Electronic Supplementary Material (ESI) for Analytical Methods.

Supplementary information

Electrochemical impedance spectroscopy of blood. Part 3: A study of the correlation between blood conductivity and sedimentation to shorten the erythrocyte sedimentation rate test

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Effective medium theory. Theoretical background

Shell-ellipsoid model for erythrocytes

We modeled blood as a mixture of rotational ellipsoid inclusions (Fig. S1). We can therefore assume that $a_x = a_y$ and consequently define the axis ratio as $\xi = a_z / a_x = a_z / a_y$.

Prolate ellipsoids (of pointy or elongated form) have ξ values of more than 1, whereas oblate ellipsoids (of planetary or flattened form) have ξ values of less than 1. The depolarization factors (L) along each axis are given by [S1]:

$$L_x = L_y = \begin{cases} \dfrac{\xi}{4p^3}\left[2\xi p + \ln\dfrac{\xi - p}{\xi + p}\right], \xi > 1 \\ \dfrac{\xi}{4q^3}\left[\pi - 2\xi q - 2\arctan\dfrac{\xi}{q}\right], \xi < 1 \end{cases}, L_z = \begin{cases} \dfrac{1}{2p^3}\left[\xi \ln\dfrac{\xi + p}{\xi - p} - 2p\right], \xi > 1 \\ \dfrac{1}{2q^3}\left[2q - \xi\pi + 2\xi\arctan\dfrac{\xi}{q}\right], \xi < 1 \end{cases}, \quad \text{(S1)}$$

in which $L_x + L_y + L_z = 1$, $p = \sqrt{\xi^2 - 1}$, and $q = \sqrt{1 - \xi^2}$.

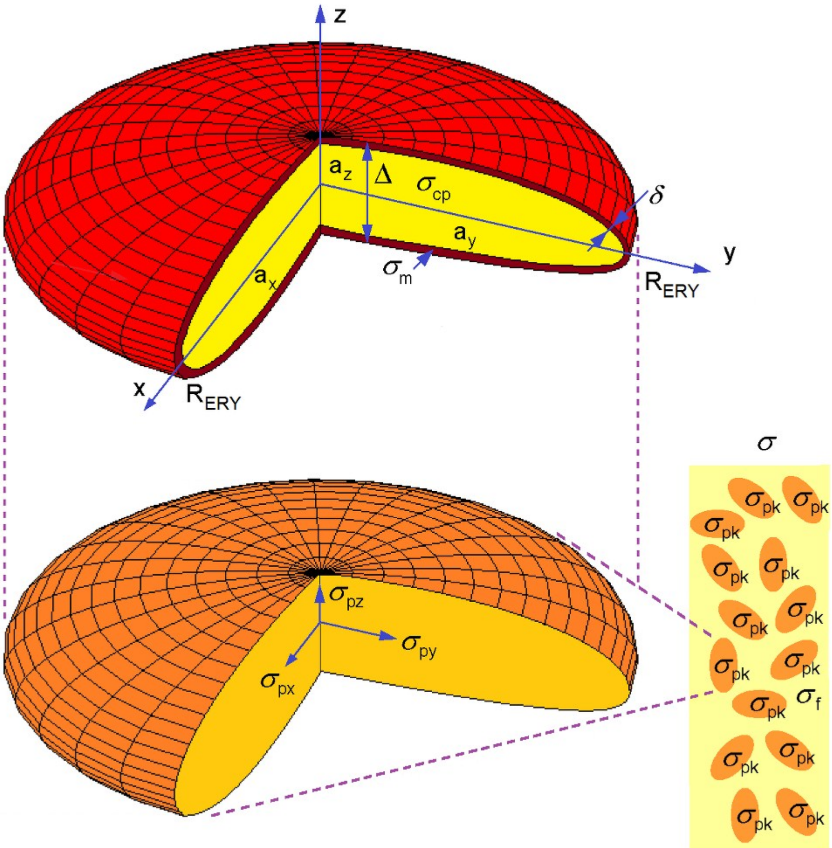

Fig. S1 Model of coated ellipsoidal particles for red blood cells.

The thickness of the erythrocyte membrane δ was very small compared with the erythrocyte radius, R_{ERY}, and its thickness, Δ (see Fig. S1). Hence, δ/a_x, δ/a_y, and δ/a_z << 1, and the volume ratio η of the inner ellipsoid to the outer ellipsoid may be approximated by:

$$\eta \approx \left(1-\frac{\delta}{a_x}\right)\left(1-\frac{\delta}{a_y}\right)\left(1-\frac{\delta}{a_z}\right) \qquad \text{(S2)}$$

The equivalent conductivity of a shell-ellipsoid is a tensor that has three components along the *x*-, *y*-, and *z*-axes of the ellipsoid: σ_{px}, σ_{py}, and σ_{pz}, respectively. For an axis *k* (*k = x, y, z*), the component σ_{pk} can be expressed as [S1]:

$$\sigma_{pk} = \sigma_m \frac{\beta_k \sigma_m + \sigma_{cp} - \beta_k \eta(\sigma_m - \sigma_{cp})}{\beta_k \sigma_m + \sigma_{cp} + \eta(\sigma_m - \sigma_{cp})} \qquad \text{(S3)}$$

where σ_m and σ_{cp} are the electrical conductivity of the membrane and cell cytoplasm, respectively, and $\beta_k = (1 - L_k)/L_k$. In this study, we assumed that the erythrocytes had random orientations and were randomly distributed in the plasma. Thus, the effective conductivity of the blood was a scalar, despite the fact that the conductivity of each cell was a tensor.

