Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

journal homepage: www.elsevier.com

Full Length Article

Interaction of semiochemicals with model lipid membranes: A biophysical approach

Sergio A. Rodriguez[a, *], O.A. Pinto[b, *], Axel Hollmann[c, d, *]

[a] Laboratory of Antioxidants and Oxidative Process, CITSE- National University of Santiago del Estero and CONICET, 4206 RN 9 Km 1125, Santiago del Estero, Argentina
[b] INBIONATEC, National University of Santiago del Estero and CONICET. 4206 RN 9 Km 1125, Santiago del Estero, Argentina
[c] Laboratory of Biointerfaces and Biomimetic Systems, CITSE- National University of Santiago del Estero and CONICET, 4206 RN 9 Km 1125, Santiago del Estero, Argentina
[d] Laboratory of Molecular Microbiology, Institute of Basic and Applied Microbiology, University of Quilmes, B1876BXD Bernal, Argentina

ARTICLE INFO

Article history:
Received 13 June 2017
Received in revised form 18 October 2017
Accepted 1 November 2017
Available online xxx

Keywords:
Semiochemicals
DPPC
Insect olfaction
Grandlure
Monte Carlo simulation

ABSTRACT

Unravelling the chemical language of insects has been the subject of intense research in the field of chemical ecology for the past five decades. Insect communication is mainly based on chemosensation due to the small body size of insects, which limits their ability to produce or perceive auditory and visual signals, especially over large distances. Chemicals involved in insect communication are called semiochemicals. These volatiles and semivolatiles compounds allow to Insects to find a mate, besides the oviposition site in reproduction and food sources. Actually, insect olfaction mechanism is subject to study, but systematic analyses of the role of neural membranes are scarce. In the present work were evaluates the interaction of different semiochemicals as α-pinene, benzaldehyde, eugenol, grandlure, among others, with a lipid membrane model using surface pressure experiments and Monte Carlo computational analysis, allowed to propose a plausible membranotropic mechanism of interaction between semiochemicals and insect neural membrane.

1. Introduction

Insects play an important role in agriculture and human health. Their communication is mainly based on chemosensation. This is likely due to the small body size of insects, which limits their ability to produce or perceive auditory and visual signals, especially over large distances [1]. Chemicals involved in insect communication are called semiochemicals and can be classified into two categories: pheromones and allelochemicals. Pheromones are produced and secreted by an organism that elicits a behavioral or physiological response in a member of the same species that receives the signal, while allelochemicals are those that elicit a response in a member of a different species [2]. Insect olfaction is essential for finding a mate and oviposition site in reproduction and the detection of food sources. The semiochemicals are detected via olfactory receptors housed in the antennae and maxillary palps of insects [3]. The antennae contain a large number of chemosensory hairs called sensilla. Odors (volatile and semivolatile organic compounds) enter through sensillar pores and bind to hydrophilic proteins, called Odorant Binding Proteins (OBPs), in the sensillum lymph. OBPs are soluble proteins, smaller than 20 kDa, present at high concentrations in the antennal sensillum lymph of insects [4–7]. Although the precise physiological role of these proteins is not completely understood, biochemical data strongly suggest that they are involved in the binding (OBP-Odor complex) and transportation of odors through the sensillum lymph [8] to specific odorant receptors (ORs) localized in the membrane of olfactory neurons [9,10]. The OBPs comprise two groups of proteins, varying in the type of odorant molecules bound: the pheromone binding proteins (PBPs) bind pheromones and the general odorant binding proteins (GOBPs) which bind odorant molecules of a general type, such as plant volatiles [11]. Once the odor interacts with the OR, signal transduction cascade starts leading to behavioral expression [12,13]. Finally, to avoid continuous stimulation of the receptors, the odorant molecules are rapidly degraded by proteins known as odorant degrading enzymes (ODEs) [8,13–15].

However, much remains to be done to provide truly convincing data for an integrated model of olfactory signal transduction. Based on the fact that ORs recognize odors even in the absence of OBPs raising questions about the OBPs physiological role [16]. Aversely, there is strong evidence that OBPs are involved in odorant discrimination, receptor sensitivity and specificity [17,18]. In this point, the membranotropic properties of the odorants could increase its local concentration at the membrane level boosting its efficiency, as was demonstrated for other drugs [19–24].

The use of semiochemical as essential key in insect pest management programs is very promising. This idea is clearly expressed in recent publications of numerous examples of insect control [25]. The advantages of using pheromones for monitoring or controlling pests include low or even null pollution impact environmental, lower costs, specificity, easy use, and high sensitivity [26,27].

* Corresponding author at: RN 9 Km 1125, CP 4206. Villa El Zanjón, Santiago del Estero, Argentina.
Email addresses: drsergiorod@gmail.com (S.A. Rodriguez); oapinto2010@gmail.com (O.A. Pinto); ahollmann@conicet.gov.ar (A. Hollmann)

https://doi.org/10.1016/j.colsurfb.2017.11.002
0927-7765/

Regardless the point of view of the research and according to our knowledge, the neuronal lipid membrane role in insect olfaction has not been focused properly. Moreover, the information is scarce being the neuronal membrane relevant in the insects' olfaction mechanism.

On the other hand, the modeling of biological systems has been very useful in recent years. In general, the models can handle details or parameters that the experiment cannot control or predict. Particularly the Monte Carlo simulation has had great impact in processes related to lipid membranes [28–31]

In this context, the main goal of this work is to evaluate the interaction of different semiochemicals with a model lipid membrane using surface pressure experiments and Monte Carlo simulation analysis and relate this interaction with its plausible function in insects' communication.

