Murray’s law revisited: Quémada’s fluids and fractal trees.

Benjamin Mauroy¹ and Baptiste Moreau²

¹Laboratoire J.A. Dieudonné - UMR CNRS 7351, Université de Nice-Sophia Antipolis, Nice, France.
²Laboratoire MSC - UMR CNRS 7057, Université Paris 7 Denis Diderot, Paris, France.

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In 1926, Murray proposed the first law for the optimal design of blood vessels. He minimized the power dissipation arising from the trade-off between fluid circulation and blood maintenance. The law, based on a constant fluid viscosity, states that in the optimal configuration the fluid flow rate inside the vessel is proportional to the cube of the vessel radius, implying that wall shear stress is not dependent on the vessel radius. Murray’s law has been found to be true in blood macrocirculation, but not in microcirculation. In 2005, Alarcón et al took into account the non-monotonous dependence of viscosity on vessel radius - Fähræus - Lindqvist effect - due to phase separation effect of blood. They were able to predict correctly the behavior of wall shear stresses in microcirculation. One last crucial step remains however: to account for the dependence of blood viscosity on shear rates. In this work, we investigate how viscosity dependence on shear rate affects Murray’s law. We extended Murray’s optimal design to the whole range of Quémada’s fluids, that models pseudo-plastic fluids such as blood. Our study shows that Murray’s original law is not restricted to Newtonian fluids, it is actually universal for all Quémada’s fluid as long as there is no phase separation effect. When phase separation effect occurs, then we derive an extended version of Murray’s law. Our analyses are very general and apply to most of fluids with shear dependent rheology. Finally, we study how these extended laws affect the optimal geometries of fractal trees to mimic an idealized arterial network.

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*benjamin.mauroy@unice.fr
Introduction.

In 1926, Murray proposed the first law for the optimal design of blood vessels, based on a trade-off between the power needed to make blood circulate in the vessel and the metabolic power needed to maintain blood. The law is formulated using Poiseuille’s regime in cylindrical vessels and the optimal configuration corresponds to the blood flow rate being proportional to the cube power of the radius of the blood vessel. The well known corollary for a bifurcation states that the cube radius of the parent vessel equals the sum of the cube radii of the daughter vessels \[1\]. In the seventies, Zamir extended this law to account for bifurcation angles \[2\] and expressed Murray’s law in term of wall shear stress being constant independently on the vessel size \[3\]. While blood arterial macrocirculation checks Murray’s law, this is not the case for microcirculation, where wall shear stress is decreasing with the sizes of the vessels. Different hypotheses were developed to explain the shifts to Murray’s law observed with microcirculation, for example by adding smooth muscles energy costs \[4\]. In 2005, Alarcón et al \[5\] used semi-empirical laws from Pries et al \[6\] and showed that wall shear stress behavior in microcirculation can be explained by phase separation effects in small blood vessels. Phase separation effects make blood viscosity become a non monotonous function of vessel radius: the Fåhræus - Lindqvist effect \[6\,\| 9\].

The last step to fully extend Murray’s law to blood circulation is now to add the dependence of vessel blood viscosity on flow amplitude. Indeed, blood is a rheo-fluidifying fluid and its local viscosity depends on the local shear rate in the vessel and local shear rate is a function of both blood flow amplitude in the vessel and vessel radius. Thus, in addition to red blood cells volume fraction and vessel radius for microcirculation, effective viscosity is expected to be also dependent on the shear rates in the vessel. We investigated this phenomena and showed how a shear rate dependent rheology can influence Murray’s optimal design. Our study is based on Quémada’s fluid rheology \[10\] that models a shear thinning (pseudo plastic) fluid such as blood, but our study can easily be extended to many fluids whose rheologies are shear rate dependent. Quémada’s law mimics the behavior of a shear thinning fluid and relates the fluid local viscosity to the fluid local shear rate and local hematocrit; it is known to give a good approximation of blood rheology with the good set of parameters \[11\,\| 14\]. In order for our results to be valid for arterial blood microcirculation, we accounted for the phase separation effect between plasma and red blood cells - Fåhræus effect - by integrating a layer of Newtonian fluid near the wall of the vessel. The thickness of the layer is deduced from Pries et al work \[6\].

First we show that if Fåhræus effect does not occur, the fluid effective viscosity in a vessel is dependent on mean shear rate and hematocrit in the branch only. If Fåhræus effect occurs, then we show that effective viscosity becomes also dependent on vessel radius. Then we apply Murray’s optimal design to both cases with and without Fåhræus effect and derive corresponding laws for optimal configuration of a vessel and of a bifurcation. Finally, we study how these laws affect optimal geometries of fractal tree structures used in arterial blood flow in small vessels. Fractal tree structures are well documented \[10\] and have been intensively studied and validated as good approximations for blood modeling \[12\,\| 14\]. The viscosity of Quémada’s fluids depends on the local shear rate $\dot{\gamma}$ and on the local red blood cells volume fraction $H$ (blood hematocrit):

$$\mu(\dot{\gamma}, H) = \mu_p \left(1 - \frac{H}{H_\infty}\right)^{-2} \left(1 + k \frac{\chi}{\chi + k}\right)^2$$  

$$k = (t_c |\dot{\gamma}|)^{\frac{3}{2}}$$  

$$\chi = \left(1 - \frac{H}{H_0}\right) / \left(1 - \frac{H}{H_\infty}\right)$$

The quantity $\mu_p$ is the viscosity of plasma and $\mu_p = 1.6 \times 10^{-3}$ Pa.s. The quantities $t_c$, $H_0$ and $H_\infty$ are function of the red blood cells volumetric fraction $H$. For blood, their expressions have been estimated in \[11\], their formulas and limitations are detailed in appendix A. Blood viscosity varies strongly for shear rates ranging from $10^{-3}$ s$^{-1}$ to 1 s$^{-1}$ and reach a high viscosity plateau for shear rates smaller than $10^{-3}$ s$^{-1}$ and a low viscosity plateau for shear rates larger than 1 s$^{-1}$. Viscosity increases with red blood cells volumetric fraction.
Blood fluid equations and effective viscosity.

