The Crucial Role of Water in a Phase Transition of Hemoglobin at Body Temperature

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The laboratories of Prof. Shu Chien and Paul Sung, the Whitaker Institute of Biomedical Engineering, UC San Diego, were the birth places of the observation of a temperature transition occurring at a critical temperature close to body temperature. The observation was found randomly and caused a series of experiments which we performed subsequently around the globe. We will present results of a couple of quite unusual experiments performed with red blood cells and hemoglobin of different species and we will work on answering the question whether or not and how hemoglobin can "sense" a species body temperature.

When aspirating human red blood cells (RBCs) into 1.3 µm pipettes (ΔP=-2.3kPa), a transition from blocking the pipette below Tc=36.3±0.3°C to passing it above occurred (micro pipette passage transition). With a 1.1 µm pipette no passage was seen and RBC volume measurements were possible. With increasing temperature RBCs lost volume significantly faster below than above a T_c=36.4±0.7 (volume transition). Colloid osmotic pressure (COP) measurements of RBCs in autologous plasma (25°C≤T≤39.5°C) showed a Tc at 37.1±0.2°C above which the COP rapidly decreased (COP transition). In NMR T1-measurements, the T1 of RBCs in autologous plasma changed from a linear (r=0.99) increment below Tc=37±1°C at a rate of 0.023 s/K into a parallel to the temperature axis above Tc (RBC T1 transition). Lately, incoherent quasielastic neutron scattering (Stadler, Zaccai, [†]Bueldt; Institut Laue-Langevin, Grenoble, France; [†]Research Centre Juelich, Juelich, Germany); experiments were performed to measure the temperature dependence of hemoglobin dynamics in human red blood cells. The technique probed average protein dynamics in the picosecond time range and Ångstrom length scale between 16.9 °C and 45.9 °C in heavy water buffer. Besides many interesting results, we found that the geometry of internal haemoglobin motion changed at 36.9 °C (Neutron scatter transition).

In conclusion: In the micropipette experiments, an amorphous hemoglobin-water gel forms within the spherical trail of the aspirated RBC. At Tc, a sudden fluidization of the gel occurs at which non-covalent bonds brake down. We suggest that this is initiated by a sudden phase transition occurring at Tc in the hemoglobin molecules entropy. All changes mentioned above happen at a distinct Tc close to body temperature. A Tc was found in hemoglobin of different species as well and all occurred at the species`body temperature. Thus, we concluded that Tc marks the set point of a normal body temperature which is inscribed in the primary structure of hemoglobin and possibly other proteins. A potential physical-biological mechanism will be presented.