2. Materials and methods

2.1. Semiochemical standards and lipids

α-pinene ((1*R*)-2,6,6-trimethylbicyclo[3.1.1]hept-2-ene, 98% of purity) and benzaldehyde (99% of purity) were purchased from Sigma-Aldrich, Buenos Aires, Argentina, and Commercial mix containing and eugenol (4-allyl-2-methoxyphenol, 99% of purity), Grandlure I, II, III and IV were purchased from ChemTica Internacional, Costa Rica. DPPC (1,2-dipalmitoyl-sn-glycero-3-phospho-1′-rac-glycerol) were purchased from Avanti Polar Lipids (Alabaster, AL, USA)

2.2. Surface pressure

Changes in the surface pressure of lipid monolayers induced by semiochemicals were measured in a Kibron Langmuir-Blodgett trough, at constant temperature (25 ± 0.5 °C). The surface of the buffer solution contained in a Teflon trough of fixed area was exhaustively cleaned by surface aspiration. Then, a chloroform solution of lipids was spread on Hepes buffer, 10 mM pH 7 to reach surface pressures of 20.5 ± 1 mN/m. Semiochemical solutions were injected in the subphase and the changes of surface pressure were recorded until a constant value was reached during at least 60 min. The surface pressure of an air−water interface upon injecting the largest concentration of compound used throughout the study was always below 17.5 mN/m (data not shown). For this reason, the lowest initial surface pressure of the lipid monolayers before the addition of the semiochemicals to the subphase was above that value, 20.5 mN/m for all assays. In this condition, the changes in the surface pressure observed upon the injection of the compound solutions could be ascribed to an effect of each compound on the monolayer instead by the accumulation of semiochemicals on the aqueous/air interface.

Pressure data obtained were adjusted using simplest isotherm model with the following equation:

$$\theta = \frac{\Delta\Pi}{\Delta\Pi_{\max}} = \frac{[semiochemical]}{k_d + [semiochemical]} \tag{1}$$

Where θ corresponds to the degree of coverage, ΔP is the surface pressure shift, [semiochemical] is the semiochemical concentration, and k_d is the apparent dissociation constant.

2.3. Computational details: model and basic definitions

In this work were used a lattice-gas model to emulate the substrate or support where the lipids are deposited. This substrate symbolizes water. In this case were considered a triangular two-dimensional lattice of lateral size L, which contain $M = L^2$ nodes. In this medium, it is possible to deposit an amount of N lipids, which will affect a certain number of nodes of this lattice. With this is possible to define a lipid density d = N/M. If d = 0 [1] the substrate is empty [full] of lipids. In our model, the empty nodes symbolized the interstitial water between lipids. Should be pointed that the surface pressure used in the experimental setup, 20.5 ± 1 mN/m, implies a homogenous monolayer with a high degree of hydration [32–34]

In turn, it is possible to inject a quantity P of semiochemical which will affect only the lipids. Then we can consider that a density of lipids with semiochemistry will be within the range $0 \le \sigma \le d$. If σ = 0, no lipid will have a chemical, however, if σ = d all lipids will have a semiochemical.

Then with these definitions, we have two states for each lipid: pure lipid (*Lp*) and lipid with semiochemical (*LSch*). On the other hand, the lipids can only interact energetically with his nearest neighbors (NN). For this was defined three types of lateral interaction energy: interaction *Lp-Lp*, w_{LpLp}/k_BT, interaction *LSch − LSch*, w_{LsLs}/k_BT and for the case of pure lipid with a chemical lipid *Lp- LSch*, w_{LpLs}/k_BT. If any of these energies are positive or negative it means that the lateral interactions are repulsive or attractive, respectively.

The energy or the Hamiltonian of the system can be expressed by:

$$H = \sum_{i}^{M} \sum_{l \in (NN,i)} \Big[w_{LpLp}\delta_{c_i,l,1} + w_{LsLs}\delta_{c_i,l,-1} + w_{Lp-Ls}\left(\delta_{c_i,1}\delta_{c_l,-1} + \delta_{c_i,-1}\delta_{c_l,1}\right)\Big] \tag{2}$$

where *l ?* (*NN*, *i*) run on all NN sites of site "i" and δ is the Kronecker function. Each node can be monitor by an occupation variable c_i can take the value zero if the node "i" is empty and equal to +1 (−1) if it is occupied with *Lp* (LSch). At equilibrium pressure p/k_BT at fixed σ, it is possible to obtain the system. Each lipid will have an environment (α) formed by six nodes with an associated energy (H_α). In turn, there will be an empty node with same environment (β), this means with the same configuration of *Lp* or *LSch* but with zero energy.

The ratio between the populations of local state α and its conjugate β in the statistical assembly must be:

$$\frac{P_\alpha}{P_\beta} = \exp\left(-\Delta H/k_BT\right) = \exp\left(-\left(H_\alpha - p\right)/k_BT\right) \tag{3}$$

Where ΔH is the energy change between populations. Then:

$$\frac{p}{k_BT} = \ln\left(\frac{P_\alpha}{P_\beta}\right) + \frac{E_\alpha}{k_BT} \tag{4}$$

Finally, we can calculate $\left\langle \frac{p}{k_BT} \right\rangle_\alpha$ by averaging over different configurations.

