fourier transform IR Spectroscopy) as a function of temperature for DMPC and DMPG liposomes in the presence and the absence of R,R4,R7 peptides. Spectra revealed a significant shift of the DMPG transition temperature for ARG4 and ARG 7 reflecting significant changes in the membrane order and the motional freedom of the methylene groups whereas the same peptides did not affect significantly DMPC transition. No changes were observed with arginine alone for both lipids. Molecular modelling showed insertion of part of R7 deeply in the DMPG bilayer that was not observed with free arginine.
Overall the data demonstrate that R7 penetrates into and destabilise the DMPG bilayer which could explain in molecular terms the cell uptake of these arginine oligopeptides. The fact that such a destabilising effect was not observed with the lysine peptides also suggest that the arginine -lipid interaction is quite specific in agreement with the phosphate_guanidine interaction identified by molecular modelling.

440-Pos
Molecular Electroporation and the Transduction of Oligoarginines
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Certain short polycations, such as TAT and polyarginine, rapidly pass through the plasma membranes of mammalian cells by an unknown mechanism called transduction as well as by endocytosis and macropinocytosis. These cell-penetrating peptides (CPPs) promise to be medically useful when fused to biologically active peptides. I offer a simple model in which one or more CPPs and the phosphatidylserines of the inner leaflet form a kind of capacitor with a voltage high enough to create a molecular electropore. The model is consistent with an empirical upper limit on the cargo peptide of about 50 amino acids. More importantly, it fits experimental data on how the transduction of a polyarginine-fluorophore into mouse C2C12 myoblasts depends on the number of arginines in the CPP and on the CPP concentration. The model makes three testable predictions.

441-Pos
Influence of Lipid Composition on the Orientational State of the Antimicrobial Peptide MSI-103 in Membranes. a Solid-State NMR Study
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The antimicrobial peptide MSI-103 is known to undergo a functionally relevant re-orientation in membranes from a surface-aligned S-state to a tilted T-state depending on the peptide concentration and lipid phase. Here, we have used solid-state NMR on the ^{2}H-labeled peptide to determine its orientational state in membranes composed of different types of lipids.
In phosphatidylcholine (PC) bilayers with different acyl chains, there is no effect of the chain length on the peptide orientation. However, a distinct difference is observed in the peptide response to saturated and unsaturated acyl chains. In unsaturated lipids, the peptide always remains in the surface-bound S-state, with its alpha-helical axis perpendicular to the bilayer normal at a tilt angle close to 90°. Only in saturated lipids it is able to insert into the membrane in a tilted T-state, with an angle of around 125°. Interestingly, when lyso-PC is added, the T-state is found to be stable also in unsaturated lipids. These results can be explained by the shape of the lipids; especially the relative area of head group and acyl chains, as will be discussed in detail. It is known that the presence of anionic lipids leads to a higher affinity of the cationic peptide towards bacterial membranes, but such electrostatic effects *per se* do not suffice to induce any change in peptide orientation. Interestingly, we found that the presence of cholesterol prevents MSI-103 from binding to the membrane in any ordered state, but rather induces the formation of immobilized peptide aggregates. This observation can essentially explain the selective membrane-permeabilizing action of MSI-103 on bacteria compared to eukaryotic cells which contain cholesterol.

442-Pos
Understanding the Importance of Residue 13 and the C-terminus on the Structure and Activity of the Amphibian Antimicrobial Peptide, Aurein 2.2
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Previous studies on the cationic antimicrobial aurein 2.2 and 2.3 peptides in DMPC/DMPG and POPC/POPG membranes have shown that bilayer thickness and PG content have significant impact on the interaction of these peptides with membrane bilayers, in a concentration- and peptide sequence-dependent manner [1]. In addition, DiSC$_3$5 assay results have indicated that aurein 2.2 induces greater membrane leakage than aurein 2.3 in *S. aureus* C622 [1]. The difference between aurein 2.2 and aurein 2.3 is a L13I mutation at residue 13.
In order to understand the importance of the nature of the residue at position 13, we have further studied L13A, L13F, and L13V mutant aurein 2.2 peptides. In addition, we have investigated a number of peptides with truncations at the C-terminus. Solution CD results demonstrate that the L13F mutation and truncation of the C-terminus by 6 residues result in decreased helical content, while the L13A or L13V mutation and truncation of the C-terminus by three residues shows no effect on the structure. Oriented CD and ^{31}P NMR spectroscopy results show that only an extensive C-terminal truncation reduces the ability of the peptide to insert into the lipid bilayers and to disorder the headgroups at lower peptide concentrations. The implication of these results in terms of antimicrobial activity will be discussed.
[1] Cheng, J.T.J. *et al.* 2009. *Biophys. J.* 96: 552-565.