We assume the vessels to be cylindric and the fluid to be axi-symmetric and fully developed in all the vessels. The viscosity $\mu(\dot{\gamma}(s), H(s))$ of the fluid at a radial position $s$ of a vessel depends on the local shear rate $\dot{\gamma}(s)$ and on the local red blood cell concentration $H(s)$, see equation (B10). The pressure drop per unit length is denoted $C$, it is assumed independent on the position. In this frame, the fluid dynamics reduce to an equation on the shear rate $\dot{\gamma}(s)$ at radial position $s \in [0, r]$:

$$
\mu(\dot{\gamma}, H) \dot{\gamma} = \frac{Cs}{2}
$$

Once the expression of the viscosity $\mu$ is known, this equation shows that the shear rate at radial position $s$, $\dot{\gamma}$, is a function of $Cs$ and $H$ only. Using Quémada’s law, it is possible to reach an analytical expression for the shear rate $\dot{\gamma}$ and consequently for the flow rate $F$ in the branch as a function of the radius of the branch $r$, of the pressure drop per unit length $C$ and of the discharge hematocrit $H_D$, see appendix B for the details. Note that for branches whose radius is sufficiently large, say larger than 300 $\mu$m, Fårhæus effect is negligible and the blood hematocrit $H$ in the branch is homogeneous and equal to the discharge hematocrit $H_D$, see figure (9).

From these relations, and the expression of the hydrodynamical resistance of a cylindrical tube of length $L$, $R = CL/F = (8\mu L)/(\pi r^4)$, we can compute the effective viscosity $\mu_{eq}$ of the fluid in a branch depending on the quantity $Cr$ in the branch and the red blood cells volumetric fraction $H_D$ in the branch:

$$
\mu_{eq}(r, C, H_D) = \frac{\pi r^4 C}{8F(r, C, H_D)} = \frac{Cr}{8\langle\dot{\gamma}\rangle(r, C, H_D)} \quad (4)
$$

When Fårhæus effect can be neglected, then the quantity $Cr$ is a function of the mean shear rate in the branch $\langle\dot{\gamma}\rangle$ and of the red blood cells volumetric fraction $H_D$, they are related through the function $g$: $Cr = g(\langle\dot{\gamma}\rangle, H_D)$. Explanations about why and how they are related are detailed in appendix B.1. Thus, when Fårhæus effect does not occur, then the effective viscosity is driven by the mean shear rate in the branch $\langle\dot{\gamma}\rangle$ and red blood cells volumetric fraction $H_D$:

$$
\mu_{eq}(\langle\dot{\gamma}\rangle, H_D) = \frac{g(\langle\dot{\gamma}\rangle, H_D)}{8\langle\dot{\gamma}\rangle} \quad (without \ Fårhæus \ effect) \quad (5)
$$

When Fårhæus effect occurs, this remains a good approximation if the vessel radius is larger than about 300 $\mu$m. For smaller vessels, we lose the independence on the radius of the branch $r$, and the effective viscosity can be expressed using a function $k$ relating $Cr$ to $\langle\dot{\gamma}\rangle$, see details in appendix B.2

$$
\mu_{eq}(\langle\dot{\gamma}\rangle, r, H_D) = \frac{Cr}{8\langle\dot{\gamma}\rangle} = \frac{k(\langle\dot{\gamma}\rangle, r, H_D)}{8\langle\dot{\gamma}\rangle} \quad (with \ Fårhæus \ effect) \quad (6)
$$

In the following, we will assume $H_D$ to be constant and thus drop it out of the equations for the sake of simplification. All the next results would nevertheless be dependent on the value of $H_D$. 

Figure 1. Quémada’s model of viscosity [10, 11]: viscosity dependence on the shear rate (blood case, $H = 0.45$).
Figure 2. Effective viscosity $\mu_{eq}$ depends on mean shear rate in branch only unless Fåhraeus effect occurs (case with mean shear rate of $2/\pi \times 10^{-3}$ s$^{-1}$).

Why Murray’s law remains true when Fåhraeus effect is negligible?

We now show that these principles extends Murray’s law to the whole range of Quémada’s fluid, and thus for blood, at least as long as Fåhraeus effects are negligible. Let us consider a fluid flow rate $F$ that is going through a vessel with radius $r$ and length $l$. The dissipated power $W$ defined by Murray [1, 5] divides into two parts:

$$W = W_H + W_M,$$

where $W_H$ is the power dissipated by the flow, and $W_M$ the energy consumption rate of the fluid (in the case of blood, this is typically a metabolic consumption rate). With the results presented earlier, we have

$$W_H = \frac{8F^2\mu_{eq}\langle \dot{\gamma} \rangle l}{\pi r^4}$$ (7)

$$W_M = \alpha_b \pi r^2 l$$ (8)

where $\alpha_b$ is the energy consumption rate per unit volume of the fluid.