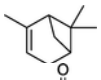
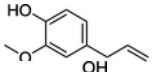
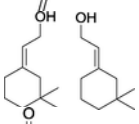
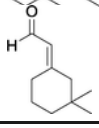
For the Monte Carlo simulations, we consider a two-dimensional lattice of size L = 180, with d = 0.5, which will remain constant throughout the compute. The lipids have been randomly distributed. Periodic contour conditions have been considered in the two dimensions.

Then a quantity of lipid, chosen at random, $\sigma \leq d$ are marked with the chemical (LSch). For the present model, the equilibrium state will be obtained using Monte Carlo Simulation in the canonical assembly [35,36] together with the Kawasaki algorithm [37].

3. Results and discussion

In insects, sensory reception involves diverse and parallel molecular components to process a nearly infinite spectrum of chemical information. While multiple, and not necessarily incompatible, models persist as to the underlying mechanisms and precise functional roles of each element in these diverse signal transduction paradigms, there is the general consensus around the idea that precise and temporally restricted odor sensing is required for many aspects of insect success and survival. Furthermore, It is well known that partitioning of a drug into the membrane compartment not only potentially depletes drug from the aqueous compartment but also concentrates drug in the local environment around the receptor [38]. In this context, we aimed to study the interaction with model lipid membranes of two pure semiochemicals and a commercial blend listed in Table 1. In order to remark the biological significance of these molecules, main references are presented where their activities as pheromones were reported (more details of the compounds in study as semiochemicals are available at www.pherobase.com).

Table 1
Semiochemicals in study.

Compound	Structure	MW (g/mol)	Ref. Pheromone[a]
1. α-pinene		136	[39–42]
2. benzaldehyde		106	[43,44]
Commercial blend			
3. eugenol 59.3%		164	[45,46]
4. grandlure I 14.79%		154	[25,47]
5. grandlure II and III mixture 19.5% and 3.83%		154	[48–50]
6. grandlureIV 2.74%		152	15,16

[a] Some references were the compound acts as an insect pheromone.

First, the effect on the DPPC lipid monolayers surfaces pressure produced by each semiochemical injected in the subphase was carried out. As revealed in Fig. 1, changes in the surface pressure (ΔΠ) vary with the semiochemical concentration in the subphase. It can be observed that besides all semiochemical tested induces changes in the surface pressure; each one induces a different response (Fig. 1a). The kinetic behavior also showed differences between each compound tested.

α-Pinene exhibited the faster kinetics, whereas commercial blend coincident with its lower affinity also shown the slowest kinetics (Fig. 1b).

In order to get an insight on semiochemical − lipid interactions, we analyze the surface pressure data using Eq. (1) described in Materials and Methods (Eq. (1)) obtaining the apparent dissociation constant (K_d) for each semiochemical (Table 2), that give us a quantitative information about the affinity of the compound to the membrane.

Interesting, each semiochemical exhibit a different affinity toward the model lipid membrane, as could be inferred from Fig. 1. Benzaldehyde was the compound that exhibits the biggest difference with the highest affinity (i.e. low Kd) and effectiveness. This effect could be attributed to the chemical nature of aldehyde group due to that can interact with polar head of DPPC monolayer, followed by a stabilization on the membrane with its benzene located in the hydrophobic acyl chains of the lipids.α-Pinene that also exhibits a high affinity toward the membrane, due it chemical hydrophobic that not present a polar substituent and cannot interact directly with DPPC polar head but are able to interact with the hydrophobic tail of the lipids. In this context result energetically favorable that this small compound quickly adopts a final position in the acyl region of the monolayer instead on the polar solvent, as its kinetic behavior shown. Finally,

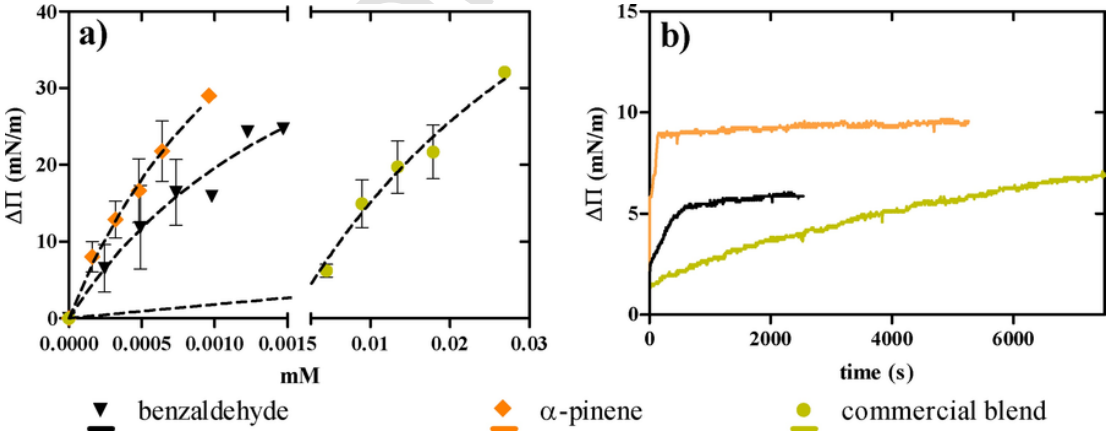


Fig. 1. Interaction of semiochemicals with lipid monolayers. (a). Changes in the surface pressure expressed as ΔΠ as a function of semiochemical concentration on pure DPPC monolayers. (b) Changes in the surface pressure expressed as ΔΠ as a function of time on pure DPPC monolayers after the first addition (Fig. 1a) each semiochemical. The initial surface pressure for all assays was 20.5 ± 0.5 mN/m for all assays. Values are presented as mean ± standard deviation with n = 3.

