University of Groningen

Antimicrobial Peptides Induce Growth of Phosphatidylglycerol Domains in a Model Bacterial Membrane

Polyansky, Anton A.; Ramaswamy, Rajesh; Volynsky, Pavel E.; Sbalzarini, Ivo F.; Marrink, Siewert J.; Efremov, Roman G.

Published in:
JOURNAL OF PHYSICAL CHEMISTRY LETTERS

DOI:
[10.1021/jz101163e](https://doi.org/10.1021/jz101163e)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2010

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Polyansky, A. A., Ramaswamy, R., Volynsky, P. E., Sbalzarini, I. F., Marrink, S. J., & Efremov, R. G. (2010). Antimicrobial Peptides Induce Growth of Phosphatidylglycerol Domains in a Model Bacterial Membrane. *JOURNAL OF PHYSICAL CHEMISTRY LETTERS*, 1(20), 3108-3111.
<https://doi.org/10.1021/jz101163e>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Supporting information

Antimicrobial Peptides Induce Growth of Phosphatidylglycerol Domains in a Model Bacterial Membrane

Anton A. Polyansky^{*,†,‡}, Rajesh Ramaswamy[§], Pavel E. Volynsky[†], Ivo F. Sbalzarini[§], Siewert J.

Marrink[‡], Roman G. Efremov[†]

[†]*M.M. Shemyakin and Yu.A. Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow, 117997, Russia, and* [‡]*Groningen Biomolecular Sciences and Biotechnology Institute & Zernike Institute for Advanced Materials, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands, and* [§]*Institute of Theoretical Computer Science and Swiss Institute of Bioinformatics, ETH Zurich, CH-8092 Zurich, Switzerland, and* [‡]*Max F. Perutz Laboratories, GmbH Campus Vienna Biocenter 5, A-1030 Vienna, Austria*

Table S1. Systems studied.

Abbreviation	Composition	MD, μs^*	A_L , $\text{\AA}^2$	D_{HH} , $\text{\AA}$
<i>Coarse-grained (CG) MD systems[#]</i>				
256 MD	180DOPE/76DOPG/2500W/76Na+	4	68.5	43.2
512 MD	360PE/152PG/8000W/152Na+	4	68.3	44.3
2048 MD	1440PE/608PG/30000W/608Na+	4	68.4	44.5
256 MD+AMPs	12 Ltc1 [†] /180PE/76PG/2500W/44Cl-	4	70.2	42.6
2048 MD+AMPs	96 Ltc1/1440PE/608PG/76000W/352Cl-	4	72.1	43.1
<i>Randomly generated CG-bilayers[‡]</i>				
256 Rnd	180DOPE/76DOPG		68.5	43.2
512 Rnd	360PE/152PG		68.3	44.3
2048 Rnd	1440PE/608PG		68.4	44.5

* hereinafter effective time⁹

[#] all systems were simulated at 315 K; the last 3 μs were used for analysis (75 snapshots), for ACF curves statistics were collected over the last 400 ns of MD (with 4 ns time resolution)

[†] Ltc1: SMWSGMWRRKLLKLLRNALKKLLKGEK

[‡] 75 randomly generated snapshots were used for the analysis.

Simulation setup and equilibration

In the initial configuration of all systems (256, 512, and 2048 lipids), water molecules and sodium counterions were randomly placed in the simulation box. The bilayer structures were obtained after 400 ns (effective time) of MD simulation. During this time, the lipid molecules self-assembled into a bilayer surrounded by solvent and sodium ions. These bilayers have no predefined packing characteristic. In both cases, PE and PG lipids are equally distributed across the bilayer leaflets, thus maintaining the initial ratio in each of the leaflets (PG content in a leaflet varies from 29 to 32 %). Subsequently, the pre-assembled bilayers undergo 4 μs MD relaxation both without and with the presence of AMPs (see Table S1). AMPs are initially placed randomly in the aqueous environment at distances >10 $\text{\AA}$ from the surface of the 256MD and 2048MD bilayers. We use five 4 μs MD trajectories (256MD, 512MD, 2048MD, 256MD+AMPs, and 2048MD+AMPs) for the analysis. The global structure parameters (area per lipid, A_L , and bilayer thickness, D_{HH}) of the “pure” bilayers reach equilibrium values ($A_L \sim 68$ $\text{\AA}^2$) after less than 400 ns. We also observe that binding of AMPs leads to the well-known effect of increasing A_L (by about 3 $\text{\AA}^2$ on average, Table S1).

Analysis details

The MD data are used for analyzing three structural and dynamic characteristics of PG-domains: (1) domain size (number of PG lipids in a domain), (2) 2D organization within the membrane plane (2D radial distribution function, RDF), and (3) characteristic relaxation times (spatially averaged time-autocorrelation function, ACF).

In order to reduce the noise at large cluster sizes we use logarithmic binning for the domain size distributions: $P(N_d)$: $2^{n-1} \leq N_d \leq 2^n - 1$, where $P(N_d)$ is the probability of finding a domain of size N_d in a given bin n .

The RDF curves are calculated over 2D grids spanning the bilayer surface (“bilayer maps”). They show the normalized average fraction of grid cells occupied by PG lipids at a distance R from any other PG cell.

ACF values are fitted by a sum of two exponential functions using the following expression:
 $ACF(t) = A \times \exp(-t/\tau_1) + B \times \exp(-t/\tau_2)$. The coefficients A and B quantify the contribution of each exponent with characteristic relaxation times τ_1 and τ_2 , respectively.

Figure S1. Sodium counterions preferably co-localize with PG heads. Pair-wise radial distribution functions (RDF) for lipid heads and sodium counterions were calculated for the 2048MD system over the last 3 μ s of the productive run.