The Role of Molecular Quantum Electrodynamics in Linear Aggregations of Red Blood Cells

K. Bradonjić, J. D. Swain, A. Widom

Physics Department, Northeastern University, Boston MA USA

Y. N. Srivastava

Physics Department, Northeastern University, Boston MA USA and Physics Department & INFN, University of Perugia, Perugia Italy

Despite the fact that red blood cells carry negative charges, under certain conditions they form cylindrical stacks, or “rouleaux”. It is observed that a form of the Casimir effect, generalizing the more well-known van der Waals forces, can provide the necessary attractive force to balance the electrostatic repulsion. Erythrocytes in plasma are modelled as negatively charged dielectric disks in an ionic solution, allowing predictions to be made about the conditions under which rouleaux will form. The results show qualitative and quantitative agreement with observations, and suggest new experiments and further applications to other biological systems, colloid chemistry and nanotechnology.

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It has been observed for many years that, under certain conditions, erythrocytes (red blood cells) form cylindrical stacks known as “linear aggregations”, or “rouleaux”.[1]. One may view blood as an ionic plasma in which red blood cells, and some other cellular colloidal particles, are suspended. Employing direct measurements of colloidal particle mobility, the red blood cells have been shown to carry a net negative charge.[2]

A long cylindrical stack of negatively charged red blood cells is shown schematically in Fig. 1. Attractive forces must exist in order to stabilize the rouleaux formation against the explosion which would take place if only the repulsive Coulomb interaction were existent[1, 2]. Our purpose is to argue that quantum radiation field Casimir forces provide the required rouleaux stability mechanism. The Casimir effect generalizes the well-known van der Waals forces by including electromagnetic retardation effects.[3]. Casimir forces are simpler in nature than the selective long range dispersion forces suggested by Fröhlich.[4, 5].

The essential physical principles underlying the Casimir forces are quite simple. When electromagnetic radiation interacts with condensed matter, the frequencies of the normal modes are Lamb shifted. Frequency shifts imply a change in the electromagnetic field free energy. In particular, at virtually zero temperature, the ground state zero point energy changes. A special case of such an energy shift may be found from the electromagnetic modes located between two parallel highly conducting plates. The energy shift then describes an attractive force between two plates and can be understood as being due to the change of zero-point modes when the distance between the plates is changed. The closer the plates, the more reduced is the vacuum energy and the greater the attractive force between the plates.[6]

For the problem at hand, we consider two dielectric plates each having cross sectional area $A$ and a dielectric constant $\varepsilon_1$. Between the two dielectric plates is a plasma medium of thickness $d$ and dielectric constant $\varepsilon_2$. The zero point electromagnetic field energy per unit plate area is calculable. If the dielectric plates both have a surface charge per unit area $\sigma$, then the electrostatic potential energy density may also be computed taking into account the Debye screening effects of a background plasma solution of ionization strength $I$. It is assumed in both calculations[7] that $d^2 \ll A$. The final result for the total free energy per unit area $u$ as a function of plate separation $d$ may be written[8]

$$u(d) = \frac{\sigma^2 A}{2\varepsilon_2} \left\{ e^{-d/A} - \left( \frac{\pi^2 h\nu\sqrt{\varepsilon_0\varepsilon_2}}{360\sigma\Lambda} \right) \frac{1}{d^3} \right\}. \quad (1)$$

