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The effect of interaction between K^+ ions and gramicidin D on the lecithin membrane interfacial tension

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Abstract

The effect of the presence of gramicidin D in a lecithin membrane on its interfacial tension has been studied. The studies have been carried out at various forming solution compositions and at various potassium ion concentrations in the electrolyte solution. Potassium chloride was used as the electrolyte. The complex was formed between the gramicidin molecule and K^+ ion. The following parameters describing the complex were determined: the surface area occupied by GK^+ complex (A_{GK^+}), the interfacial tension of the GK^+ membrane complex (γ_{GK^+}), and the stability constant of the gramicidin–K^+ complex (K). These values are 156 $Å^2$, 1.89 mN m^{-1} and 0.033 m^3 mol^{-1}, respectively.

Keywords: Interfacial tension; Lecithin; Bilayer lipid membranes; Gramicidin D

1. Introduction

Membranes are present in all known biological systems, which are able to live independently. They separate the cell from its environment, and they can separate it' interior into smaller regions having different functions [1–3].

Experiments are carried out with simple membrane models, e.g., artificial phospholipids membranes, for a better understanding of the properties of natural membranes. Such membranes have been obtained either as a single lipid layer on an aqueous solution surface, as a lipid double-layer membrane formed in the Teflon partition, or as liposomes [3].

Lipid bilayers have been most widely used in modelling transport phenomena (mainly in the case of electrolytes) across biological membranes. A class of transport promoting substances are the modifiers forming so-called ionic channels in lipid membranes; gramicidin, alamecithin, monamosicin, nystatin, and hemocyanin belong to this group. Molecules of these modifiers are incorporated into the membrane and form water-saturated pores (ionic channels), which constitute the ion passage paths [2–4].

The gramicidin peptide forms the smallest known protein ion channel, a dimmer consisting of two gramicidin molecules that contain 15 amino acid residues each. Because of a small size, its relative easy partitions into membranes to form channels and is relatively easy synthesized [5–7]. Gramicidin has been used as a useful model system allowing to study membrane permeability, the principles of membrane protein structure, and the mechanisms of protein–lipid interactions [8–10].

Different experimental techniques have been used to elucidate the permeability characteristics of the gramicidin channel. Single [11–13] and multichannel [14] current–voltage measurements have been particularly popular.

Many details about the topology and function of ion channels have been unveiled by using a variety of techniques including molecular biology, mutagenesis, patch-clamp recordings, and molecular dynamic simulation. As bacterial membranes provide powerful systems for expressing channel proteins at a high level for the crystallization and X-ray analysis, the three-dimensional

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structures of channel proteins have begun to come into sight. For example, a crystal structure of a bacterial K^+ channel (KcsA) has been resolved at a resolution of 3.4 Å [15]. This structure is remarkably similar to the model inferred from years of electrophysiological studies on mutated and wild type K^+ channels [16].

A study of the effect of the presence of gramicidin D on the interfacial tension of the lecithin membrane as a function on electrolyte solution concentration and membrane composition is the aim of this work.

2. Theory

Gramicidin is the compound, which can be integrally built-in into the membrane. The length of two connected gramicidin molecules is similar to the thickness of the hydrophobic part of lecithin bilayers. For this reason, the effect of the presence of gramicidin in the bilayer on interfacial tension can be described as similar to that of cholesterol [17]; that is, the interfacial tension of such membrane should be a sum of lecithin and gramicidin interfacial tensions values.

