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Comparing Antifouling Strategies on Silica Nanoparticles

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Motivation

Protein adsorption onto nanoparticles immersed in biological fluids alters fundamental surface properties and ultimately modifies the interaction of nanomaterials with biological systems.[1] Thus, finding antifouling strategies has been an active subfield of research within nanomedicine since its very origin.[2] In this context, developing theoretical tools for rapid screening of potential antifouling candidates is of paramount importance.

This work presents a theoretical study of antifouling strategies to prevent protein adsorption on silica nanoparticles using a molecular theory approach.[3] We evaluated surface modifications with short zwitterions (sulfobetaine, ZS), with PEG against the adsorption of lysozyme. This cationic protein is strongly adsorbed onto negatively born surfaces, thus representing a big challenge for antifouling coatings.[4] Theoretical results were compared with experimental characterizations using DLS, and UV-Vis spectroscopy.

Theoretical Approach

Molecular theory is a methodology based on mean field self-consistent approximations. It formulates the thermodynamic potential is considering all the relevant physicochemical contributions. Namely, conformational and translational entropy, electrostatic interactions, van der Waals attractions, steric repulsions, and acid-base equilibrium.

Simulations were performed at coarse-grain level, considering planar surfaces. Bare silica surfaces containing two silanol groups with pKa = 8.5 (75%) and = 4.5 (25%) were considered. PEG was represented by EO units. ZS was represented by methylene, quaternary amine (charge = +1) and sulfonate units (charge = -1). In coated surfaces with PEG or ZS, in addition to the coating groups, remnant silanols were considered. For lysozyme, each aminoacid was represented by its volume and pKa. For lysozyme, each aminoacid was represented by its volume and pKa.

References

(1) Corbo, C. et al. Nanomedicine 2016, 11, 81.

(2) Schlenoff, J. B. Langmuir 2014, 30, 9625.

(3) Ramirez, P. G. et al. J. Colloid Interf. Sci. 2019, 552, 701.

(4) Galdino, F. E. et al. Colloids Surfaces B Biointerfaces 2020, 186, 110677.

Acknoledgements

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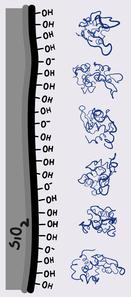
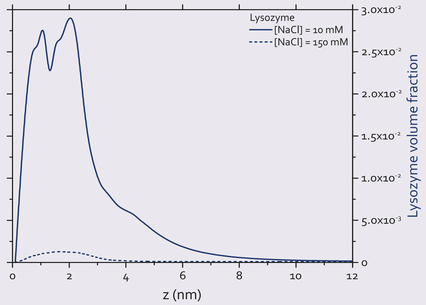
SIMULATIONS

Bare Silica

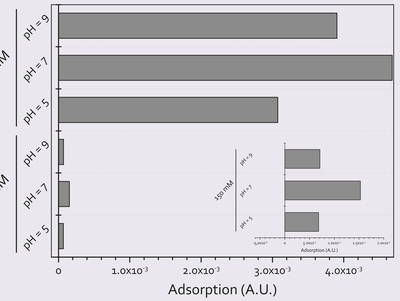


Simulated volume fraction of lysozyme with increasing distance (z) from silica surface at pH=7 and NaCl 10 and 150 mM. Bare silica surface was modelled with 4.6 silanols/nm²

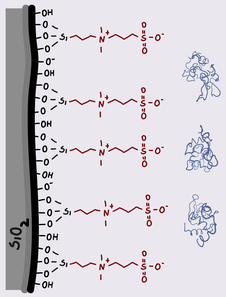
Bare silica was modelled containing 4.6 silanols/nm² on the surface.



Predicted lysozyme adsorption adsorption onto bare silica. The adsorption is mainly driven by electrostatic attraction. Thus, at higher ionic strength less adsorption is predicted.

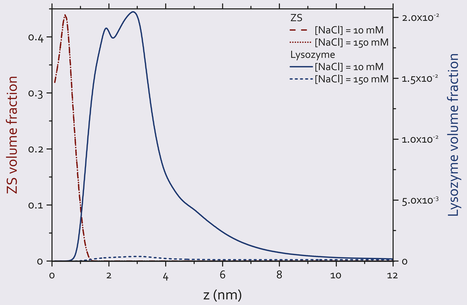


Silica-ZS

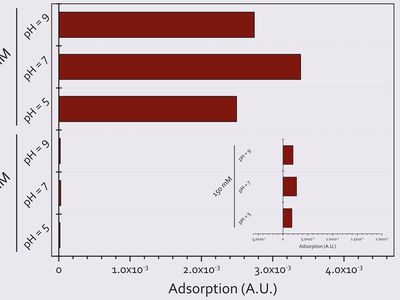


Simulated volume fraction of ZS and lysozyme with increasing distance (z) from silica surface pH=7 and NaCl 10 and 150 mM.

