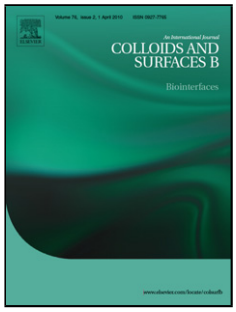

Title: Implications of lipid monolayer charge characteristics on their selective interactions with a short antimicrobial peptide

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<AT>Implications of lipid monolayer charge characteristics on their selective interactions with a short antimicrobial peptide

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<ABS-Head><ABS-HEAD>Graphical abstract
<ABS-P>► Influence of membrane surface charges on the selective binding of antimicrobial peptide G4 ($G(IIKK)_4I\text{-}NH_2$), where DPPC stands for 1,2-dipalmitoyl-sn-glycero-3-phosphocholine and DPPG for 1,2-dipalmitoyl-sn-glycero-3-phospho-(1'-rac-glycerol) (sodium salt).
<ABS-HEAD>Highlights► Effects of lipid monolayer charges on the binding of antimicrobial peptides; ► Structure and composition of lipid monolayers; ► Impact upon antimicrobial peptide binding; ► Relevance to antimicrobial activity.
<ABS-HEAD>Abstract
<ABS-P>Many antibacterial peptides (AMPs) target bacterial membranes and they kill bacteria by causing structural disruptions. One of the fundamental issues however lies in the selective responses of AMPs to different cell membranes as a lack of selectivity can elicit toxic side effects to mammalian host cells. A key difference between the outer surfaces of bacterial and mammalian cells is the charge characteristics. We report a careful study of the binding of one of the representative AMPs, with the general sequence $G(IIKK)_4I\text{-}NH_2$ (G_4), to the spread lipid monolayers of DPPC (1,2-dipalmitoyl-sn-glycero-3-phosphocholine) and DPPG (1,2-dipalmitoyl-sn-glycero-3-phospho-(1'-rac-glycerol) (sodium salt)) mimicking the charge difference between them, using the combined measurements from Langmuir trough, Brewster angle microscopy (BAM) and neutron reflectivity (NR). The difference in pressure rise upon peptide addition into the subphase clearly demonstrated the different interactions arising from different lipid charge features. Morphological changes from the BAM imaging confirmed the association of the peptide into the lipid monolayers, but there was little difference between them. However, NR studies revealed that the peptide bound 4 times more onto DPPG monolayer than onto the DPPC monolayer. Importantly, whilst the peptide could only be associated with the head groups of DPPC it was well penetrated into the entire DPPG monolayer, showing that the electrostatic interaction strengthened the hydrophobic interaction and that the combined molecular interactive processes increased the power of G_4 in disrupting the charged membranes. The results are discussed in the context of general antibacterial actions as observed from other AMPs and membrane lytic actions.