Then the design principle proposed by Murray is to search for a minimum of $W$ relatively to the radius of the vessel, thus solving $\frac{\partial W}{\partial r} = 0$. This leads to the following non linear equation that depends only on $\langle \dot{\gamma} \rangle$ and not anymore on the flow $F$ or the radius $r$ of the vessel:

$$\frac{1}{\pi rl} \frac{\partial W}{\partial r} = -8 \langle \dot{\gamma} \rangle^2 \left( 4\mu \langle \dot{\gamma} \rangle + 3 \langle \dot{\gamma} \rangle \frac{\partial \mu_{eq}}{\partial \langle \dot{\gamma} \rangle} \langle \dot{\gamma} \rangle \right) + 2\alpha_b = 0$$ (9)

Consequently Murray’s design principle applied to Quémada’s fluids says not only that the optimal configuration is reached as soon as the mean shear rate in the vessel solves the preceding equation, but also that the mean shear rate does not depend on both flow rate $F$ or vessel size $r$ and $l$.

Let us apply this result to a bifurcation where the flow rate in the parent branch is $F_p$ and in the two daughter branches $F_1$ and $F_2$. There respective radii are denoted $r_p$, $r_1$ and $r_2$. If $\langle \dot{\gamma} \rangle_{noF}$ is the solution of the preceding equation (9), then $\langle \dot{\gamma} \rangle_{noF}$ is the optimal mean shear rate in the three vessels and $\langle \dot{\gamma} \rangle_{noF} = \frac{F_p}{\pi r_p^3} = \frac{F_1}{\pi r_1^3} = \frac{F_2}{\pi r_2^3}$. By flow conservation, we have an additional equation which is $F_p = F_1 + F_2$. Combining these equations finally leads to Murray’s original law:

$$r_p^3 = r_1^3 + r_2^3$$ (10)

Our method and result are most general and apply to any fluid whose viscosity is monotonously driven by the shear rate in the vessel. The fact that mean shear rate drives the optimal behavior makes it interesting to study its consequences on tree structures. The optimal shear rates are the smallest possible shear rates standing on the plateau of low viscosities of the fluid rheogram, see figure [1].

Murray’s law with Fåhraeus effect.

Fåhraeus effect is a phase separation effect due to the biphasic characteristics of blood. Some estimation about Fåhraeus effect strength can be estimated from [1] (equation (B8) in appendix B2), and Fåhraeus effects can reasonably
be forgotten for diameters larger than 300 $\mu$m, see an example figure \[3\]. For smaller diameter, to estimate the role of Fähræus effects on Murray’s law, we approximated this effect by assuming there was a red blood cell depleted layer near the wall of the branch, see details in appendix \[B2\]. The thickness of this depleted layer depends on the branch radius and thus the whole fluid dynamics in the tube. As a consequence, the effective viscosity in a branch where Fähræus effect occurs is not anymore dependent on the mean shear rate only, it also becomes dependent on the radius of the branch through the value of $\dot{\gamma}(r)$:

$$\mu_{eq}(\langle \dot{\gamma} \rangle, r) = \frac{k(\langle \dot{\gamma} \rangle, r)}{4 \langle \dot{\gamma} \rangle}$$

![Figure 3. Effective viscosity variation versus branch radius and mean shear rate in branch. When Fähræus effect occurs (small radii), the effective viscosity $\mu_{eq}$ depends on the mean shear rate in the branch and on the radius on the branch ($H_D$ = 0.45).](image)

In this case the power dissipation in the fluid used for computing Murray’s law is, with the fluid flow rate in the branch $F$ a constant:

$$W_H = \frac{8F^2\mu_{eq}(\langle \dot{\gamma} \rangle, r)l}{\pi r^4}$$ (11)

The energy consumption rate of the fluid $W_M$ remains the same, $W_M = \alpha_0 \pi r^4 l$. Then, the radius that minimizes the total work $W = W_H + W_M$ solves $\frac{\partial W}{\partial r} = 0$, i.e.

$$\frac{1}{\pi rl} \frac{\partial W}{\partial r} = -8 \langle \dot{\gamma} \rangle^2 \left(4\mu_{eq}(\langle \dot{\gamma} \rangle, r) + 3 \langle \dot{\gamma} \rangle \frac{\partial \mu_{eq}}{\partial \langle \dot{\gamma} \rangle} (\langle \dot{\gamma} \rangle, r) - r \frac{\partial \mu_{eq}}{\partial r} (\langle \dot{\gamma} \rangle, r) \right) + 2\alpha_0 = 0$$ (12)

This equation shows that the minimum power is reached on a curve $r \to \langle \dot{\gamma} \rangle^*_F(r)$ that depends on the red blood cells volumetric fraction $H_D$, blood case is plotted on figure (1). When $r$ is large enough, say larger than about 300 $\mu$m \[6\], then the dependence on $r$ is lost and $\langle \dot{\gamma} \rangle^*_F(r) = \langle \dot{\gamma} \rangle^*_{noF}$.

Let us now consider a bifurcation where the mean shear rate in the parent branch is $\langle \dot{\gamma} \rangle_p$ and in the two daughter branches $\langle \dot{\gamma} \rangle_1$ and $\langle \dot{\gamma} \rangle_2$. There respective radii are still denoted $r_p$, $r_1$ and $r_2$. Using flow conservation through the bifurcation, we can deduce that the optimal radii check the following equality

$$\langle \dot{\gamma} \rangle^*_F(r_p) r_p^3 = \langle \dot{\gamma} \rangle^*_F(r_1) r_1^3 + \langle \dot{\gamma} \rangle^*_F(r_2) r_2^3$$ (13)

As expected, when Fähræus effect vanishes, the previous equation simplifies into equation \[10\].

*Behavior of shear rates in a fractal tree structure.*

We are now looking at a tree structure which is a cascade of cylinders. The branches divides regularly into $n$ smaller identical branches. The number of divisions between a vessel and the root vessel of the tree defines its generation index. The tree root stands at generation 0 and the tree leaves stand at generation $N$. The size of the branches are defined thanks to the homothety ratio $h$ \[13\] \[16\] that corresponds to the relative change in vessels diameter and lengths in a bifurcation, i.e. if $r_i$ is the radius of vessels of generation $i$, then the radii of vessels of generation $i + 1$ are $r_{i+1} = h \times r_i$. 

