# An in-silico Virtual-Patient Modelling of the effective transport of Drug-Carrying particles to treat Atherosclerosis

Traditional treatments have proven impotent as drug molecules act non-specifically by simply diffusing freely throughout the body, leading to undesirable side effects and are detrimental in achieving the required doses for positive outcomes. On the other hand, medical applications of nanotechnology have proven proficient enough to deliver protagonistic clinical breakthroughs in the diagnosis and treatment of several diseases using drug-carrying particles (DCPs). The use of DCPs provides promising and more effective alternative treatments, compared to traditional ones, to fight several diseases of the circulatory system, such as atherosclerosis (when the vascular wall thickens due to deposition of dead cells, like cholesterol, on the vascular wall), thrombosis (formation of a blood clot inside a vessel) and cerebrovascular amyloid angiopathy (when amyloid proteins build up on the walls of brain arteries).

To be able to perform such in-silico trials, however, a reliable and accurate constitutive model is needed addressing the vascular flow of DCPs. In most theoretical studies of NP transport in blood, the methodology employed is too simplistic. The aim of the project "An in-silico Virtual-Patient Modelling of the effective transport of Drug-Carrying particles to treat Atherosclerosis" was the development of in-silico tools which shall provide the means to test DCPs in virtual-patients and allow for their tailor-design in treating atherosclerosis. This will reduce the size and duration of, as well and as enable the design of more effective, human clinical trials, and lower both the development and time-to-market costs of new DCPs for treating atherosclerosis.

At the heart of such a procedure lies a mathematical model (a set of evolution/transport equations) which will allow the description of the vascular flow behavior of particles. This model is developed via the use of non-equilibrium thermodynamics (NET) and for this reason it will be, by construction, thermodynamically admissible, i.e. obeying the laws of thermodynamics. We compare the predictions of this new model against the experimental data of Antonova et al. (2014) [Antonova, N. Koseva, A. Kowalczuk, P. Riha, I. Ivanov, "Rheological and Electrical Properties of Polymeric Nanoparticle Solutions and their Influence on RBC Suspensions", Appl. Rheol. 24, 35190 (2014)] in the following figure for both spherical [part (a)] and rod-like nanoparticles [part (b)]. The comparison is very satisfactory.

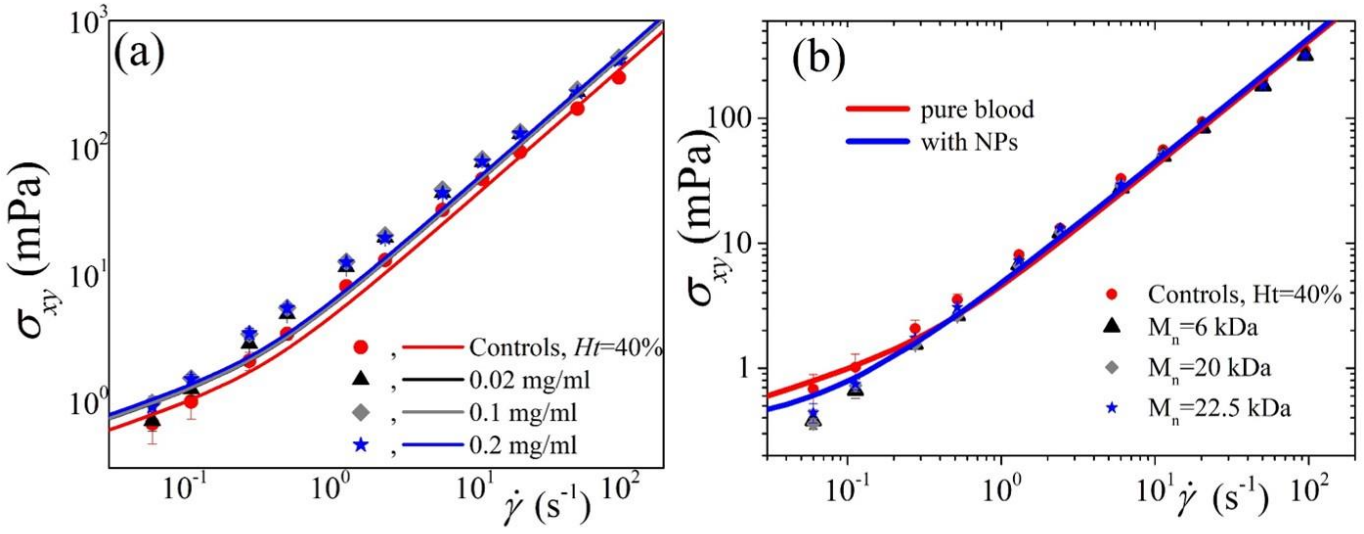


**Figure**: Comparison of the shear stress model predictions for a blood-nanoparticle suspension with *Ht*=40% using (a) spherical (R=14 nm) and (b) rod-like nanoparticles against the experimental rheological data of Antonova et al.

We have published three (3) papers at three international peer-reviewed journals:

1) P. S. Stephanou, and I. Ch. Tsimouri, A constitutive hemorheological model addressing the deformability of red blood cells in Ringer solutions, *Soft Matter* 16, 7585 (2020)

2) P. S. Stephanou, A constitutive hemorheological model addressing both the deformability and aggregation of red blood cells, *Physics of Fluids* 32, 103103 (2020)

3) P. S. Stephanou, Elucidating the rheological implications of adding particles in blood, *Rheologica Acta* 60, 603–616 (2021)].


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