The K^+ ion forms a complex with gramicidin molecule in the membrane:

$$G + K^+ \Leftrightarrow GK^+ \tag{1}$$

The membrane interfacial tension, γ, can be written taking advantage of additivity of individual gramicidin-lipid membrane component contributions:

$$\gamma = \gamma_L S_L + \gamma_G S_G + \gamma_{GK^+} S_{GK^+} \tag{2}$$

$$S_L + S_G + S_{GK^+} = 1$$

$$A_L a_L = S_L$$

$$A_G a_G = S_G$$

$$A_{GK^+} a_{GK^+} = S_{GK^+}$$

The respective components of interfacial tension are denoted by γ_L, γ_G, γ_{GK^+}[mN m^{-1}] and represent the interfacial tensions of the membrane formed from lecithin, gramicidin, and the GK^+ complex, respectively; S_L, S_G, S_{GK^+} are the surface fractions occupied by lecithin, gramicidin, and the GK^+ complex, respectively; A_L, A_G, A_{GK^+}[m^2 mol^{-1}] are the surface areas occupied by lecithin, gramicidin, and the GK^+ complex, respectively; and a_L, a_G, a_{GK^+}[mol m^{-2}] are the activities of lecithin, gramicidin, and the GK^+ complex, respectively.

The association constant of the gramicidin–K^+ complex can be presented in the form:

$$K = \frac{a_{GK^+}}{a_G a_{K^+}} \tag{3}$$

where a_{K^+}[mol m^{-3}] is K^+ ions activity in the solution.

The lecithin and the analytical gramicidin concentration ratio in the membrane are denoted by n_G. We make an assumption that the gramicidin and lecithin ratio in the membrane is the same like in forming solution. Thus, n_G is described by the equation:

$$\frac{a_L}{a_G + a_{GK^+}} = \frac{m_L M_G}{m_G M_L} = n_G$$

where m_L, m_G are the masses of lecithin and gramicidin in the forming solution, respectively, M_L and M_G, are the molar masses of lecithin and gramicidin, respectively.

The solutions with gramicidin to lecithin weight equal to 1:10, 1:20, 1:30, 1:40 ratios were used in the experiments.

Elimination of S_L, S_G, S_{GK^+}, a_L, a_G, a_{GK^+} yielded the equation:

$$\gamma = -\frac{\left(A_L n_G^{-1} + A_{GK^+}\right)K}{A_L n_G^{-1} + A_G} a_{K^+}\gamma + \frac{\left(\gamma_L A_L n_G^{-1} + \gamma_{GK^+} A_{GK^+}\right)K}{A_L n_G^{-1} + A_G} a_{K^+} + \frac{\gamma_L A_L n_G^{-1} + \gamma_G A_G}{A_L n_G^{-1} + A_G} \tag{4}$$

Eq. (4) presents the dependence of modified lipid membrane on gramicidin D in the K^+ ion solution as a function of interfacial tension.

3. Experimental

3.1. Methods

The interfacial tension, γ, of the lipid bilayer was determined by measuring the curvature radius, R, of the convex surface formed by applying a pressure difference, Δp, on its sides. This method was based on Young and Laplace's equation [18].

$$2\gamma = R\Delta p.$$

3.2. Measurements

The apparatus and the measurement method of the interfacial tension were described in the papers [17,19,20]. The membranes were formed by the Mueller–Rudin method [21] on the flat end of the Teflon element. Both chambers of the measuring vessel were filled with the electrolyte solution. The forming solution was brought with a micropipette to the flat wall of the Teflon element. Then, a pressure was applied to the left chamber using a manometer (VEB).

The convexity of the lipid membrane cap was measured with a 0.05-mm precision instrument reading. This value together with the Teflon element diameter corresponding to the lipid cap diameter yielded the radius of curvature.

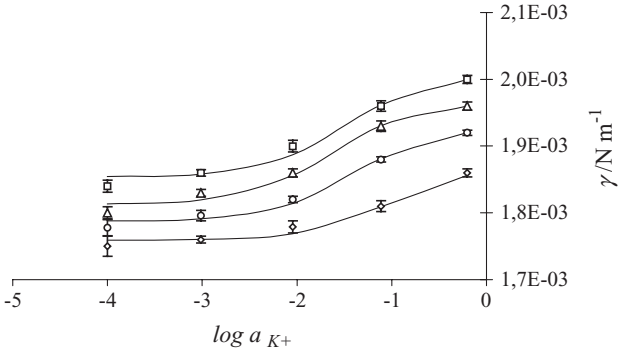

Fig. 1. The dependence of the interfacial tension of a lipid membrane formed from phosphatidylcholine modified with gramicidin D on the electrolyte solution concentration for different PC/G ratios: (□)—1:40, (△)—1:30, (○)—1:20, (◇)—1:10; the experimental values are marked by points and the theoretical ones by curves.