The length $\Lambda$ describes electrolytic Debye screening and $\nu$ is the electromagnetic velocity parameter $\nu = c (\varepsilon_1 - \varepsilon_2)/(\varepsilon_1 + \varepsilon_2)^2$. The first term on the right hand side of Eq.(1) describes the Coulomb repulsion between red blood cells while the second term on the right hand side of Eq.(1) describes the Casimir attraction between red blood cells. The relative strength of the two effects is
quantitatively described by the dimensionless parameter

\[ a = \left( \frac{\pi^2 \hbar \sqrt{\varepsilon_0 \varepsilon_2}}{360 \sigma^2 \Lambda^4} \right) = \left( \frac{\pi^2 \hbar c \sqrt{\varepsilon_0 \varepsilon_2}}{360 \sigma^2 \Lambda^4} \right) \left( \frac{(\varepsilon_1 - \varepsilon_2)}{(\varepsilon_1 + \varepsilon_2)} \right)^2 \]  \hspace{1cm} (2)

where the Debye screening length \( \Lambda \) is related to the ionization strength \( I \) via \( \Lambda^2 = \{\varepsilon_2 k_B T / e^2 I\} \). The ionization strength in physical units is \( I = \sum z^2 n_a \) where \( n_a \) is the number of ions per cubic meter having an ionic charge \( z_a e \). In chemical units of moles per liter, one employs the ionization strength \( I = [10^{-3} \text{meter}^3/\text{liter}] (I/N_A) \) where Avogadro’s \( N_A \) is the number of ions per mole.

The above theory assumes that the parallel plates are maximally overlapping. If the plates were to slide over one another yet remaining parallel but not maximally overlapping, then the energy would be increased. Thus, there is a force parallel to the plates tending to pull them back into a maximally overlapping state. This force represents a lateral Casimir effect which, though rather obvious, does not appear to have been previously noted in the literature. It is centrally important in the context of the rouleaux formation problem since it supplies a force which will tend to align two plates so that they directly face each other with the largest possible area overlap. When many plates are stacked in a cylinder, the lateral force tends to give the cylinder transverse structural stability. With regard to compression stability, one must find a local minimum in the free energy per unit area \( u(d) \) with respect to the distance between the plates. A metastable equilibrium distance between plates arises from the local minimum at \( d_0 \) found from equating the force per unit area to zero; i.e. \( u'(d_0) = 0 \). There exists a critical parameter \( a_c \approx 1.57 \) such that a local rouleaux minimum exists if \( a < a_c \) and a local rouleaux minimum does not exist if \( a > a_c \). The resulting free energy per unit area \( u(d) \) is plotted in Fig.2 for several values of \( a \).

We fix the parameters in the model so that the capacitor plates correspond to erythrocytes and we employ room temperature. This leaves the ionic strength \( I \) and the relative to the vacuum permeability \( (\varepsilon_2/\varepsilon_0) \) of the blood plasma as free parameters. The phase diagram showing in which regions the rouleaux are stable is then exhibited in Fig.3. To stabilize the rouleaux it is theoretically necessary to have sufficiently small ionic strength and/or sufficiently large relative dielectric strength \( (\varepsilon_2/\varepsilon_0) \). The temperature dependence of the Casimir energy is very weak for the problem at hand. Temperature dependencies may be of importance in other biochemical systems.

It is important to note that rouleaux formations are usually observed in significantly artificially diluted blood. It is also known that such formations can be unstable in solutions of sufficiently high ionic strength. It would be of great interest for this model to investigate quantitatively the complete phase diagram.

In addition to providing an explanation for the otherwise mysterious attractive force which compensates the electrostatic repulsion of erythrocytes in rouleaux, this work opens up the possibility of numerous experimental tests, both in blood and in novel colloids with nonspherical particles in suspension. The fact that the Casimir energies involved are significant suggests that studies of colloidal systems such as blood may provide novel approaches to studies of the Casimir effect which avoid the extremely difficult techniques employed in past studies. It also suggests that the Casimir effect will be of importance in the burgeoning field of nanotechnology as devices approach the size of single cells.

FIG. 2: The variation of the free energy per unit area with the separation distance. The rouleaux formation can exist at the local minimum only if the parameter \( a \) in Eq. 2 is sufficiently small.

FIG. 3: The phase diagram showing the regions in which room temperature rouleaux formations are stable and in which regions such rouleaux formations are unstable. The reference ionization strength \( I_0 = 0.05 \text{ moles/liter} \) has been employed.
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