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Short communication

New stochastic microsensors based on oleamides

Catalina Cioates Negut [a,b], Raluca-Ioana Stefan-van Staden [c,*,1], Iuliana Moldoveanu [c], Eleonora-Mihaela Ungureanu [b,*,1], Camelia Stanciu-Gavan [d]

[a] National Institute for Chemical–Pharmaceutical Research and Development ICCF, Bucharest, Romania
[b] Faculty of Applied Chemistry and Materials Science, Politehnica University of Bucharest, Bucharest, Romania
[c] Laboratory of Electrochemistry and PATLAB Bucharest, National Institute of Research for Electrochemistry and Condensed Matter, Romania
[d] Department of Surgery 4, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania

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ABSTRACT

Six oleamides: oleoylethanolamide, (Z)-N-[(1S)-2-hydroxy-1-(phenylmethyl)ethyl]-9octadecenamide, N-phenethyloleamide, N-[2-(4-methoxyphenyl)ethyl]oleamide, N-[1]naphthyloleamide, N-cyclohexyloleamide were synthesized and used as modifiers for the design of new stochastic microsensors based on graphite paste. Carcinoembryonic antigen (CEA) was used as a model analyte to prove the stochastic behavior of the microsensors. CEA was determined directly from whole blood samples with recoveries higher than 94.00%, favorizing pattern recognition of CEA in whole blood samples. The most sensitive stochastic microsensor was the one based on the physical immobilization of N-[2-(4-methoxyphenyl)ethyl]oleamide in graphite paste.

1. Introduction

Stochastic sensors are based on a single molecule interaction with pores/channels [1], the molecules entering the pores in an order given by their size, geometry, conformation, velocity of unfolding (i.e., for proteins), and velocity of going into the pores/channels, as defined earlier by Bayley and Cremer [1]. Therefore, stochastic sensors were able to perform reliable qualitative analysis of an analyte in a complex matrix [1–3]. Based on channel/pore conductivity, it is a need to explore new nanostructured materials that are able to provide the required signal for stochastic sensing. The "evil protein" was one of the first used molecules for single molecule detection using stochastic sensing [1]. The group of Stefan-van Staden introduced substances from different classes like porphyrin, maltodextrin, cyclodextrin, for the design of the stochastic microsensors which improved their signal [2,3]. Oleamides are new materials presenting in 3D a "V" conformation, miming the necessary pores needed for the design of the stochastic sensors due to their ability of providing the necessary channels/pores for sensing. Therefore, for this paper, the oleamides were immobilized in the graphite paste to give the stochastic microsensor.

Carcinoembryonic antigen (CEA) — a tumor marker used for clinical diagnosis and evaluation of treatment for different types of cancer [4] was selected as a model analyte for the new designed stochastic microsensors. CEA is a highly glycosylated cell surface glycoprotein (180–200 kDa), belonging to a group of substances known as the tumor-associated antigens (TAA) [5,6]. Its concentration is usually as low as 4.6 ng mL^{-1} in the blood of healthy adults. But in the blood of the patients who suffer from some cancers, such as colorectal cancer, liver cancer and pancreatic cancer, the average CEA concentration is obviously higher than for healthy adults.

Sensitive detection of tumor markers is significant in early clinical diagnosis and evaluation of the recovery of patients [7–10]. Laboratory measurements of serum tumor markers, such as CEA [11–13], cytokeratin 19 fragment marker (CYFRA 21-1) [14,15], α-fetoprotein (AFP) [16] and cancer antigen 125 (CA125) [17,18] have been used for the diagnosis, prognostic evaluation and treatment monitoring of cancer patients [19–23].

In this paper we proposed six new stochastic microsensors based on physical immobilization of oleoylethanolamide (1), (Z)-N-[(1S)-2-hydroxy-1-(phenylmethyl)ethyl]-9octadecenamide (2), N-phenethyloleamide (3), N-[2-(4-methoxyphenyl)ethyl]oleamide (4), N-[1]naphthyloleamide (5), N-cyclohexyloleamide (6) (Fig. 1) in graphite paste, for the assay of the model analyte — carcinoembryonic antigen in the human whole blood.

2. Experimental

2.1. Reagents and solutions

Oleamides 1–6 (Fig. 1) were synthesized accordingly, in house [24,25]. Graphite powder (1–2 μm) was supplied by Aldrich and

* Corresponding authors.
E-mail addresses: ralucavanstaden@gmail.com (R.-I. Stefan-van Staden), em_ungureanu2000@yahoo.com (E.-M. Ungureanu).
[1] Member of ISE.