The interfacial tension was measured on freshly created bilayer lipid membrane 12–15 times for each electrolyte solution. For each membrane, about 10 instrument readings of the lipid spherical cap diameter, formed by pressure difference applied on both sides, were made. These measurements were made within the whole range, from the very low values of the lipid spherical cap diameter to those almost equal to the Teflon element radius. From all of instrument readings (100–150), the arithmetic mean and standard deviation were enumerated. Measurements with preparation of the electrolyte solution were made two to three times in order to test the repeatability of these determinations. The experimental results are presented in the Fig. 1 with error bars.

3.3. Materials

The lipid bilayer was formed from Fluka (Switzerland) production of 99% egg lecithin (3-*sn*-phosphatidylcholine) and from gramicidin D produced by Sigma (USA). Lecithin was dissolved in chloroform, and the solvent was evaporated in an atmosphere of argon. Gramicidin D was used without any purification. The lecithin and gramicidin solutions containing 20 mg substance per 1 cm^3 of solvent (*n*-decane) were prepared. Proper diluting and mixing of the stock solutions prepared forming solutions containing various lecithin and gramicidin amounts. Forming solutions contained lecithin, gramicidin, and lecithin–gramicidin mixtures of 1:10, 1:20, 1:30, and 1:40 weight ratio. The membrane components were dissolved in *n*-decane. The solvent was distilled, and their purity was checked by measurements of the refraction coefficient.

Potassium chloride solutions were used as electrolytes. The electrolyte solutions were prepared from mili-Q water and KCl from POCh (Poland). 1 M, 0.1 M, 0.01 M, 1 mM, and 0.1 mM electrolyte solutions were used for experiments. Potassium chloride was calcinated to remove organic impurities. All experiments were carried out at room temperature (22–24 °C).

4. Results and discussion

The dependence of interfacial tension of the lipid membrane modified with gramicidin D on the K^+ ion concentration is presented in Fig. 1 for various gramicidin D concentrations in the membrane. As previously mentioned, the effect of gramicidin D in the lecithin bilayer on its interfacial tension in a K^+ ion solution was expressed by Eq. (4). This Eq. (4) can be written in the form:

$$y = m_1 x_1 + m_2 x_2 + b.$$

The m_1, m_2, and b constants were determined using the linear regression of the Excel 2000 program. Eight constants are present in the equation, whereas three constants only are available. Therefore, combinations of individual constants only can be calculated instead of the constants themselves. The coefficients determined by the regression were applied to present the agreement of the Eq. (4) data (solid lines) with the experimental data (points) in Fig. 1 using Eq. (5) presented below:

$$\gamma = \frac{m_2 a_{K^+} + b}{1 - m_1 a_{K^+}} \tag{5}$$

The m_1, m_2, and b parameters, presented in the Table 1, were used for calculation of the following constants: the surface areas occupied by gramicidin membrane and GK^+ complex, interfacial tensions of the gramicidin membrane and GK^+, and the stability constant of the gramicidin–K^+ complex. The parameters m_1, m_2, and b were described by Eqs. (6)–(8):

$$-\frac{\left(A_L n_G^{-1} + A_{GK^+}\right)K}{A_L n_G^{-1} + A_G} = m_1 \tag{6}$$

$$\frac{\left(\gamma_L A_L n_G^{-1} + \gamma_{GK^+} A_{GK^+}\right)K}{A_L n_G^{-1} + A_G} = m_2 \tag{7}$$

and

$$\frac{\gamma_L A_L n_G^{-1} + \gamma_G A_G}{A_L n_G^{-1} + A_G} = b \tag{8}$$

All magnitudes γ_G, γ_{GK^+}, A_G, A_{GK^+}, and K can be determined from the Eqs. (6)–(8) and from the lecithin membrane interfacial tension, γ_L, and the area occupied by lecithin membrane, A_L, values equal to 1.623 mN m^{-1} and

