MINIMIZING SIGNAL INTERFERENCE FROM THE BIOLOGICAL SAMPLE MATRIX IN A BIOSENSOR FOR SEPSIS: THE PIVOTAL ROLE OF WATER

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Water is essential to Life. This understatement stems from the vital role this ubiquitous fluid plays in a wide variety of biological and other processes due to its many unique dissolving, dissociating/lysing and solvating properties. It thus should not come as a surprise that water has been hypothesized to also be a key element in the antifouling of surfaces, although the precise underlying mechanism is still a matter of debate. Being a topic of great interest in both fundamental and applied biophysical chemistry, we recently set out to try and solve this puzzle through the aid of a series of both empirical and computational studies conducted with new organosiloxane surface chemistry. A key finding from initial experiments relying on ultra-high frequency acoustic wave sensor technology was the observation that, among a series of ultrathin coatings with systematically-varied chemical structure, only the monoethylene glycol (MEG) variety incorporating a single, internal ether oxygen atom in the chains was able to dramatically alter full serum adsorption – the synergy being strongest for the MEG-OH system featuring distal hydroxyl moieties. We proposed this antifouling behaviour to be deeply rooted in the coatings' state of hydration, the internal ether atoms of oxygen being pivotal in the instigation of a special intrafilm zone of hydration from which an interfacial phase of water physically distinct from ordinary bulk would stem. Neutron reflectometry later corroborated this hypothesis revealing the existence of such a distinctive hydration pattern for MEG-OH. This result, and that of molecular dynamic simulations, collectively allowed for a molecular-level antifouling mechanism to be rationalized in terms of a set of basic requirements (surface hydrophilicity, kosmotropicity, and hydration strength, as well as water dynamicity). Their fulfilment would give rise to a stable permeant network of water, whose disturbance *via* dehydration upon (serum) protein adsorption would constitute an energetic penalty and generate repulsive forces. Overall, our investigation yielded solid evidence to suggest that the remarkable antifouling properties of MEG-OH surface chemistry are indeed intimately linked to its hydrogel-like characteristics.

It is the object of the present contribution – in order to minimize signal interference from the biological sample matrix – to integrate antifouling MEG-OH surface chemistry into a real-world biosensor capable of detecting bacterial lipopolysaccharide (LPS), also known as 'endotoxin', one of the most potent activators of sepsis (a life-threatening condition affecting millions of individuals worldwide). LPS detection is conducted using ultra-high frequency acoustic wave sensing in tandem with an ethylene glycol-based mixed organosiloxane hydrogel coating imposed on piezoelectric quartz discs and biofunctionalized with polymyxin B, a cyclic peptide antibiotic with high affinity for LPS target analyte. Dose-response measurements are performed in a real-time and label-free fashion using full human blood plasma microsamples (50 µL) over a wide range of LPS concentrations. In terms of analytical performance, this hydrogel-based biosensor assay is able to qualitatively differentiate low from high endotoxin levels (~300 pg/mL LPS cut-off) in a rapid manner (~35 min per replicate). Such an achievement offers, in principle, the possibility for clinicians to expeditiously determine the appropriate course of action to adopt for patients suspected of being afflicted with LPS-induced sepsis.