Figure 4. In black, the optimal mean shear rate in a branch as a function of the radius of the branch with Fähraeus effect (function \( r \to \langle \dot{\gamma} \rangle_{\text{optF}} \) in text), in red dotted line, the optimal mean shear rate without Fähraeus effect. Blood case: \( H_D = 0.45 \) and \( \alpha_b = 77.8 \text{ J.m}^{-3}.\text{s}^{-1} \) \[4, 5\].

Figure 5. Tree network structure with \( n = 2 \) and \( N = 6 \). The tree is dichotomous and the vessels size decreases at each generation: their diameters and lengths are multiplied by the homothety factor \( h < 1 \) after each bifurcation.

The mean shear rate in a branch of generation \( i \) is computed as the ratio between the mean fluid velocity in the branch over the branch radius. Denoting \( F_i \) the blood flow in a branch of generation \( i \) and \( S_i = \pi r_i^2 \) the surface of its circular cross section, then the mean shear rate in that branch is

\[
\langle \dot{\gamma}_i \rangle = \frac{F_i}{r_i} = \frac{F_i}{\pi r_i^3}
\]

Since the tree branches are assumed to divides into \( n \) smaller identical branches, the total blood flow in a branch of generation \( i \) is twice the total blood flow in a branch of the next generation \( i + 1 \). Then the mean shear rate in a branch of generation \( i + 1 \) is

\[
\langle \dot{\gamma}_{i+1} \rangle = \frac{F_{i+1}}{\pi r_{i+1}^3} = \frac{F_i}{\pi r_i^3} \frac{1}{nh^3} = \langle \dot{\gamma}_i \rangle \frac{1}{nh^3}
\] (14)

Thus, the regularity of the structure (fractal) leads to an interesting scaling law on how mean shear rates vary with generations as a function of the homothetic factor \( h \). This scaling law depends only on the homothetic ratio \( h \). Depending on the position of the factor \( \frac{1}{nh^3} \) relatively to 1, the mean shear rate has different behaviors:

- if \( h > (\frac{1}{n})^{1/3} \), then the mean shear rate decreases along the generations, consequently blood viscosity tends to increase along the generations.
- if \( h = (\frac{1}{n})^{1/3} \), then the mean shear rate remains constant along the generations and so for blood viscosity.
- if \( h < (\frac{1}{n})^{1/3} \), then the mean shear rate increases along the generations, consequently blood viscosity tends to decrease along the generations.
Figure 6. Mean viscosity variation in a dichotomous tree \((n = 2)\) with \(N = 10\) generations for three different values of the homothety reduction factor \(h\). In the case plotted Fåhræus effect is negligible and the shear rate in the root branch of the tree is \(640\) \(s^{-1}\).

Blood viscosity depends on shear rate in a non linear way, with a plateau of high viscosities at low shear rates and a plateau of lower viscosities for high shear rates. Between the two plateaus, for medium shear rates, blood viscosity varies quickly, as shown on figure 1A. When the shear rate decreases or increases along the generations of the tree, then viscosity will vary more strongly if shear rate variation makes the viscosity go through the strongest slope. Consequently, the amplitude of viscosity variation depends on the initial mean shear rate \(\langle \dot{\gamma}_0 \rangle\) in the root branch of the tree: a high shear rate in the root branch can induce notable viscosity variations throughout the tree only if shear rate is decreasing enough along generations; similarly, a low shear rate in the root branch can induce notable viscosity variations throughout the tree only if the shear rate increases enough along the generations. In any other case, the viscosity is stalled, either in one of the two plateaus or because mean shear rate does not vary much if \(h \sim (\frac{1}{n})^{1/3}\).

These results are summarized in table I.

| \(h\) | Behavior of viscosity along the generations as a function of the homothety ratio \(h\) and the initial mean shear rate \(\langle \dot{\gamma}_0 \rangle\). |
|-------|----------------------------------------------------------------------------------------------------------------------------------|
| \(h < (\frac{1}{n})^{\frac{2}{3}}\)  |
| low \(\langle \dot{\gamma}_0 \rangle\) (high viscosity in root) | Decrease of viscosity |
| high \(\langle \dot{\gamma}_0 \rangle\) (low viscosity in root) | Low viscosity, small positive variations |
| \(h = (\frac{1}{n})^{\frac{2}{3}}\)  |
| high mean shear rate | High constant viscosity |
| \(h > (\frac{1}{n})^{\frac{2}{3}}\)  |
| high viscosity, small negative variations |
| low constant viscosity | Increase of viscosity |

Table I. Behavior of viscosity along the generations as a function of the homothety ratio \(h\) and the initial mean shear rate \(\langle \dot{\gamma}_0 \rangle\).

Optimal tree structure in the sense of Murray’s optimal design without Fåhræus effect.

As stated previously, Murray’s law extended to Quémada’s fluid implies that the dissipative power \(W\), see equations 7 and 8, is minimal in all branches if the mean shear rate in all the branch is equal to the optimal mean shear rate \(\langle \dot{\gamma} \rangle^*\) which solves equation 9. Since the mean shear rate is following a scaling law in the tree, the only way for the tree to minimize the dissipative power throughout the tree is for the scaling parameter \(\frac{1}{nh^*}\) to be equal to 1, i.e.

\[ h^* = \left(\frac{1}{n}\right)^{\frac{2}{3}} \]

This implies that optimal configuration corresponds to constant mean shear rates and effective viscosities throughout the tree. This result is fully compatible with blood arterial macrocirculation 6. For blood, it has been estimated that \(\alpha_b = 77.8 \ J.m^{-3}.s^{-1}\) and \(H_D = 0.45\) 4 5, with these numbers, the optimal mean shear rate predicted by our study is \(\langle \dot{\gamma} \rangle^*_{\text{noF}} \sim 12.47\ s^{-1}\), which is in agreement with the mean shear rates measured in arterial macrocirculation 6. The case of arterial microcirculation is more complex, because it includes phase separation effects (Fåhræus effects).