Table 1
The parameters m_1, m_2, and b determined from Eq. (4) used to calculate the γ_G, γ_{GK^+}, A_G, A_{GK^+}, and K constants

Gramicidin D: phosphatidylcholine ratio	n_G^{-1}	m_1	m_2	b
1:10	6.19×10^{-2}	−0.03027	6.076×10^{-5}	0.001854
1:20	3.10×10^{-2}	−0.04382	8.612×10^{-5}	0.001813
1:30	2.06×10^{-2}	−0.02539	4.89×10^{-5}	0.001788
1:40	1.55×10^{-2}	−0.01058	1.98×10^{-5}	0.001759

85 Å^2, respectively. These constants were determined by us earlier and have been presented in the papers [19,20].

In order to calculate the constants A_{GK^+} and γ_{GK^+}, we derived the linear equation by elimination the constants K and A_G from Eqs. (6) and (7).

We have:

$$-A_L n_G^{-1} - \gamma_L A_L n_G^{-1} \frac{m_1}{m_2} = \gamma_{GK^+} A_{GK^+} \frac{m_1}{m_2} + A_{GK^+} \qquad (9)$$

This is the equation of the type $y=ax+b$, where $y=-A_L n_G^{-1}-\gamma_L A_L n_G^{-1}\{\{m_1\}/\{m_2\}\}$; $x=\{\{m_1\}/\{m_2\}\}$; $a=\gamma_{GK^+}A_{GK^+}$ and $b=A_{GK^+}$.

This calculation was illustrated in the Fig. 2. Values obtained for the interfacial tension of the gramicidin–K^+ ions complex, γ_{GK^+}, and the area occupied by gramicidin–K^+ ions complex, A_{GK^+}, from Eq. (9) are equal to 156 Å^2 and 1.89 mN m^{-1}, respectively.

Then, we calculated the values A_G and γ_G from the Eq. (8) by a similar method using the equation presented below:

$$\gamma_L A_L n_G^{-1} - A_L n_G^{-1} b = A_G b + \gamma_G A_G \qquad (10)$$

This is also the equation of the type $y=ax+b$, where $y=\gamma_L A_L n_G^{-1}-A_L n_G^{-1} b$; $x=b$; $a=A_G$ and $b=\gamma_G A_G$.

This calculation was illustrated graphically in Fig. 3. The determined values of the area occupied by gramicidin membrane and interfacial tension of the gramicidin membrane from Eq. (10) are equal to 188 Å^2 and 1.76 mN m^{-1}, respectively.

The resulting area occupied by the gramicidin molecule in the bilayer is 188 Å^2, which is in a good agreement with 115–225 Å^2 value given in the literature [22–24]. The last value, the stability constant of gramicidin–K^+ ions complex, K, was determined from Eqs. (6) and (7) by substitution of the determined earlier values of parameters γ_G, γ_{GK^+}, A_G, A_{GK^+}, and it is presented graphically, relatively to values m_1 or m_2. The value of constant K was determined from two separate equations Eqs. (6) and (7); the obtained values are identical and are equal to 0.033 m^3 mol^{-1}.

In the present study, we also calculated the surface energy of membrane formed from gramicidin or the

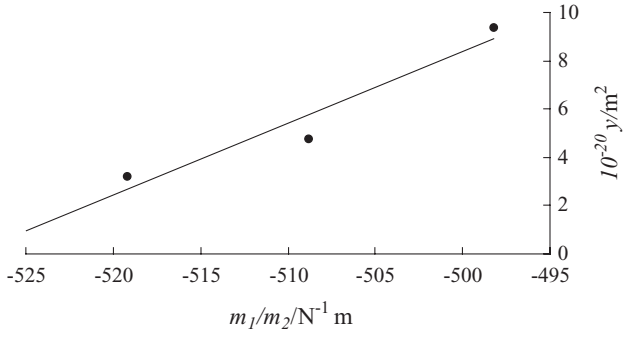

Fig. 2. A plot illustrating Eq. (9) for calculation of the constants: the surface area occupied by GK^+ complex, A_{GK^+}, and the interfacial tension of the GK^+ membrane complex, γ_{GK^+}, where $y=-A_L n_G^{-1}-\gamma_L A_L n_G^{-1}\{\{m_1\}/\{m_2\}\}$.

