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What can we learn from Einstein and Arrhenius about the optimal flow of our blood?

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ABSTRACT

Background: The oxygen flow in humans and other higher animals depends on the erythrocyte-to-blood volume ratio, the hematocrit. Since it is physiologically favourable when the flow of oxygen transport is maximum it can be assumed that this situation has been achieved during evolution. If the hematocrit was too low, too few erythrocytes could transport oxygen. If it was too high, the blood would be very viscous, so that oxygen supply would again be reduced.
Methods: The theoretical optimal hematocrit can be calculated by considering the dependence of blood viscosity on the hematocrit. Different approaches to expressing this dependence have been proposed in the literature. Here, we discuss early approaches in hydrodynamics proposed by Einstein and Arrhenius and show that especially the Arrhenius equation is very appropriate for this purpose.
Results & conclusions: We show that despite considerable simplifications such as neglecting the deformation, orientation and aggregation of erythrocytes, realistic hematocrit values of about 40% can be derived based on optimality considerations. Also the prediction that the ratio between the viscosities of the blood and blood plasma at high shear rates nearly equals Euler's constant (2.718) is in good agreement with observed values. Finally, we discuss possible extensions of the theory. For example, we derive the theoretical optimal hematocrit for persevering divers among marine mammals to be 65%, in excellent agreement with the values observed in several species.
General significance: These considerations are very important for human and animal physiology since oxygen transport is an important factor for medicine and physical performance.

"Blood is thicker than water."(German and English proverb)

1. Introduction

In higher animals, oxygen is transported in the blood by red blood cells (erythrocytes). Obviously, it is physiologically favourable when the flow of oxygen transport is at the maximum. This can be phrased as an optimality principle. Such principles are often used in biology, based on Darwinian evolutionary theory.

The oxygen flow in animals depends on the erythrocyte-to-blood volume ratio, the hematocrit (HCT). Within hemorheology (hydrodynamics of the blood), a theoretical framework called 'optimal hematocrit theory' has been established [1–6]. It is an interesting question whether that theory allows one to calculate HCT values that are in agreement with the observed values in healthy humans. Various approaches have been put forward to calculate this [2,4,5,7,8]. If the HCT was very low, too few erythrocytes would be present to transport oxygen. If it was too high, the blood would be very viscous and could not flow quickly, so that oxygen supply to the tissues would again be reduced (Fig. 1).

In healthy humans, the HCT amounts to about 40%. There is a difference in HCT between men and women: 45.8 ± 2.7% vs. 40.0 ± 2.4%, respectively [9]. A scatter plot of numerous experimental data depending on age [10–13] is shown in Fig. 2. In contrast, the mean plasma viscosity values are not significantly different between men and women [14]. Altered HCT values occur in numerous diseases such as in fatty liver disease [15] and heart failure [16]. Changes in HCT and viscosity are also investigated in ageing research [17,18].

Many other higher animals show nearly the same HCT values as humans, while several others show different values. For example, many deep-diving marine mammals have a higher HCT. We will investigate this special case below.

Blood is a very complicated fluid involving a lot of effects. Erythrocytes are not usually spheres. In humans, they are biconcave discs. They show phenomena such as aggregation, orientation, and deformation. Interestingly, for complex situations or processes, simple formulas sometimes lead to surprisingly good results and enable better understanding, even if they do not have a sound theoretical basis. This is, in fact, the essence of mathematical modelling, since a model is a simplified

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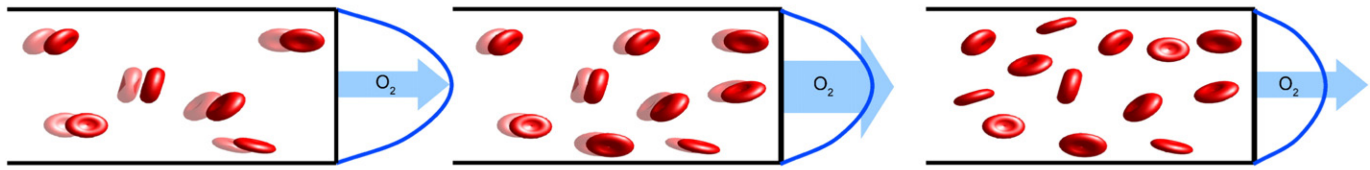

Fig. 1. Parabolic velocity profile (blue) and oxygen transport (arrow) in the case of homogeneous concentration. While the hematocrit increases from left to right, the velocity of flow decreases due to the increasing viscosity. Thus, the oxygen transport flow reaches a maximum in the middle panel.

representation of some aspect of reality. Different models can be built for the same process, and it is decided by practical application which one works best.

Here, our aim is to simplify the description of blood flow to concentrate on the essential properties, even more than in earlier approaches in optimal hematocrit theory [7,19]. It turns out that equations proposed in hydrodynamics very early by Einstein and Arrhenius are highly appropriate for this purpose. We show that despite the simplifications, realistic HCT values can be derived based on optimality considerations.

