

# The structural response of albumin to oxidation

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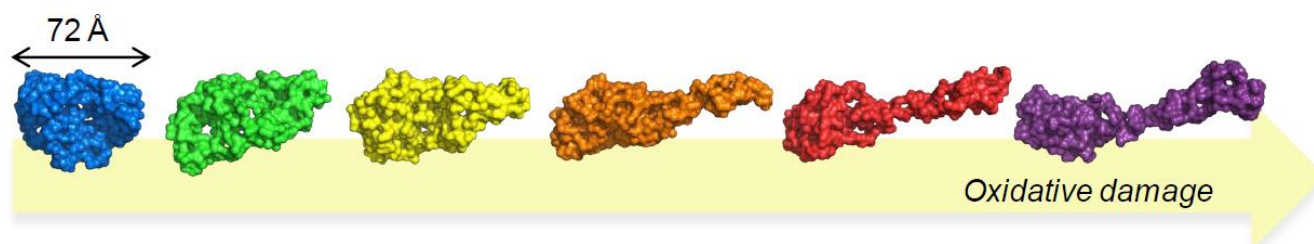
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The most abundant plasma protein, Human Serum Albumin (HSA), plays a key part in the body antioxidant defense against reactive species [1]. This study was aimed at correlating oxidant-induced chemical and structural effects on HSA and was performed thanks to the use of a multi-probe platform allowing for the simultaneous collection of small angle x-ray scattering (SAXS), UV-vis absorption spectra and fluorescence emission [2].

We demonstrated that, despite the chemical damage of the protein occurs since the very first addition of the potent oxidant sodium hypochlorite, its structure is fairly preserved up to relevant oxidative modification (oxidant/HSA molar ratio of 80). At stronger oxidation conditions a dose-dependent unfolding of HSA occurs in a critical range of oxidant/HSA molar ratio of 80-120 that is given by a progressive detachment of one of the protein end-domains (Figure 1). This conformational variation, which implies the loss of roughly one third of the  $\alpha$ -helix and the increase of the protein negative charge (detected by means of complementary circular dichroism and zeta potential measurements), is highly reproducible and represents a further fundamental property of this widely studied protein. The ability to tolerate high level of oxidation in a folded or only partially unfolded state, together with the stability to aggregation, confer to albumin optimal feature as a biological buffer to local formation of oxidants.



**Figure 1** Representative dummy-residue models fitting SEC-SAXS data of increasingly oxidized HSA samples. The hypochlorite/HSA molar ratios are: 0 (blue), 80 (green), 90 (yellow), 105 (orange), 120 (red), 170 (violet).

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[1] M. Roche, P. Rondeau, N. R. Singh, E. Tarnus and E. Bourdon, E., *FEBS Lett.*, 2008, **582**, 1783.

[2] S. Haas, T. S. Plivelic and C. Dicko, *J. Phys. Chem. B*, 2014, **118**, 2264.