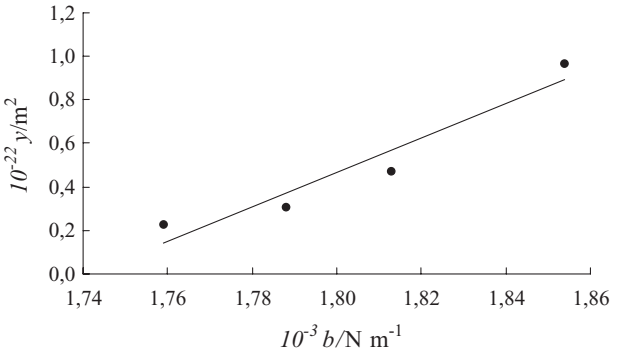

Fig. 3. A plot illustrating Eq. (10) for calculation of the constants: the surface area occupied by gramicidin, A_G, and the interfacial tension of the gramicidin membrane, γ_G, where $y=\gamma_L A_L n_G^{-1}-A_L n_G^{-1} b$.

gramicidin–ion K^+ complex. This is the energy needed to change the surface for 1 mol. For these calculations, it is necessary to find the surface concentration of membrane built from gramicidin and gramicidin–K^+ complex. These constants were calculated from Eq. (11).

$$s = \frac{1}{A \cdot N_A} \qquad (11)$$

where A [Å^2] is the surface occupied by the gramicidin or the gramicidin–K^+ complex, N_A[mol $^{-1}$] is the Avogadro's constant. These concentrations for gramicidin and the gramicidin–K^+ complex are equal to 8.82×10^{-7} and 1.06×10^{-6} mol m^{-2}, respectively. Knowing the surface concentrations of the membrane from the pure gramicidin and pure gramicidin–K^+ complex and its interfacial tensions, we can calculate the surface energy of these substances using Eq. (12).

$$E_p = \frac{\gamma}{s} \qquad (12)$$

where γ[mN m^{-1}] is the interfacial tension of the membrane formed from gramicidin or the gramicidin–K^+ complex, s[mol m^{-2}] is the surface concentration of the gramicidin or the gramicidin–K^+ complex.

The obtained value of the surface energy for gramicidin membrane is equal to 1995.7 J mol^{-1}, and for gramicidin–ion K^+ complex membrane, it is equal to 1782.5 J mol^{-1}. The result of subtraction of these energies (−213.2 J mol^{-1}) is the energy required for entrance of the K^+ ions into pore of the gramicidin channel. It is very difficult to interpret these values because the energy required for entrance of K^+ ions into pore of the gramicidin channel has a small value. It is very difficult to compare this value with different sizes of the energy of bonds. The gramicidin channel has about a 0.4-nm diameter and is full with water. It permits water and the partly hydrated K^+ ions to pass through a membrane. The energy necessary for K^+ ions to enter the pore of the gramicidin channel that we determined (−213.2 J mol^{-1}) is the energy connected with the pushing out of the water from the gramicidin channel and inserting the ion K^+ inside the channel.