Optimal tree structure in the sense of Murray’s optimal design with Fåhræus effect.

The optimal configuration of each division in the tree checks the extended Murray’s law equation 13 with the hypothesis that the daughter branches are identical. In addition, the optimal configuration also checks the scaling
law for the branch radii, i.e. $r_{i+1} = hr_i$. These equations make the scaling factor $h$ generation dependent, thus we now index scaling factors by their generation index $i$; The optimal $h_i$ in term of Murray’s design checks the equation:

$$nh_i^3 \langle \gamma \rangle_p^{**}(h_{i,s}, r_{i,s}) = \langle \gamma \rangle_p(r_{i,s})$$

![Diagram A](image1.png)  
![Diagram B](image2.png)

Figure 7. Example for blood circulation in a tree with $n = 2$, root radius of 800 $\mu$m, length over radius of the branches 10; Blood properties are from [1][5]: $H_D = 0.45$ and $\alpha_0 = 77.8$ $J.m^{-3}.s^{-1}$. A: Optimal scaling factor with Fahraeus effect (black) and without Fahraeus effect (red) Fahraeus effect allows an optimal configuration with slightly tighter branches. B: Mean shear stress versus pressure within the tree. The deepest generations are on the left (low pressures) and the upper generations are on the right (high pressure). The drop of mean shear stress in the smaller generations is due to Fahraeus effect.

We computed numerically the optimal scaling factors for the case of blood in a dichotomical tree, the results are shown on figure (7A). We chose the root branch to be 800 $\mu$m, thus Fahraeus effect is negligible in the root. Consequently, the optimal configuration consists in three first generations bifurcating with a scaling factor of $\left(\frac{1}{2}\right)^{\frac{1}{3}} \sim 0.7937$. Fahraeus effect becomes influential near about the fourth generation and affects the optimal scaling factors of the next generations. The function $r \rightarrow \langle \gamma \rangle_p(r)$ is a decreasing function, thus $h_{i,s} < \left(\frac{1}{2}\right)^{\frac{1}{3}} = h_*$. Thus the optimal configuration has tighter branches where Fahraeus effect occurs than the optimal configuration without Fahraeus effect. Indeed, Fahraeus effect improves the lubrication of the fluid in the tube because the red blood cell depleted layer near the wall is less viscous that the core layer. Consequently, effective viscosities decrease and mean shear rates increase along the generations as soon as Fahraeus effect occurs, as shown by table [4] and equation (14).

The mean shear stress in the branch is $\sigma_{i,s} = \mu_{eq}(\gamma)_{p}^{**}(r_{i,s}, r_{i,s}) \langle \gamma \rangle_p(r_{i,s}) = \frac{k}{3} k(\gamma)_{p}^{**}(r_{i,s}, r_{i,s})$. Since $k$ is an increasing function of the mean shear rate, see appendix B, the mean shear stress increases along the generations when Fahraeus effect occurs. Because pressure is decreasing along the generation, the mean shear stress is a decreasing function of pressure within the tree, which is in agreement with the observations made in the literature for arterial blood microcirculation when Fahraeus effect occurs [6]. Blood example is plotted on figure (7B).

Conclusion.

We extended Murray’s law to Quémada’s fluids; since our study is based on the fact that viscosity’s dependence on fluid mechanics is a monotonous function of the shear rate only, our results also holds for any other similar fluid. In a cylindrical tube, we showed that the mean shear rate drives the behavior of the effective viscosity of the tube and thus of the power dissipated in the flow. The consequence is that Murray’s optimization principle in a cylindrical tube brings an universal optimal mean shear rate that does not dependent on the flow amplitude or on the size of the tube. In the case of Quémada’s law mimicking blood behavior, we found that this optimal mean shear rate is $\langle \gamma \rangle_{noF}^{**} = 12.47$ $s^{-1}$. This value is in accordance with arterial macrocirculation data where the mean shear rates in the successive vessels remain almost constant at about $10$ $s^{-1}$. This optimal value is the smallest possible mean shear rate that allows viscosity to remain in its lowest plateau, see figure (1). Applied to a fractal tree whose branches divide into a identical smaller branches, we found that the optimal scaling factor remains the same as for a Newtonian fluid, i.e. $\left(\frac{1}{n}\right)^\frac{1}{3}$.

However, if the tube diameter is small enough, the phase separation effect, called Fahraeus effect, occurs and a plasma only layer appears near the wall of the tube, thus making the effective viscosity dependent not anymore on the mean shear rate only, but also on $r$. Consequently, we derived a new optimal configuration from Murray’s optimisation principle in a tube, which formulate into a decreasing function relating the optimal mean shear rate in a tube and the radius of the tube $r \rightarrow \langle \gamma \rangle_p(r)$. For large $r$, the function coincides with the optimal mean shear
rate without Fähræus effect. The function behavior highlights the fact that Fähræus effect induces a lubrication phenomena into the tube. The case of Quémada’s fluid mimicking blood is plotted on figure [4]. We also derived the optimal configuration of a fractal tree when Fähræus effect occurs. We showed that the optimal scaling factors become dependent on the generation index, on the size of the root of the tree and on the function \( r \rightarrow \langle \dot{\gamma} \rangle_F (r) \), i.e. \( nh^1_i \langle \dot{\gamma} \rangle_F (h_i, r_{i,*}) = \langle \dot{\gamma} \rangle_F (r_{i,*}) \). Optimal configuration of the fractal tree allows tighter branches when Fähræus effect occurs and induces a drop in mean shear stresses along the tree, which has been reported in the literature for blood arterial microcirculation.