The influence of erythrocyte aggregation on the effective conductivity of blood

Erythrocyte aggregation affects whole blood conductivity. Erythrocytes can form rouleaux aggregates, which resemble a pile of coins. We use the term aggregate size to specify the number of 'coins' in a pile. Because we studied the initial stage of aggregation, the aggregate consisted of several erythrocytes. Fig. S2a depicts an aggregate with an aggregate size of 5. In contrast, a disaggregated mixture has an aggregate size of 1.

We considered a suspension of randomly distributed rouleaux with the same aggregate sizes. It was necessary to simplify the model to allow theoretical calculations. A rouleaux of erythrocytes could be approximated as a heterogeneous cylinder, as shown in Fig. S2b. In the next step of simplification, we considered an anisotropic homogeneous cylinder. The principal conductivities of the anisotropic cylinders had three components $\sigma_{px} = \sigma_{py}$ and σ_{pz} (Fig. S2c). To determine the principal conductivity, we applied eqn (S3) in the limits under which a_x and a_y tend to infinity, yielding $\sigma_{px} = \sigma_{py}$ = 0.0253 S/m, or a_z tends to infinity, yielding σ_{pz} = 0.00658 S/m. Unfortunately, there is no known analytical solution for the equivalent conductivity of a mixture of randomly oriented short cylinders. We therefore used the model of prolate ellipsoids, instead of cylinders (Figure S2(d)).

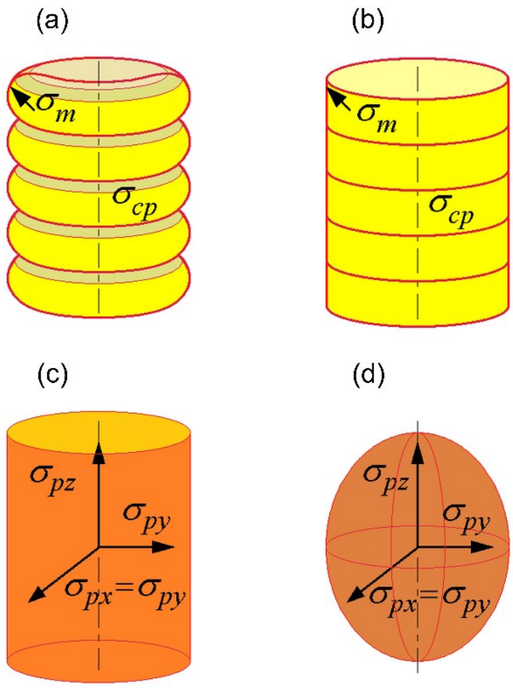

Fig. S2 Models for erythrocyte aggregation in rouleaux formation. The figure shows consistent simplification of the models that were used for theoretical calculations of blood conductivity during aggregation. (a) Erythrocyte aggregate for which the aggregate size was 5. (b) Model of heterogeneous cylinders. (c) An anisotropic homogeneous cylinder. (d) An anisotropic prolate ellipsoid.

We calculated the conductivities of blood samples that had HCT values of 35%, 45%, and 55% and contained aggregates of various sizes (Fig. S3). The maximum electrical conductivity was achieved with an aggregate size of 4 for all HCT values. The increase in conductivity was approximately 0.075 S/m for all levels of HCT, as compared with the conductivities of the corresponding disaggregated suspensions. In our experiments, we observed a maximum conductivity increase of 0.02 S/m for blood sample #2 (Fig. 2d).

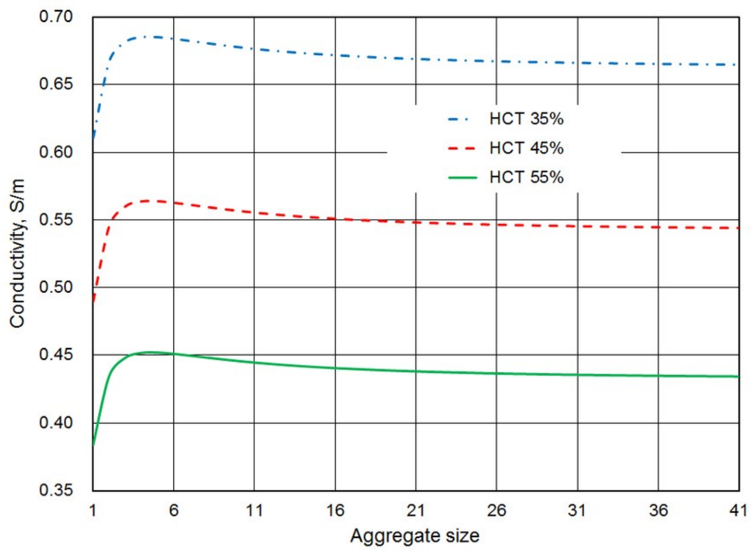

Fig. S3 Changes in blood conductivity with the aggregation of erythrocytes.

The theoretically calculated conductivities of the disaggregated erythrocyte suspension were σ = 0.611, 0.490, and 0.384 S/m with HCT values of 35%, 45%, and 55%, respectively (aggregate size of 1). The maximum electrical conductivities were σ_{max}(35%) = 0.685, σ_{max}(45%) = 0.564, and σ_{max}(55%) = 0.452 S/m with an aggregate size of 5 for all HCT values. Saturation was found to occur at a high aggregate size.

Reference

S1. Asami K. Characterization of heterogeneous systems by dielectric spectroscopy. Prog Polym Sci. 2002;27: 1617-1659.