Many authors determined the energy required for the entrance of the K^+ ions into pore of by molecular dynamic simulation. The structures of the channel and this process play a prominent role as a test for theories of ion permeation. Permeation studies using ions of different crystal radii lead to the suggestion [25] that the diameter of the filter region was between 3 and 3.3 Å. A widely accepted view is that filter is better adapted for contacts with a desolvated potassium ion (crystal radii=1.33 Å) than with a desolvated sodium ion (crystal radii=0.95 Å). In the literature, there were a lot of mathematical simulation data reporting the energy required for entrance of K^+ ions into the pore of the gramicidin channel, using molecular dynamics simulations (MD simulations). The ion parameters used in the MD simulation were those from Quanta package [26]. For K^+, these values are r_{min}=2.350 Å and e=−0.010 kcal mol^{-1}, and for Na^+, r_{min}=1.650 Å and e=−0.026 kcal mol^{-1}. The authors [26] compared these parameters for potassium and sodium ions with those from various other studies reported in the literature; for example, those used by Åqvist and Luzhakov [27–29] (for K^+, r_{min}=2.66 Å and e=-3.28×10^{-4} kcal mol^{-1}, and for Na^+, r_{min}=2.053 Å and e=-8.45×10^{-4} kcal mol^{-1}). Simple calculation between ions and a single water and also between ions and *N*-methylacetamide (NMA) reveal that the parameters used in paper [26] give a difference in energy (compared to those used by Åqvist and Luzhakov [27]) for the ion–water interaction by 1 kcal/mol and for ion–NMA by 0.2 kcal/mol. The authors note in the paper [26] that the difference they have observed in the channel is in the order of 25 kcal mol^{-1}.

Theoretical values determined by many authors of the energy required for entrance of K^+ ions into the pore of the gramicidin channel using an MD simulation method are of a similar value to the energy needed for K^+ ions to enter the pore of the gramicidin channel calculated by us, which is equal to −213.2 J mol^{-1} (−0.0509 kcal mol^{-1}).

5. Conclusions

The dependence of the interfacial tension of lecithin membranes modified with gramicidin D on lipid membrane composition and on electrolyte concentration was studied. The complex was formed between the gramicidin molecule and K^+ ion. The parameters describing the complex were determined using theoretical equations: surface area occupied by GK^+ complex, the interfacial tension of the membrane formed from GK^+ complex, and the stability constant of the gramicidin–K^+ complex.

It was very interesting to estimate the values of the surface energy for membrane formed from gramicidin and gramicidin–ion K^+ complex. These values are equal to 1995.7 and 1782.5 J mol^{-1}, respectively. The result of subtraction of these energies (−213.2 J mol^{-1}) is the energy required for entrance of K^+ ions to the pore of the gramicidin channel.