Table 2
Dissociation constants, *Kd, ΔΠ and* Effectiveness of the process, determined from surface pressure changes.1.α-pinene

Semiochemical	K_d [a]	*Δπ at higher conc. assayed*	*Effectiveness of the process* ($\Delta\pi_{max}$ [b]/K_d)
1. α-pinene	0,0019 ± 0.001	29.0 ± 1.3	29660,49
2. benzaldehyde	0,0015 ± 0.001	24.7 ± 0.4	48172,95
1. Commercial blend	0,046 ± 0.01	32.1 ± 3.1	1832,90

[a] Values are presented as mean ± standard deviation with n = 3.

[b] Theoretical maximum obtained by Eq.(1) fitting.

commercial blend witch poses hydrophilic molecules that could easily stabilize in the polar solvent requires higher amount of compound and time to induce similar changes on the surface pressure probably through a primary interaction with the polar head of the lipid and final stabilization with the allyl groups in the hydrophobic region of the monolayer. However due the size of this molecules are those that result in a greater perturbation of the membrane (i.e. highest Δπ).

With the aim of improving our knowledge on semiochemical − lipid interactions computational simulation were made using *Lattice-gas model*. Here we describe the simplest model including pairwise interactions between lipids, as was well used for this kind of system [52–54]. The model design was based on previous developments with mixture lipids [55–57].

Fig. 2 (a–c) shows experimental pressure [MC pressure] versus semiochemical concentration [σ] for experimental and MC data (Note that two scales are used), for each semiochemical indicated. For the simulations repulsive interactions were considered in particular that $w_{LpLp} << w_{LsLs}, w_{LpLs}$.

As we can see in Fig. 2, the model reproduces phenomenologically the experimental results.

The behavior obtained from the model exhibit a similar trend for the three compounds studied with significant higher values of energy for the pair *Lipid- Semiochemical* (LSch)/*Lipid − Semiochemical* (LSch). However each compound, as was observed from pressure data, exhibited different nominal values.

In order to dissect the behavior of the compounds after reach the membrane, the inset in Fig. 3(i) shows a MC pressure versus σ, for the commercial blend in a specific region. Three different concentration of semiochemical was analyzed. These are indicated by a red point and labeled by A, B, and C. Insets (ii-iv) shows a "snapshots" of the mentioned states of the system. Green dots represent Lp and red dots to LSch. When compounds accumulate into the membrane a clustering effect of the lipids carrying semiochemical was observed. The three compounds studied reveal a similar behavior (data not shown).

This finding strongly suggests that semiochemical after the interaction with the membrane is grouped in clusters that implied a high concentration of drug in restricted spatial domains of the membrane.

At the highest concentration of semiochemical tested, the membrane pressure up cto around 50 mN/m, which is close to collapse pressure of pure DPPC monolayer [58]. However, should be that collapse on pure DPPC monolayer, is mainly due at high packing of DPPC with an area per lipid of around 46 Å^2. In our experiments, lipids amounts and area remains constant, with an initial area per lipids around 65 Å^2. In the contexts of the present work, the increase in the surface pressure could be interpreted as an increase in the area per lipid due to the interaction of the lipids with the semiochemical tested by the formation of a lipid-semiochemical complex with a resulted in the higher area (red dots in Fig. 3). This increase in the area per lipid with the concomitant increase in the monolayer tension could contribute at the clustering of the lipids carrying semiochemical in order to achieve an energetically more favorable conformation.

It is well established that the concentrating effects of membrane-associated drugs, lateral diffusion of drugs across the two-dimen-