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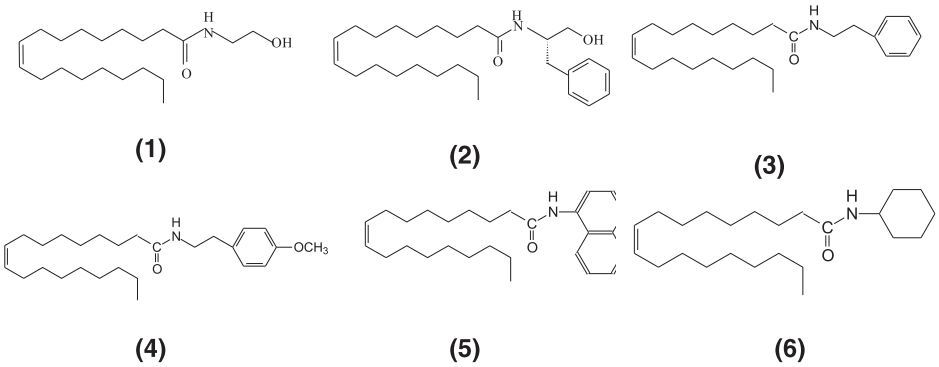
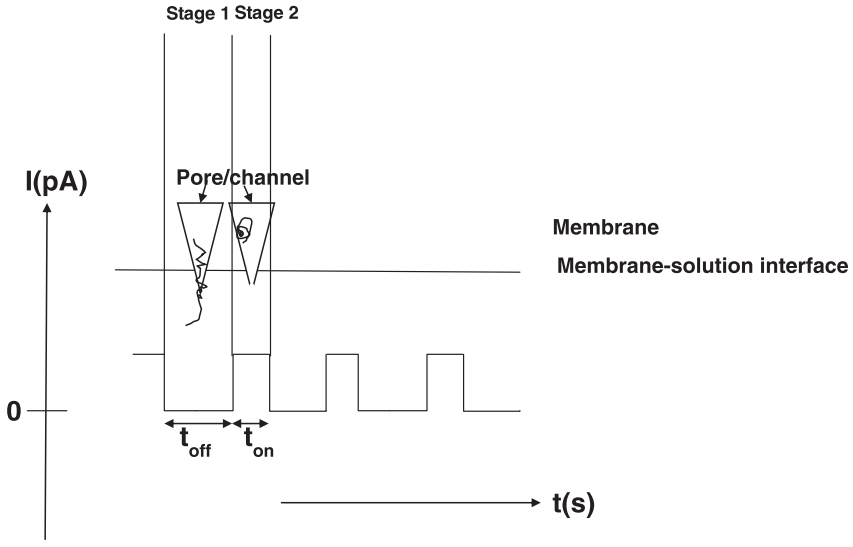


Fig. 1. Structures of oleamides 1–6, used for stochastic microsensors' design.



Scheme 1. Current development at the membrane–solution interface, for stochastic sensors.

paraffin oil by Fluka (Buchs, Switzerland), monosodium phosphate and disodium phosphate were purchased from Reagent, Bucharest. Deionized water obtained from a Millipore Direct-Q 3 System (Mosheim, France) was used for the preparation of all solutions. 0.1 mol/L phosphate buffer solution (PBS) was prepared in the laboratory using monosodium and disodium phosphates. Working standard CEA solutions of 10^{-11} to 10^{-2} mg/mL were prepared using the serial dilution method.

2.2. Samples

Whole blood samples were kindly provided by the University of Medicine and Pharmacy "Carol Davila" (UMF) in tubes containing EDTA. The blood samples were obtained from UMF with informed consent patients in accordance with the rules of the Ethical Committee no. 11/2013. The samples were measured as provided by the hospital.

Table 1
Response characteristics of stochastic microsensors based on oleamides.

Stochastic microsensors based on graphite paste & oleamide	Signature of the analyte t_{off} (s)	Equation of calibration and correlation coefficient*	Linear concentration range (mg mL^{-1})	Sensitivity (s^{-1}/mg mL^{-1})	Limit of determination (mg mL^{-1})
1	1.8	$1/t_{on} = 1.29 \times 10^6 \times C + 0.0321$; $r = 0.9998$	1.6×10^{-10}–1.6×10^{-7}	1.29×10^6	1.6×10^{-10}
2	1.5	$1/t_{on} = 1.06 \times 10^4 \times C + 0.0480$; $r = 0.9982$	1.6×10^{-8}–1.6×10^{-6}	1.06×10^4	1.6×10^{-8}
3	3	$1/t_{on} = 6.99 \times 10^5 \times C + 0.0311$; $r = 1.0000$	1.6×10^{-9}–1.6×10^{-7}	6.99×10^5	1.6×10^{-9}
4	2	$1/t_{on} = 8.97 \times 10^6 \times C + 0.1793$; $r = 0.9996$	1.6×10^{-10}–1.6×10^{-8}	8.97×10^6	1.6×10^{-10}
5	2.4	$1/t_{on} = 2.65 \times 10^5 \times C + 0.0460$; $r = 1.0000$	1.6×10^{-9}–1.6×10^{-7}	2.65×10^5	1.6×10^{-9}
6	2	$1/t_{on} = 1.66 \times 10^5 \times C + 0.0555$; $r = 0.9970$	1.6×10^{-9}–1.6×10^{-6}	1.66×10^5	1.6×10^{-9}

* $1/t_{on}$ is expressed in s^{-1} and C in mg mL^{-1}.