Buffer Specificity as a Governing Principle at Nano-Bio Interfaces

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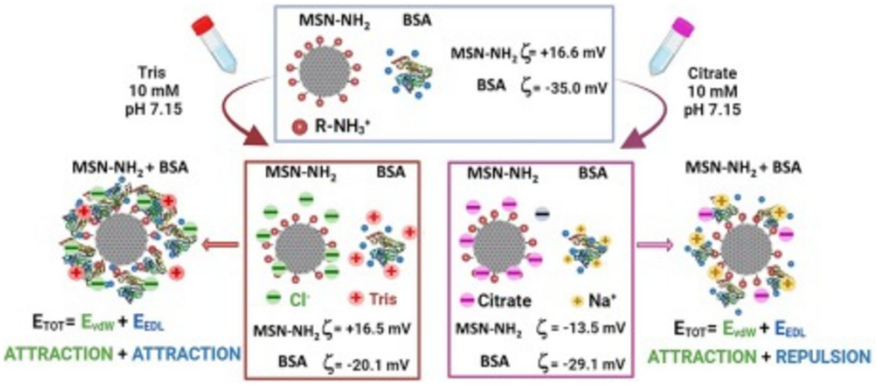
Specific ion effects are known to modulate biological interactions beyond what is predicted by pH and ionic strength alone. However, buffer species are still commonly treated as chemically inert components acting solely as pH regulators. Here, we show that buffer specificity constitutes a governing principle at nano–bio interfaces, controlling interfacial structure, interaction strength, and functional behaviour across different systems.

Within this framework, interactions at charged nano–bio interfaces are intrinsically buffer dependent. DNA–lipid bilayers and proteins adsorbing at solid surfaces display clear buffer hierarchies and non-monotonic dependencies on monovalent cations, revealing the limits of classical mean-field electrostatic descriptions [1]. These trends originate from the interplay between ion hydration, electrostatic screening, and ion-specific dispersion forces, which renormalize effective surface charge and interaction potentials. The same physical picture governs protein corona formation on amino-functionalized mesoporous silica nanoparticles. At identical pH and ionic strength, protein adsorption varies strongly with buffer identity, while buffer-induced surface charge modulation marks a breakdown of purely electrostatic models and highlights the role of ion-specific dispersion interactions [2]. Buffer specificity further affects mesoscopic organisation and biological function in ionizable lipid nanoparticles. In this case, buffer-dependent shifts of pH-controlled structural transitions in ionizable lipid/cholesterol mesophases alter curvature elasticity and stabilize or destabilize fusogenic inverse phases. These structural changes directly modulate endosomal escape and transfection efficiency, providing a clear mechanistic connection between ion-specific interfacial energetics and macroscopic functional outcomes [3].

Overall, these results demonstrate that buffers must be treated as active components of the interfacial free energy in nano–bio systems. Incorporating buffer-specific ion effects provides a unified conceptual framework connecting molecular interactions, mesoscopic organization, and biological function, with important implications for experimental reproducibility, predictive theory, and the rational design of biointerfaces and nanomedicine platforms.

Keywords:
ion and buffer-specific effects; nano–bio interfaces; DNA–lipid interactions; protein corona; lipid nanoparticles



Specific buffer effects on BSA adsorption on functionalized mesoporous silica nanoparticles (MSN-NH2) at pH 7.15

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