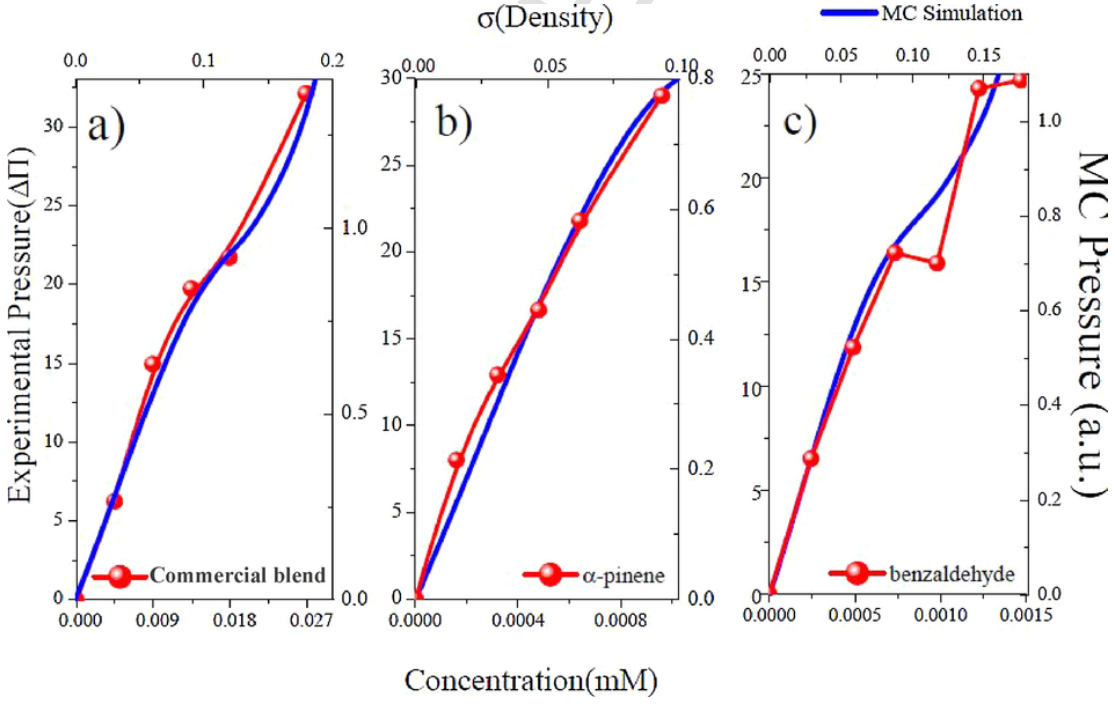


Fig. 2. Experimental pressure [MC pressure] versus semiochemical concentration [σ] for experimental and MC data. Energies used were: a) Commercial blend, $w_{LsLs}/k_BT = 32.0$, $w_{LpLs}/k_BT = 4.0$, b) α-pinene, $w_{LsLs}/k_BT = 24.0$, $w_{LpLs}/k_BT = 3.0$ *and* c) Benzaldehyde. $w_{LsLs}/k_BT = 40$, $w_{LpLs}/k_BT = 5.0$.

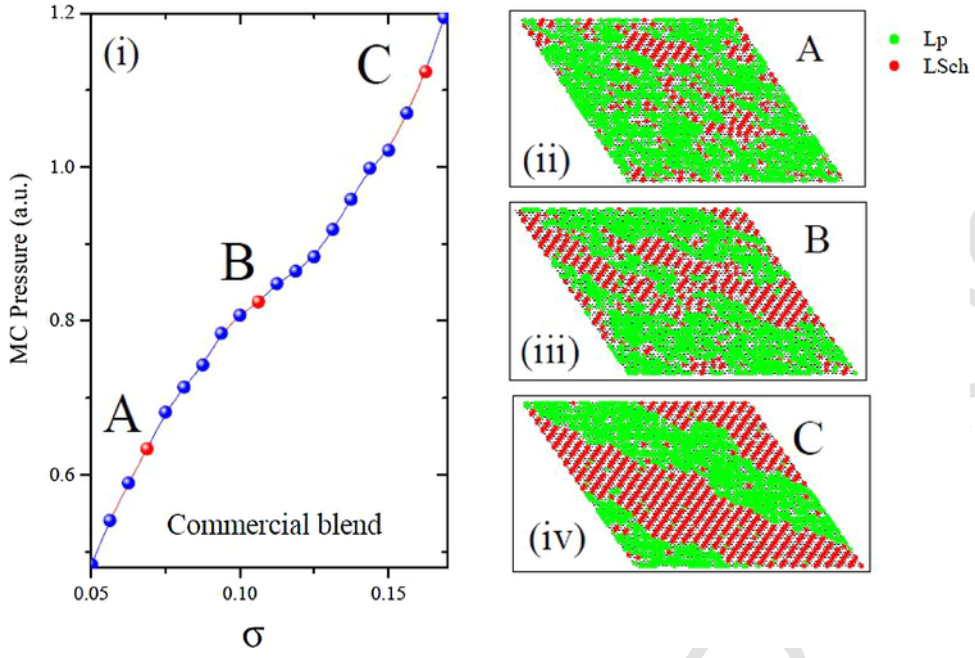


Fig. 3. (i) MC pressure versus σ, for the commercial blend. Insets (ii–iv): snapshots at three different concentration A–C.

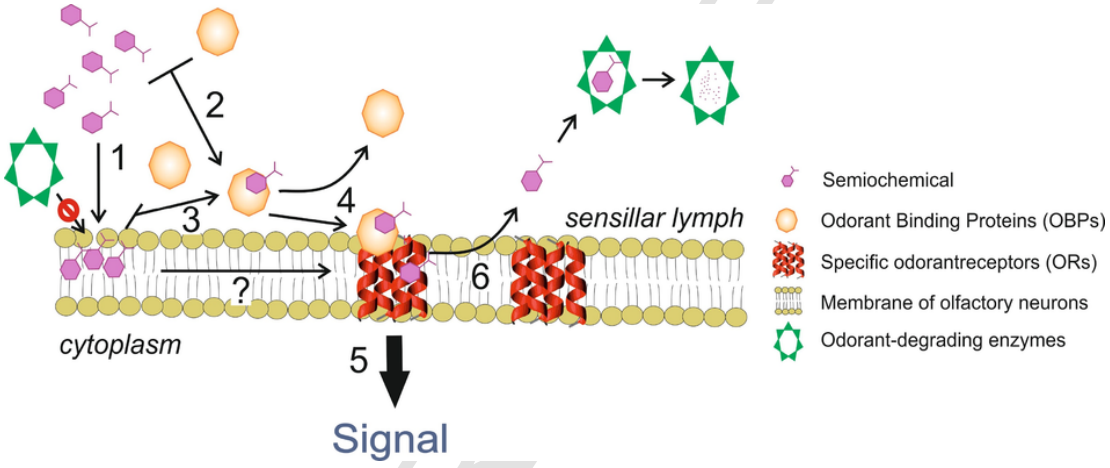


Fig. 4. Putative model of the role of membrane association of semiochemical in the context of olfactory receptor functions.

sional surface (rather than three dimensions in aqueous bulk) could also increase reaction rates with receptors in a mechanism referred to as "reduction of dimensionality" rate enhancement [38,51].