Further studies may focus on aspects related to blood circulation physiology. Hence, the role of inertia, turbulence or heart beating that occur in blood large circulation may influence Murray’s optimal design. In the microcirculation, the role of glycocalyx on the effective radius of the blood vessels may also play a role [17]. Because the power dissipation in Murray’s optimal design is not symmetric relatively to its optimal value, biological noise affecting the vessel sizes may also influence the optimal configuration [16][18], thus the inclusion of such a noise in Murray’s optimal design may bring interesting insights on blood vessels size distribution in the arterial network.

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APPENDIX

Appendix A: Quémada’s law

The local viscosity $\mu$ is a function of both local shear rate $\dot{\gamma}(s)$ and local hematocrit $H(s)$ as stated by Quemada’s law:

$$
\mu(\dot{\gamma}, H) = \mu_p \left(1 - \frac{H}{H_\infty(H)}\right)^{-2} \left(\frac{1 + k(H)}{\chi(H) + k(H)}\right)^2
$$

with $k(H) = (t_c(H)|\dot{\gamma}|)^{1/2}$, $\chi(H) = \left(1 - \frac{H}{H_\infty(H)}\right) / \left(1 - \frac{H}{H_\infty(H)}\right)$; $\mu_p$ is the viscosity of plasma and $\mu_p = 1.6 \times 10^{-3}$ Pa.s.

The quantities $t_c$ (seconds), $H_0$ and $H_\infty$ are functions of the red blood cells volumetric fraction $H$. We use the fits from [11]:

$$
t_c(H) = e^{6.1508 - 27.293H + 25.60H^2 - 3.697H^3}
$$

$$
H_\infty(H) = 2 e^{-1.3435 + 2.803H - 2.711H^2 + 0.6479H^3}
$$

$$
H_0(H) = 2 e^{-3.8740 + 10.410H - 13.80H^2 + 6.738H^3}
$$

The formulas for $t_c$, $H_\infty$ and $H_0$ come from data fitting, they are valid for red blood cells volumetric fraction up to 0.7 [19] and for moderate shear rates, i.e. larger than about 0.1 s$^{-1}$. Other fitting methods using second order polynomials can be used, see for example [14]. Using such alternative fit induces very few differences on the results predicted in this work.

Appendix B: Computation of the effective viscosity

1. Without Fåhraeus effect.

In this section, we consider a cylindrical branch with radius $r$ and length $L$. Blood flow in the branch is assumed to be fully developed and axi-symmetrical. The quantity $C$ is the pressure drop per unit length in a vessel, it is assumed to be a constant in the whole vessel. We do not take Fåhraeus effect into account, thus red blood cells volume fraction $H$ is assumed constant in the whole vessel. The shear rate at radial position $s$ is then denoted $\dot{\gamma}(s, C, H)$ and the fluid dynamics in the branch with these hypotheses reduces to and is the solution of the following equation:

$$
\mu(\dot{\gamma}(s, C, H), H(s)) \dot{\gamma}(s, C, H) = \frac{C s}{2}
$$

(B1)

The first consequence of this equality is that the shear rate $\dot{\gamma}(s, C, H)$ can actually be seen as a function of $Cs$ and $H$ only: $\dot{\gamma}(Cs, H)$. The quantity $Cs$ is a constraint; denoting $x$ the axis of the branch, $2\pi Cs dx$ represents the infinitesimal increase of the pressure force felt by a particle of fluid whose radial position in the branch is $s$ and which moves a distance $dx$ forward into the branch.

The second consequence of equation (B1) is that we can compute an analytical solution for the local shear rate $\dot{\gamma}(Cs, H)$:

$$
\dot{\gamma}(Cs, H) = \left(\frac{\sqrt{\gamma_1(Cs, H)} - \sqrt{\gamma_3(H)}}{2} + \sqrt{\left(\frac{\sqrt{\gamma_1(Cs, H)} - \sqrt{\gamma_3(H)}}{2}\right)^2 + 4\sqrt{\gamma_1(Cs, H)\gamma_2(H)}}\right)^2
$$

(B2)
with \( \dot{\gamma}_1(C_s, H) = \frac{|C_s|}{2\mu_P} \left(1 - \frac{H}{H_{\infty}(H)}\right)^2 \), \( \dot{\gamma}_2(H) = \frac{\chi(H)}{t_c(H)} \) and \( \dot{\gamma}_3(H) = \frac{1}{t_c(H)} \). Then the flow \( F \) in a branch is:

\[
F = -2\pi \int_0^r \dot{\gamma}(C_s, H) s^2 \frac{ds}{2}
\]

(B3)

Consequently, the mean shear rate in the branch \( \langle \dot{\gamma} \rangle \) is a function of \( Cr \) and \( H \), as shown by the following equalities:

\[
\langle \dot{\gamma} \rangle = \frac{F}{\pi r^3} = -\int_0^r \dot{\gamma}(C_s, H) s^2 \frac{ds}{r^3} = -\int_0^{Cr} \dot{\gamma}(y, H) \frac{y^2}{r^3} \frac{dy}{(Cr)^3} = \langle \dot{\gamma} \rangle \langle Cr, H \rangle
\]

(B4)

Moreover, the mean shear rate \( \langle \dot{\gamma} \rangle \) is a strictly increasing function of the pressure drop per unit length (and as a matter of fact of the radius of the branch too, since it depends on \( Cr \)), thus there exists a function \( g \) such that \( Cr = g(\langle \dot{\gamma} \rangle, H) \) that relates the mean shear rate \( \langle \dot{\gamma} \rangle \) to \( Cr \) and \( H \). No analytical expression for \( g \) is available but it can be easily computed numerically by inverting equation (B4).