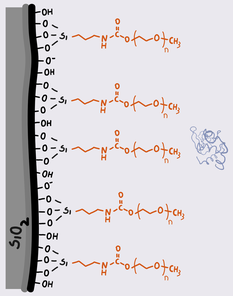
Silica – ZS was modeled containg 1 ZS group/nm² on the surface and 1 remnant silanol/nm²



Predicted lysozyme adsorption adsorption onto silica-ZS. Similar behavior than bare silica is observed at lower ionic strength. Different from bare silica, at higher ionic strength the adsorption is almost negligible.

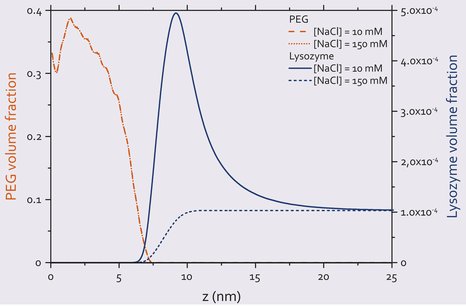


Silica-PEG

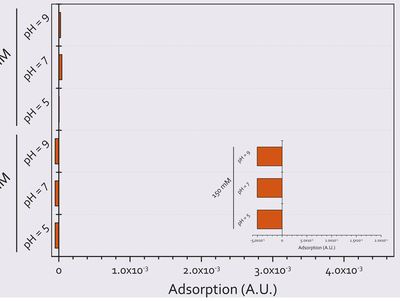


Simulated volume fraction of PEG and lysozyme with increasing distance (z) form silica surface pH=7 and NaCl 10 and 150 mM.

Silica – PEG was modeled containg 1 PEG (Mn = 1000) group/nm² on the surface and 1 remnant silanol/nm²

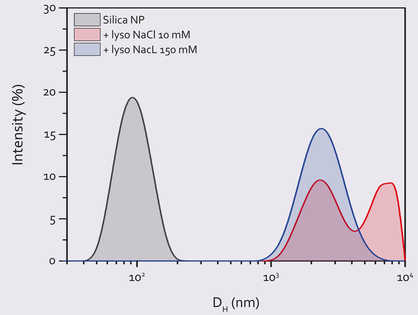


Predicted lysozyme adsorption adsorption onto silica-PEG. At NaCl 10mM, the adsorption is almost negligible. At higher ionic strengths the adsorption is negative. As can be seen, at both ionic strengths, PEG is better for preventing lysozyme adsorption. This can be attributed to steric repulsions.

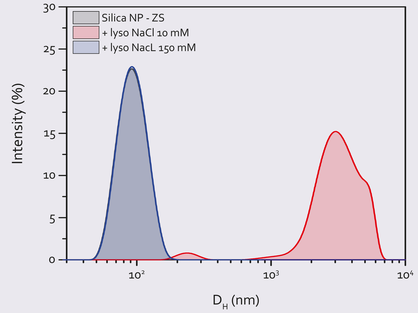


DLS results

Bare Silica NPs (Dh ~ 90nm) were incubated with lysozyme at pH 7.4 and 10 mM or 150 mM of NaCl. Upon adsorption of lysozyme, the silica surface negative charge is neutralized/decreased. Consequently, massive nanoparticle aggregation is observed.



Silica – ZS NPs prepared from the above bare silica NPs. were incubated with lysozyme at pH 7.4 and 10 mM or 150 mM of NaCl. At NaCl=10 mM Silica – ZS NPs behave as bare silica NPs. In contrast and as predicted by theory, at higher ionic salt concentration, the NPs do not adsorb lysozyme and, consequently, do not exhibit aggregation.



Silica-PEG NPs prepared from the above bare silica NPs. were incubated with lysozyme at pH 7.4 and 10 mM or 150 mM of NaCl. No modifications of Dh are observed at both salt concentrations, implying non detectable adsorption of lysozyme. However, at low salt concentration, residual lysozyme adsorption is detected (see inset showing Bradford analysis over NPs).