In terms of signaling activity, the possibility of a clustering effect of the semiochemicals could promote the interaction with OBP by an increase of local concentration and/or even induce a direct stimulation of ORs without the need of OBPs participation as some authors suggested [16].

4. Conclusions

In this work, we demonstrated that two known semiochemicals and a commercial blend are able to interact with membrane lipid models. In order to rationalize these findings in the context of olfactory receptor functions, was proposed a putative model were the lipid interaction could play a passive catalytic role Fig. 4.

Membranotropic properties were described as a key step in many therapeutic compounds, due can increase their local concentration at the membrane level, in this way enhancing the efficiency of the drug. In our model, the "pre" concentration of the semiochemicals in the neuronal membranes could catalyze the subsequent interaction with the OBPs (pathway 1 in Fig. 4), and also play a role to avoid the premature degradation by the odorant-degradative enzymes. Furthermore, some authors have been reporting that some semiochemicals could activate the odorant receptors without an OBP [16], in this situation the affinity toward lipid membrane could become essential to achieve the odorant receptor and trigger the odorant signal.

Acknowledgements

This work was supported by grants from Agencia Nacional de Promoción Científica y Tecnológica, ANPCyT- MINCyT, Argentina (PICT 2013-1482; PICTO-UNSE 2012-001), CONICET-UNSE

PIO145201401000l3CO and CONICET-PIP 11220130100383CO. SAR, OAP, and AH are members of the Research Career of CONICET.

The numerical calculations were done using the Huauke parallel cluster located in Instituto de Bionanotecnología (INBIONATEC-CONICET), Universidad Nacional de Santiago de Estero, Argentina.