From these results, we can get an analytical formula of the effective viscosity of the fluid in a branch as a function of \( Cr \) and \( H \):

\[
\mu_{eq}(Cr, H) = \frac{\pi r^4 C \langle \dot{\gamma} \rangle}{8F} = \frac{1}{8} \frac{Cr}{\langle \dot{\gamma} \rangle (Cr, H)} \left( \int_0^r \dot{\gamma}(C_s, H) s^2 \frac{ds}{2} \right)^{-1}
\]

(B5)

or using \( \langle \dot{\gamma} \rangle \) as the variable:

\[
\mu_{eq}(\langle \dot{\gamma} \rangle, H) = \frac{1}{8} \frac{g(\langle \dot{\gamma} \rangle, H)}{\langle \dot{\gamma} \rangle}
\]

(B6)

2. With Fåhræus effect.

In this section, we consider a cylindrical branch with radius \( r \) and length \( L \). Blood flow in the branch is assumed to be fully developed and axi-symmetrical. The quantity \( C \) is the pressure drop per unit length in a vessel, it is assumed to be a constant in the whole vessel. Blood hematocrit is not anymore assumed constant in the whole vessel since we account for Fåhræus effect in this section.

Red blood cells distribution in a vessel.

We assume that red blood cells stand only in the core of the vessel where the hematocrit is constant and equal to \( H \) (core hematocrit). The radius of the core is \( \xi \leq r \). Plasma flows in the layer near the wall (its flow is \( F_{layer} \)). We neglect the role of the glycocalyx layer [17] since its thickness, of about 1 micron, is small relatively to the diameters of the vessels considered, that are larger than 50 microns. Plasma and red blood cells flow in the core (their flow is \( F_{core} \)), see figure 8.

![Figure 8. Scheme of the blood flow inside an axi-symmetric vessel.](image)

The red blood cells depletion near the vessel wall induces the Fåhræus effect that corresponds to a decrease of the mean hematocrit in the vessel relatively to the discharge hematocrit \( H_D \) in large vessels. Since the blood that circulates into the vessel comes from larger vessels, by flow conservation [6, 8] we can relate discharge hematocrit \( H_D \) to core hematocrit \( H \)

\[
H_D = \frac{H(r, C, H_D) F_{core}(r, C, H_D)}{F_{core}(r, C, H_D) + F_{layer}(r, C, H_D)}
\]

(B7)
The dependence of the mean red blood cells volumetric fraction in a vessel, called tube hematocrit $H_T$, with tube radius and discharge hematocrit is well documented [6]: if the radius of the tube $r$ is measured in microns, then

$$H_T(r, H_D) = H_D \times (H_D + (1 - H_D) \times (1 + 1.7e^{-0.415 \times 2r} - 0.6e^{-0.011 \times 2r})$$  \tag{B8}

Finally, tube hematocrit is related to core hematocrit by $H_T(r, H_D) \pi r^2 = H(r, C, H_D)\pi \xi(r, C, H_D)^2$ and

$$H_T(r, H_D) = H(r, C, H_D) \frac{\xi(r, C, H_D)^2}{r^2}$$  \tag{B9}

We can thus define the following function, which represents how red blood cells volumetric fraction varies along the radius of the vessel:

$$\begin{cases}
\text{if } 0 \leq s \leq \xi \text{ (core), } & H(s) = H(r, C, H_D) = \frac{r^2}{\pi(r, C, H_D)^2} H_T(H_D, 2r) \\
\text{if } \xi < s \leq r \text{ (wall layer), } & H(s) = 0
\end{cases}$$  \tag{B10}

In order to be able to compute the values of $H(r, C, H_D)$ and $\xi(r, C, H_D)$, we need to add to this set of equations the equations of fluid dynamics.

**Fluid mechanics.**

The shear rate $\dot{\gamma}$ at radial position $s$ is the solution of the following equation:

$$\mu (\dot{\gamma}(s, C, H(s)), H(s)) \dot{\gamma}(s, C, H(s)) = \frac{Cs}{2}$$  \tag{B11}

As in the case with no Fåhræus effect, this shows that shear rate at radial position $s$ is a function of $Cs$ and $H(s)$. However, on the contrary of the case without Fåhræus effect, the dependence of $\dot{\gamma}$ on $s$ remains through the dependence of $H(s)$ on $s$. From equation (B11), we can compute an analytical solution for the local shear rate $\dot{\gamma}(Cs, H(s))$:

$$\begin{cases}
\text{if } 0 \leq s \leq \xi \text{ (core), } & \dot{\gamma}(Cs, H(s)) = \left(\frac{\sqrt{\gamma_1(Cs, H(s))}}{2} - \frac{\sqrt{\gamma_2(H(s))}}{2} + \sqrt{\left(\sqrt{\gamma_1(Cs, H(s))} - \sqrt{\gamma_2(H(s))}\right)^2 + 4\sqrt{\gamma_1(Cs, H(s))}\gamma_2(H(s))}\right)^2 \\
\text{if } \xi < s \leq r \text{ (wall layer), } & \dot{\gamma}(Cs, H(s)) = \frac{Cs}{2\mu r}
\end{cases}$$  \tag{B12}

with $\dot{\gamma}_1(Cs, H(s)) = \frac{|Cs|}{2\mu r} \left(1 - \frac{H(s)}{H_T(H_D)}\right)^2$, $\dot{\gamma}_2(H(s)) = \frac{\gamma(H(s))^2}{\mu(H(s))}$ and $\dot{\gamma}_3(H(s)) = \frac{1}{\mu(H(s))}$.