443-Pos
Temperature Dependence of the Interaction of Antimicrobial Peptides With Mixed Lipid Bilayers
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The interactions of two α-helical antimicrobial peptides, aurein 1.2 (13 residues) and maculatin 1.1 (21 residues), with model membranes have been examined using solid-state NMR and surface plasmon resonance techniques. P-31 NMR of multilamellar (MLV) dimyristoylphosphatidycholine (DMPC) vesicles with aurein 1.2 revealed minor disruptions in the bilayer above the gel-liquid phase transition. However, below the phase transition temperature an isotropic signal was observed, indicating that the peptide disrupted the bilayer and formed small, rapidly tumbling aggregates ~ 22 nm in diameter as determined by light scattering measurements. However, the isotropic signal was not seen with the longer peptide. Additional experiments conducted using different lipid compositions revealed that both fluidity and temperature influence the peptide interaction. Gel phase lipid bilayers were more strongly affected by the peptide although similar effects were observed at lower temperatures in unsaturated chain lipid bilayers in the liquid crystalline state.
A preliminary study on membranes mimicking the lipid composition of S. aureus has demonstrated a disruptive effect on the bilayer organization by addition of maculatin 1.1, a potent antibacterial peptide. As revealed in P-31 static NMR spectra of MLV composed of dimyristoylphosphatidylglycerol (DMPG) and tetramyristoylcardiolipin (TMCL), the peptide promoted formation of a dominant isotropic phase at 15°C, well below the liquid-crystalline transition temperature; while the lamellar organization was mainly restored above 50°C and an intermediate state was observed at 30°C. Interestingly, relaxation experiments on MLV without peptide indicated coexistence of two populations in the temperature range 30-50°C, most likely composed of fluid DMPG and rigid TMCL. The antimicrobial peptide may insert preferentially at domain boundaries, using defects in membrane packing to lower energy costs. Further experiments are ongoing to determine the nature of the isotropic phase and its relevance to antimicrobial activity.

444-Pos
Determination of a High-Definition Structure of Antimicrobial Piscidin-3 At the Water-Bilayer Interface
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Piscidins are a family of naturally occurring host-defense antibiotics that are short, cationic, and amphipathic in structure. Extensive NMR studies of membrane-bound Piscidin 1 (p1), a 22-mer, have shown that the peptide is composed of two alpha-helical segments that lie in the plane of the lipid bilayer. These segments are joined by a kink at residue glycine 13 (G_{13}). Previous studies of Piscidin 3 (p3), another isoform of piscidin, have revealed decreased antimicrobial and hemolytic activity when compared to p1. The goal of this research is to create a high-definition backbone structure of membrane-bound p3 in order to discern the atomic-level structural features that account for the differences in activity of the two peptides. Understanding the mechanistic differences is critical for the development of novel antimicrobial drugs.
Circular dichroism has previously shown that p3 adopts an alpha-helical structure in the presence of micelles and phospholipid bilayers. Using hydrated, oriented lipid bilayers that mimic bacterial cell membranes and 2D HETCOR (Heteronuclear Correlation) solid-state NMR experiments, high-resolution ^{15}N and ^{1}H Chemical Shifts (CS), and ^{15}N-^{1}H Dipolar Couplings (DC) have been obtained from selectively ^{15}N-backbone labeled p3. Spectra collected at high and ultra high magnetic field have been analyzed to obtain the backbone structure and orientation of membrane-bound p3. This analysis has revealed that p3 also consists of two alpha-helical segments kinked at G_{13}. Interestingly, the rotational angles of p1 and p3 about their own helical axes within the plane