References

[1] M.D. Greenfield, Signalers and Receivers: Mechanisms and Evolution of Arthropod Communication, Oxford University Press, 2002.
[2] J.Y. Yew, H. Chung, Insect pheromones: an overview of function, form, and discovery, Prog. Lipid Res. 59 (2015) 88–105.
[3] J. Zhang, W.B. Walker, G. Wang, Pheromone reception in moths: from molecules to behaviors, Prog. Mol. Biol. Transl. Sci. 130 (2015) 109–128.
[4] R.G. Vogt, G.D. Prestwich, M.R. Lerner, Odorant-binding-protein subfamilies associate with distinct classes of olfactory receptor neurons in insects, J. Neurobiol. 22 (1991) 74–84.
[5] J.C. Dickens, F.E. Callahan, W.P. Wergin, C.A. Murphy, R.G. Vogt, Odorant-binding proteins of true bugs. Generic specificity, sexual dimorphism, and association with subsets of chemosensory sensilla, Ann. N. Y. Acad. Sci. 855 (1998) 306–310.
[6] R.G. Vogt, E. Grosse-Wilde, J.J. Zhou, The Lepidoptera odorant binding protein gene family: gene gain and loss within the GOBP/PBP complex of moths and butterflies, Insect Biochem. Mol. Biol. 62 (2015) 142–153.
[7] R.G. Vogt, The molecular basis of pheromone reception: its influence on behaviour, in: G.D. Prestwich, G.L. Blomquist (Eds.), Pheromone Biochemistry, Academic Press, Orlando,FL, 1987, pp. 385–431.
[8] R.G. Vogt, L.M. Riddiford, Pheromone binding and inactivation by moth antennae, Nature 293 (1981) 161–163.
[9] G.D. Prestwich, G. Du, S. LaForest, How is pheromone specificity encoded in proteins?, Chem. Senses 20 (1995) 461–469.
[10] G.J. Blomquist, R.G. Vogt, Biosynthesis and Detection of Pheromones and Plant Volatiles-introduction and Overview, In: Insect Pheromone Biochemistry and Molecular Biology, 20033–18.
[11] R.G. Vogt, R. Rybczynski, M.R. Lerner, Molecular cloning and sequencing of general odorant-binding proteins GOBP1 and GOBP2 from the tobacco hawk moth Manduca sexta: comparisons with other insect OBPs and their signal peptides, J. Neurosci. 11 (1991) 2972–2984.
[12] R.G. Vogt, F.E. Callahan, M.E. Rogers, J.C. Dickens, Odorant binding protein diversity and distribution among the insect orders as indicated by LAP, an OBP-related protein of the true bug Lygus lineolaris (Hemiptera, Heteroptera), Chem. Senses 24 (1999) 481–495.
[13] P. Pelosi, R. Maida, Odorant-binding proteins in insects, Comparative biochemistry and physiology. Part B, Biochem. Mol. Biol. 111 (1995) 503–514.
[14] K.E. Kaissling, Olfactory perireceptor and receptor events in moths: a kinetic model revised, J. Comp. Physiol. A 195 (2009) 895–922.
[15] K.E. Kaissling, Kinetics of olfactory responses might largely depend on the odorant-receptor interaction and the odorant deactivation postulated for flux detectors, J. Comp. Physiol. A 199 (2013) 879–896.
[16] I. Gaillard, S. Rouquier, D. Giorgi, Olfactory receptors, Cell. Mol. Life Sci. 61 (2004) 456–469.
[17] H.J. Ko, S.H. Lee, E.H. Oh, T.H. Park, Specificity of odorant-binding proteins: a factor influencing the sensitivity of olfactory receptor-based biosensors, Bioprocess Biosyst. Eng. 33 (2009) 55.
[18] H.J. Ko, T.H. Park, Enhancement of odorant detection sensitivity by the expression of odorant-binding protein, Biosens. Bioelectron. 23 (2008) 1017–1023.
[19] M.A.R.B. Castanho, M.X. Fernandes, Lipid membrane-induced optimization for ligand-receptor docking: recent tools and insights for the membrane catalysis model, Euro. Biophys. J. 35 (2006) 92–103.
[20] H.G. Franquelim, L.M. Loura, N.C. Santos, M.A.R.B. Castanho, Sifuvirtide screens rigid membrane surfaces. establishment of a correlation between efficacy and membrane domain selectivity among HIV fusion inhibitor peptides, J. Am. Chem. Soc. 130 (2008) 6215–6223.
[21] P.M. Matos, M.A.R.B. Castanho, N.C. Santos, HIV-1 fusion inhibitor peptides enfuvirtide and T-1249 interact with erythrocyte and lymphocyte membranes, PLoS One 5 (2010) e9830.
[22] P.M. Matos, T. Freitas, M.A.R.B. Castanho, N.C. Santos, The role of blood cell membrane lipids on the mode of action of HIV-1 fusion inhibitor sifuvirtide, Biochem. Biophys. Res. Commun. 403 (2010) 270–274.
[23] A.S. Veiga, N.C. Santos, L.M. Loura, A. Fedorov, M.A.R.B. Castanho, HIV fusion inhibitor peptide T-1249 is able to insert or adsorb to lipidic bilayers. Putative correlation with improved efficiency, J. Am. Chem. Soc. 126 (2004) 14758–14763.
[24] S. Veiga, S. Henriques, N.C. Santos, M.A.R.B. Castanho, Putative role of membranes in the HIV fusion inhibitor enfuvirtide mode of action at the molecular level, Biochem. J 377 (2004) 107–110.
[25] S. Tewari, T.C. Leskey, A.L. Nielsen, J.C. Piñero, C.R. Rodriguez-Saona, Use of pheromones in insect pest management, with special attention to weevil pheromones, in: D.P. Abrol (Ed.), Integrated Pest Management: Current Concepts and Ecological Perspective, Elsevier Inc., 2014, pp. 141–168.
[26] L. Pélozuelo, B. Frérot, Monitoring of European corn borer with pheromone-baited traps: review of trapping system basics and remaining problems, J. Econ. Entomol. 100 (2007) 1797–1807.
[27] C. Wall, Principle of monitoring, in: R.L. Ridgway, R.M. Silverstein, M.N. Inscoe (Eds.), Behavior-Modifying Chemicals for Insect Management, Marcell Dekker, Inc., New York, 1990, pp. 9–23.
[28] O.G. Mouritsen, M. Bloom, Models of lipid-protein interactions in membranes, Annu. Rev. Biophys. Biomol. Struct. 22 (1993) 145–171.
[29] I.P. Sugar, R.L. Biltonen, N. Mitchard, Monte Carlo simulations of membranes: phase transition of small unilamellar dipalmitoylphosphatidylcholine vesicles, Methods Enzymol. 240 (1994) 569–593.
[30] O.A. Pinto, A.M. Bouchet, M.A. Frias, E.A. Disalvo, Microthermodynamic interpretation of fluid states from FTIR measurements in lipid membranes: a Monte Carlo study, J. Phys. Chem. B 118 (2014) 10436–10443.
[31] T. Heimburg, R.L. Biltonen, A Monte Carlo simulation study of protein-induced heat capacity changes and lipid-induced protein clustering, Biophys. J . 70 (1996) 84–96.
[32] E.A. Disalvo, A. Hollmann, M.F. Martini, Hydration in lipid monolayers: correlation of water activity and surface pressure, Subcell. Biochem. 71 (2015) 213–231.
[33] E.A. Disalvo, A. Hollmann, L. Semorile, M.F. Martini, Evaluation of the Defay-Prigogine model for the membrane interphase in relation to biological response in membrane-protein interactions, Biochim. Biophys. Acta 1828 (2013) 1834–1839.
[34] E.A. Disalvo, M.F. Martini, A.M. Bouchet, A. Hollmann, M.A. Frias, Structural and thermodynamic properties of water-membrane interphases: significance for peptide/membrane interactions, Adv. Colloid Interface Sci. 211 (2014) 17–33.
[35] K. Binder, Monte Carlo methods in statistical physics, Top. Curr. Phys. 7 (1986).
[36] D.W. Heermann, K. Binder, Monte Carlo Simulation in Statistical Physics, Springer-Verlag, Berlin Heidelberg, 2010.
[37] K. Kawasaki, Diffusion constants near the critical point for time-dependent Ising models. I, Phys. Rev. 145 (1966) 224.
[38] D.A. Sykes, C. Parry, J. Reilly, P. Wright, R.A. Fairhurst, S.J. Charlton, Observed drug-receptor association rates are governed by membrane affinity: the importance of establishing micro-pharmacokinetic/pharmacodynamic relationships at the β2-adrenoceptor, Mol. Pharmacol. 85 (2014) 608–617.
[39] D.W. Ross, G.E. Daterman, A.S. Munson, Spruce beetle (Coleoptera: scolytidae) response to traps baited with selected semiochemicals in Utah, West. North Am. Nat. 65 (2005) 123–126.
[40] D.S. Pureswaran, R. Gries, J.H. Borden, Antennal responses of four species of tree-killing bark beetles (Coleoptera: scolytidae) to volatiles collected from beetles, and their host and nonhost conifers, Chemoecology 14 (2004) 59–66.
[41] D.P. Huber, R. Gries, J.H. Borden, H.D. Pierce Jr., A survey of antennal responses by five species of coniferophagous bark beetles (Coleoptera: scolytidae) to bark volatiles of six species of angiosperm trees, Chemoecology 10 (2000) 103–113.
[42] A. Schierling, K. Seifert, S.R. Sinterhauf, J.B. Rieß, J.C. Rupprecht, K. Dettner, The multifunctional pygidial gland secretion of the Steninae (Coleoptera: staphylinidae): ecological significance and evolution, Chemoecology 23 (2013) 45–57.
[43] T.C. Leskey, V. Hock, G. Chouinard, D. Cormier, K. Leahy, D. Cooley, A. Tuttle, A. Eaton, A. Zhang, Evaluating electrophysiological and behavioral responses to volatiles for improvement of odor-baited trap tree management of conotrachelus nenuphar (Coleoptera: curculionidae), Environ. Entomol. 43 (2014) 753–761.
[44] D. Hu, J. Feng, Z. Wang, H. Wu, X. Zhang, Effect of nine plant volatiles in the field on the sex pheromones of Leguminivora glycinivorella, Nat. Prod. Commun. 8 (2013) 393–396.
[45] K.H. Tan, R. Nishida, Methyl eugenol: its occurrence, distribution, and role in nature especially in relation to insect behavior and pollination, J. Insect Sci. 12 (2012) 1–60.
[46] R.-z. Chen, M.G. Klein, C.-f. Sheng, Y. Li, Q.-y. Li, Male and female Popillia quadriguttata (Fabricius) and Protaetia brevitarsis (Lewis)(Coleoptera: scarabaeidae) response to Japanese beetle floral and pheromone lures, J. Asia-Pac. Entomol. 16 (2013) 479–484.
[47] D. Szczerbowski, G.G. Torrens, M.A. Rodrigues, O. Trevisan, S.M. Gomes, A. Tröger, K. Mori, W. Francke, P.H. Zarbin, (1R, 6R)-2, 2, 6-Trimethyl-3-oxabicyclo [4.2. 0] octan-4-one, a new monoterpene lactone produced by males of the cocoa borer Conotrachelus humeropictus (Col.: Curculionidae), Tetrahedron Lett. 57 (2016) 2842–2844.
[48] Z. Szendrei, A. Averill, H. Alborn, C. Rodriguez-Saona, Identification and field evaluation of attractants for the cranberry weevil, Anthonomus musculus Say, J. Chem. Ecol. 37 (2011) 387–397.
[49] F.J. Eller, R.J. Bartelt, B.S. Shasha, D.J. Schuster, D.G. Riley, P.A. Stansly, T.F. Mueller, K.D. Shuler, B. Johnson, J.H. Davis, Aggregation pheromone for the