2. Calculating the theoretical optimal hematocrit

In rheology, a distinction is made between Newtonian and non-Newtonian fluids. Newtonian fluids represent the simpler case. In these liquids, viscosity depends neither on the velocity distribution nor on shear stress. Since blood is a complex mixture, it is a non-Newtonian fluid. Phenomena such as aggregation, orientation and deformation of red blood cells cause its viscosity not to be constant [7,9]. Nevertheless, several basic properties of the blood can be explained even for the idealized case where we consider it to be a (quasi-)Newtonian fluid. The Hagen–Poiseuille law is a good approximation for blood flow provided the appropriate value for the apparent viscosity is used [20]. Higher shear stresses lead to decreasing viscosity.

When a Newtonian fluid flows along a cylindrical tube, its velocity distribution (profile) is a quadratic function of the radial coordinate, that is, of the distance from the tube axis. The total flow J, that is, the volume flowing per time unit, can be described by the Hagen–Poiseuille law [20–24]:

$$J = \frac{\pi \Delta p R^4}{8 \eta l} \tag{1}$$

with the following significance of symbols: Δp: pressure difference; R, tube radius, η, viscosity, l, tube length.

For the following calculations, the exact expression of the function (Eq. (1)) is irrelevant, as long as J is inversely proportional to η:

$$J = \frac{K}{\eta}. \tag{2}$$

As shown by Mortensen et al. [25], this form applies to flows of Newtonian fluids along tubes with cross-sections other than circular, for example, elliptical. Moreover, flows through porous media can be described by Darcy's law [26,27]. This equation fits into the general form (Eq. (2)) as well. Thus, we may assume that the calculations are valid for a wide range of geometries of blood vessels (e.g. liver sinusoids), even if the Hagen–Poiseuille law does not apply strictly.

To compute the optimal HCT, it is important to know the dependence of viscosity on HCT. To what extent the flow gets slower (due to an increase in viscosity) if the HCT is increased? It is non-trivial to derive this dependence because the suspended particles perturb the flow of the pure liquid. No less a scientist than Albert Einstein dealt with this question. In [28,29], he derived the function:

$$\eta = \eta_0 (1 + 2.5\varphi). \tag{3}$$

This is a linear dependence. As mentioned by Einstein himself [28,29], it only holds true for dilute suspensions, that is, for low φ. For example, Eirich found Eq. (3) to be applicable for suspensions of fungal spores up to $\varphi = 2\%$ [30,31]. In the case where φ tends to 100%, that is, where there is almost no liquid anymore, Einstein's equation would predict a viscosity of 3.5 η_0. The real viscosity, however, is much higher in that case of an almost solid, granular medium. Therefore, several authors have suggested nonlinear equations, which describe a steep increase of viscosity at large φ.

The Swedish physicochemist Svante Arrhenius, who is well-known for his equation describing the dependence of activation energy on temperature, proposed an exponential function:

$$\eta = \eta_0 e^{a\varphi}. \tag{4}$$

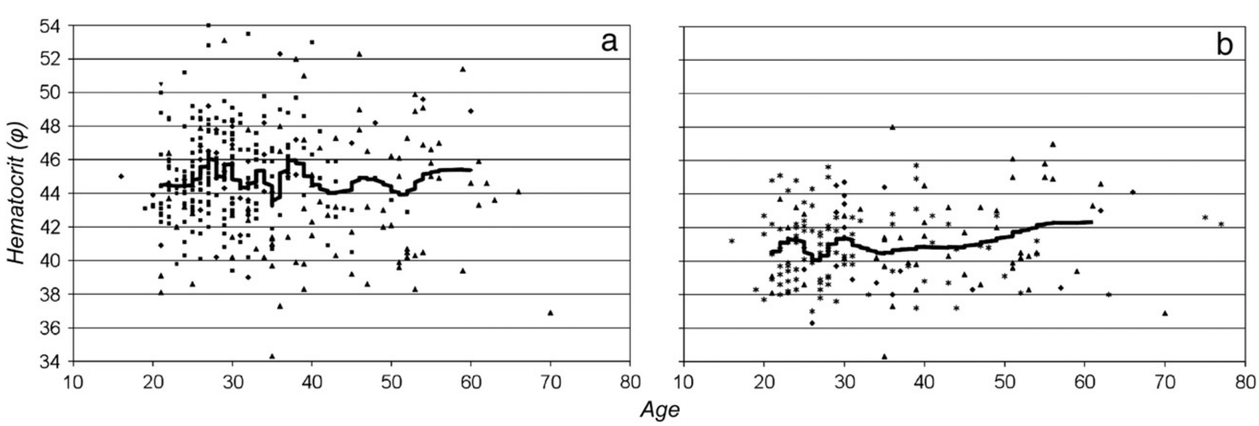

Fig. 2. Plot of the hematocrit vs. age in a) men (n = 333) and b) women (n = 171), based on data from [11] (squares), [13] (stars), [12] (diamonds) and [10] (triangles). In b), the increase in the hematocrit after menopause can clearly be seen. Solid line, sweeping average.