How does the antimicrobial peptide NK-2 distinguish between procaryotic and eucaryotic membranes?

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Antimicrobial peptides are part of the innate immune system of many animals and plants and may kill bacteria via permeabilization of the bacterial cell membrane. A peptide showing high antimicrobial activity combined with low toxicity for eucaryotic cells is the highly cationic and alpha-helical peptide NK-2 [1]. Its selectivity for procaryotes is attributed to the difference in lipid composition of the outer leaflets of pro- and eucaryotic cell membranes [2]. In vitro studies by others have revealed significant affinity of NK-2 for phosphatidyl-ethanolamine (PE) exposed by procaryotes but not phosphatidyl-choline (PC) exposed by eucaryotes, both lipids being zwitterionic. We reproduce this behavior by means of molecular dynamics simulations using a coarse grained model and thermodynamic integration and reveal the underlying mechanism.

[1] T. Jacobs, H. Bruhn, I. Gaworski, B. Fleischer, and M. Leippe, *Antim. Agent. Chemot*h. , **2003,** 47**,** 607

[2] R. Willumeit, M. Kumpugdee, S. S. Funari, K. Lohner, B. P. Navas, K. Brandenburg, S. Linser, and J. Andrä, *Biochim. Biophys. Acta-Biomemebr.*, **2005**, 1669(2), 125