pepper weevil, Anthonomus eugenii Cano (Coleoptera: curculionidae): identification and field activity, J. Chem. Ecol. 20 (1994) 1537–1555.
[50] J.C. Dickens, G.D. Prestwich, Differential recognition of geometric isomers by the boll weevil, Anthonomus grandis Boh. (Coleoptera: curculionidae): evidence for only three essential components in aggregation pheromone, J. Chem. Ecol. 15 (1989) 529–540.
[51] M.A. McCloskey, M. Poo, Rates of membrane-associated reactions: reduction of dimensionality revisited, J. Cell Biol 102 (1986) 88–96.
[52] I.P. Sugár, T.E. Thompson, R.L. Biltonen, Monte Carlo simulation of two-component bilayers: DMPC/DSPC mixtures, Biophys. J. 76 (1999) 2099–2110.
[53] O. Mouritsen, A. Boothroyd, R. Harris, N. Jan, T. Lookman, L. MacDonald, D. Pink, M. Zuckermann, Computer simulation of the main gel-fluid phase transition of lipid bilayers, J. Chem. Phys 79 (1983) 2027.
[54] T. Heimburg, Thermal Biophysics of Membranes, 20071.
[55] P.F. Almeida, A. Best, A. Hinderliter, Monte carlo simulation of protein-induced lipid demixing in a membrane with interactions derived from experiment, Biophys. J. 101 (2011) 1930–1937.
[56] M. Fidorra, T. Heimburg, H.M. Seeger, Melting of individual lipid components in binary lipid mixtures studied by FTIR spectroscopy, DSC and Monte Carlo simulations, Biochim. Biophys. Acta Biomembr. 1788 (2009) 600–607.
[57] J. Ehrig, E.P. Petrov, P. Schwille, Phase separation and near-critical fluctuations in two-component lipid membranes: Monte Carlo simulations on experimentally relevant scales, New J. Phys. 13 (2011).
[58] M.F. Martini, E.A. Disalvo, Superficially active water in lipid membranes and its influence on the interaction of an aqueous soluble protease, Biochim. Biophys. Acta Biomembr. 1768 (2007) 2541–2548.