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References

[1] R.B. Gennis, Biomembranes: Molecular Structure and Function, Springer-Verlag, New York, 1989.
[2] L. Stryer, Biochemistry, W.H. Freeman, San Francisco, CA, 1981.
[3] S. Przestalski, Błony Biologiczne, WP, Warsaw, 1983.
[4] W. Jing, Z. Wu, E. Wang, Electrochemical study of gramicidin D forming ion-permeable channels in the bilayer lipid membranes, Electrochim. Acta 44 (1998) 99–102.
[5] S.W. Chiu, S. Subramaniam, E. Jacobsson, Simulation study of a gramicidin/lipid bilayer system in excess water and lipid: I. Structure of the molecular complex, Biophys. J. 76 (1999) 1929–1938.
[6] S. Alonso-Romanowski, L.M. Gassa, J.R. Vilche, An investigation by EIS of gramicidin channels in bilayer lipid membranes, Electrochim. Acta 40 (1995) 1561–1567.
[7] L.M. Gassa, A.E. Vallejo, S. Alonso-Romanowski, J.R. Vilche, Identification of channel membrane processes in bilayer lipid membranes by electrochemical techniques, Bioelectrochem. Bioenerg. 42 (1997) 187–192.
[8] R. Krivanek, P. Rybar, E.J. Prenner, R.N. McElhaney, T. Hianik, Interaction of the antimicrobial peptide gramicidin S with dimyristoyl-phosphatidylcholine bilayer membranes: a densitometry and sound velocimetry study, Biochim. Biophys. Acta 1510 (2001) 452–463.
[9] P. Vitovič, S. Krešak, R. Naumann, S.M. Schiller, R.N.A.H. Lewis, R.N. McElhaney, T. Hianik, The study of the interaction of a model α-helical peptide with lipid bilayers and monolayers, Bioelectrochemistry 63 (2004) 169–176.
[10] J.A. Szule, R.P. Rand, The effects of gramicidin on the structure of phospholipid assemblies, Biophys. J. 85 (2003) 1702–1712.
[11] O.S. Andersen, Ion movement trough gramicidin A channels. Studies of the diffusion-controlled association step, Biophys. J. 41 (1983) 119–133.
[12] O.S. Andersen, Ion movement trough gramicidins A channel. Interfacial polarization effects on single-channel current measurements, Biophys. J. 41 (1983) 147–165.
[13] O.S. Andersen, Ion movement trough gramicidin A channels. Single-channel measurements at very big high potentials, Biophys J. 41 (1983) 135–146.
[14] O.S. Andersen, Gramicidin channels, Annu. Rev. Physiol. 46 (1984) 531–548.
[15] D.A. Doyle, J.M. Cabral, R.A. Pfuetzer, A. Kuo, J.M. Gulbis, S.L. Cohen, B.T. Chait, R. MacKinnon, The structure of the potassium channel: molecular basis of K+ conduction and selectivity, Science 280 (1998) 69–77.
[16] S.R. Durell, H.R. Guy, Structural model of the outer vestibule and selectivity filter of the Shaker voltage-gated K+ channel, Neuropharmacology 35 (1996) 761–773.
[17] A.D. Petelska, Z.A. Figaszewski, Interfacial tension of the two-component bilayer lipid membrane modelling of cell membrane, Bioelectrochem. Bioenerg. 46 (1998) 199–204.
[18] A.W. Adamson, Physical Chemistry of Surfaces, Interscience Publishers, New York, 1960, pp. 4–9.
[19] A.D. Petelska, Z.A. Figaszewski, Effect of pH on the interfacial tension of the lipid bilayer membrane, Biophys. J. 78 (2000) 812–817.
[20] A.D. Petelska, Z.A. Figaszewski, Effect of pH on the interfacial tension of the lipid bilayer membrane formed from phosphatidylcholine or phosphatidylserine, Biochim. Biophys. Acta 1561 (2002) 135–146.

[21] P. Mueller, D.O. Rudin, H.T. Tien, W.C. Wescott, Methods for the formation of single bimolecular lipid membranes in aqueous solution, J. Phys. Chem. 67 (1963) 534–535.
[22] M. Diociaiuti, F. Bordi, A. Motta, A. Carosi, A. Molinari, G. Arancia, C. Coluzza, Aggregation of gramicidin A in phospholipid Langmuir–Blodgett monolayers, Biophys. J. 82 (2002) 3198–3206.
[23] M. Naumowicz, Z. Figaszewski, Impedance analysis of phosphatidylcholine membrane modified with gramicidin D, Bioelectrochemistry 61 (2003) 21–27.
[24] H. Tournois, P. Gieles, J. de Gier, B. de Kruijff, Interfacial properties of gramicidin and gramicidin–lipid mixtures measured with static and dynamic monolayer techniques, Biophys. J. 55 (1989) 557–569.
[25] B. Hille, Potassium channels in myelinated nerve: selective permeability to small cations, J. Gen. Physiol. 61 (1973) 669–686.
[26] P.C. Biggin, G.R. Smith, I. Shrivastava, S. Choe, M.S.P. Sansom, Potassium and sodium ions channel studied by molecular dynamics simulations, Biochim. Biophys. Acta 1510 (2001) 1–9.
[27] J. Åqvist, V. Luzhakov, Ion permeation of the potassium channel, Nature 404 (2000) 881–884.
[28] J. Åqvist, Ion–water interaction potentials derived from free energy perturbation simulations, J. Phys. Chem. 94 (1990) 8021–8024.
[29] V. Luzhakov, J. Åqvist, K(+)/Na(+) selectivity of the KcsA potassium channel from microscopic free energy perturbation calculations, Biochim. Biophys. Acta 1548 (2001) 194–202.