

## Hindered diffusion of proteins in crowded solutions Implication of oxygen capture by Red Blood Cells

Stéphane LONGEVILLE<sup>1</sup> and Wolfgang DOSTER<sup>2</sup>

<sup>1</sup>Laboratoire Léon Brillouin (CEA-CNRS), CEA Saclay, 91191 Gif-sur-Yvette

<sup>2</sup>Physik Department e13 TU-München, James Franck Strasse, D-85747 Garching, Germany

E-mail: slongeville@cea.fr

The interior of cells is filled with a wide variety of objects with respect to size and shape. The major fraction is composed of proteins at millimolar concentration. The overall corresponding volume fraction can range up to 0.3 in particular cells. Protein crowding will affect those processes which depend on diffusion such as protein-assisted transport of small molecules like oxygen [1]. One of the central goal of our project is to clarify the question, whether the mobility of different components can be understood based on their intermolecular interactions... How much is the diffusion coefficient depressed with concentration? How does the diffusion coefficient behave in the vicinity of the intermolecular structure factor maximum, where the interaction is most pronounced? Can we discriminate between short-time and long-time diffusion coefficient? How is hydrodynamic interaction between proteins affecting diffusion?

We have combined SANS and NSE study of myoglobin and hemoglobin to study the effect of direct and indirect interactions on protein diffusion at a molecular level[2]. Myoglobin solutions were studied *in vitro* as a function of the concentration under physiological conditions and hemoglobin, that is inside red blood cells, directly *in vivo*.

We show that the mobility reduction is mainly due to hydrodynamic interactions up to volume fraction of  $\Phi \sim 0.2$ . The theories that describe accurately the hydrodynamic interactions for non charged colloids significantly fail for protein solutions [3].

By simple calculation we show the relevance of hemoglobin diffusion in oxygen uptake in the lungs. Without any free parameter we show that hemoglobin concentration in red blood cells is optimum for maximizing oxygen transport [4].

[1] R. John Ellis, Trends in Biochemical sciences, **26** (2001) 597-604. S. H. Northup, Current opinion in structural biology, **4** (1994), 269.

[2] S. Longeville, W. Doster and G. Kali, Chem. Phys. **292** (2003) 413-424

[3] S. Longeville and W. Doster (submitted).

[4] S. Longeville and W. Doster (in preparation).