As a consequence of the dependence of the shear rate on $s$, the mean shear rate and the effective viscosity in the branch are both dependent on the radius of the branch $r$:

$$\langle \dot{\gamma}\rangle (r, C, H_D) = \frac{F_{core}(r, C, H_D) + F_{layer}(r, C, H_D)}{\pi r^4}$$  \tag{B13}

$$\mu_{eq}(r, C, H_D) = \frac{Cr}{8 \langle \dot{\gamma}\rangle (r, C, H_D)}$$  \tag{B14}

Once $r$ and $H_D$ are fixed, the mean shear rate $\langle \dot{\gamma}\rangle$ in the branch is a strictly increasing function of the pressure drop per unit length $C$, thus there exists a function $k$ such that $Cr = k(\langle \dot{\gamma}\rangle, r, H_D)$. The function $k$ is computed numerically (see next section). Thus, effective viscosity can be reformulated into new variables:

$$\mu_{eq}(\langle \dot{\gamma}\rangle, r, H_D) = \frac{k(\langle \dot{\gamma}\rangle, r, H_D)}{8 \langle \dot{\gamma}\rangle}$$  \tag{B15}
Solving the system.

In this section, we first explain how the diameter of the red blood cells core $\xi$ and the volumetric fraction of red blood cells in the core, $H$, are computed once we know the radius of the branch $r$, the pressure drop per unit length in the branch $C$ and the discharge hematocrit $H_D$. Then we explain how we obtain the function $k$ that relates $C$ to the mean shear rate in the branch $\langle \dot{\gamma} \rangle$.

The red blood cells core $\xi$ and the volumetric fraction of red blood cells in the core $H$ are the solution of the following system that regroup the conservation equations in the branch and the equations from fluid dynamics (see previous sections):

$$
\begin{align*}
H &= H_D F_{\text{core}}(r,C,H_D) + F_{\text{layer}}(r,C,H_D) \\
\xi^2 &= \frac{H_T(r,H_D)}{H} \\
F_{\text{core}}(r,C,H_D) &= 2\pi \left( v(\xi) \frac{\xi^2}{2} - \int_0^\xi \dot{\gamma}(Cs,H(s)) \frac{\xi^2}{2} ds \right) \\
F_{\text{layer}}(r,C,H_D) &= -2\pi \left( \int_0^r \dot{\gamma}(Cs,H(s)) \frac{\xi^2}{2} ds + v(\xi) \frac{\xi^2}{2} \right) \\
v(\xi) &= \frac{C}{4\mu} (r^2 - \xi^2) \\
\dot{\gamma}(Cs,H(s)) &= \text{given by equation (B2)}
\end{align*}
$$

(B16)

The system (B16) is normalized and solved using Matlab, thanks to the fsolve command (based on a Newton method). To compute the two integrals in equation (B16), we use the quad command (adaptative Simpson quadrature).

The mean shear rate in the branch $\langle \dot{\gamma} \rangle (Cr,H_D)$ is then computed using equation (B13). The function $k$ that relates the quantity $Cr$ to the mean shear rate $\langle \dot{\gamma} \rangle$ is then computed numerically by numerical inversion of the function $\langle \dot{\gamma} \rangle (Cr,H_D)$.

![Graph A](image1.png)

![Graph B](image2.png)

![Graph C](image3.png)

Figure 9. A: Fähraeus effect plays a role on branch with small radii only, typically smaller than 300 $\mu$m. B: Effective viscosity $\mu_{eq}$ depends on mean shear rate in branch unless Fähraeus effect occurs, case with mean shear rate of $2/\pi \times 10^{-3}$ $s^{-1}$. C: Dependence of effective viscosity $\mu_{eq}$ with mean shear rate (example with tube radius 200 $\mu$m where Fähraeus effect occurs and plays a role mainly at low mean shear rates ($< 0.1$ $s^{-1}$)).
Appendix C: Optimisation of Murray’s cost.

The numerical example we gave in this work for optimal mean shear rate use Quémada’s fluid and the set of parameters corresponding to blood (see appendix A). They were computed with $H_D = 0.45$ and $\alpha_b = 77.8 \text{ J.m}^{-3}.\text{s}^{-1}$. The numerical method depends on whether Fåhræus effects occur or not. The first step is always to build the function relating the effective viscosity to mean shear rate, hematocrit and, in the case where Fåhræus effect occurs, with vessel radius, see appendices B.

When Fåhræus effect does not occur, then we solved directly equation (9), recalled below:

$$\frac{1}{\pi rl} \frac{\partial W}{\partial r} = -8 \langle \dot{\gamma} \rangle^2 \left( 4\mu \langle \dot{\gamma} \rangle + 3 \frac{\partial \mu_{eq}}{\partial \langle \dot{\gamma} \rangle} \langle \dot{\gamma} \rangle \right) + 2\alpha_b = 0$$

The derivative $\frac{\partial \mu_{eq}}{\partial \langle \dot{\gamma} \rangle}$ is computed numerically using a first order method.

When Fåhræus effect occurs, then we minimize using a gradient method the cost $W = W_H + W_M$, recalled below:

$$W = \frac{8F^2 \mu_{eq}(\langle \dot{\gamma} \rangle, r)}{\pi^2 r^4} + \alpha_b r^2$$

A value for the fluid flow rate $F$ is chosen as stated in Murray’s optimal design, then we compute the optimal radius $r^*(F)$. Finally, by spanning the whole range of interesting fluid flow rates $F$, we can compute the function relating the mean shear rate in the vessel to the vessel radius with the formula: $\langle \dot{\gamma} \rangle^* (r^*(F)) = \frac{F}{\pi (r^*(F))^3}$. 