spatially averaged (0D) dynamic model of blood flow

Let $\Delta x \approx l, V = lS$

$$\frac{\partial Q}{\partial t} + \frac{1}{\Delta x} \Delta \left(\alpha \frac{Q^2}{S} \right) + \frac{S}{\rho} \frac{\Delta P}{\Delta x} = K_r u \quad \Big| \times \frac{\rho \Delta x}{S}$$

$$\rho \frac{\Delta x}{S} \frac{\partial Q}{\partial t} + \cancel{\frac{\rho}{S} \Delta \left(\alpha \frac{Q^2}{S} \right)} - \rho K_r \frac{\Delta x}{S^2} Q + \Delta P = 0$$

$$\rho \frac{l^2}{V} \frac{dQ}{dt} - \rho K_r \frac{l^3}{V^2} Q + \Delta P = 0$$

Spatially averaged (0D) dynamic model of blood flow

$$\frac{\rho l^2}{V} \frac{dQ}{dt} - \frac{\rho l^3 K_r}{V^2} Q + \Delta P = 0$$

$$I \frac{d^2 V}{dt^2} + R_h \frac{dV}{dt} + \Delta P = 0$$

$$I = \frac{\rho l^2}{V}, \quad R_h = 2\pi\nu(\gamma + 2) \frac{\rho l^3}{V^2}$$

Spatially averaged (0D) dynamic model of blood flow

$$I \frac{d^2 V}{dt^2} + R_h \frac{dV}{dt} + \Delta P = 0$$

$$\Delta P = P(V) - P_{ext} - P_{ch}$$

Variable elasticity model³: $P(V) = P_0 + E(t) (V - V_0)$

External contractions (myocardium, cuff)⁴: $P_{ext} = f(t) < 0$

Viscoelasticity, rheology: $R_h = R_h(\nu(Q), P)$

³Suga H. Cardiac energetics: from E_{MAX} to pressure-volume area. Clinical and Experimental Pharmacology and Physiology 2003, 30, 580–585

⁴Kholodov A.S. Some dynamical models of multi-dimensional problems of respiratory and circulatory systems including their interaction and matter transport, in: Computer Models and Medicine Progress, Nauka, Moskva, 2001, 127–163

	1D	0D
Dynamic	✓	✓
Static	✗	✓

Spatially averaged (0D) static model of blood flow

$$\cancel{\frac{\partial Q}{\partial t}} + \cancel{\frac{\partial}{\partial x} \left(\alpha \frac{Q^2}{S} \right)} + \frac{S}{\rho} \frac{\partial P}{\partial x} = K_r u,$$

$$\frac{S}{\rho} \frac{\Delta P}{\Delta x} = K_r u \longrightarrow \Delta P = R_h Q, R_h = \frac{2\mu(\gamma + 2)}{\pi d^4} \Delta x$$

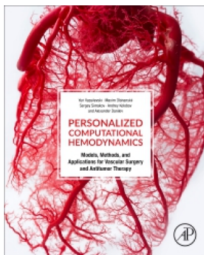
$$\sum Q = 0$$

Non-Newtonian effects for low velocities: $R_h^{-1} = \frac{\pi \kappa_1 d^4}{8\mu \Delta x} (1 + \kappa_2 Q^2)$

	1D	0D
Dynamic	✓	✓
Static	✗	✓



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