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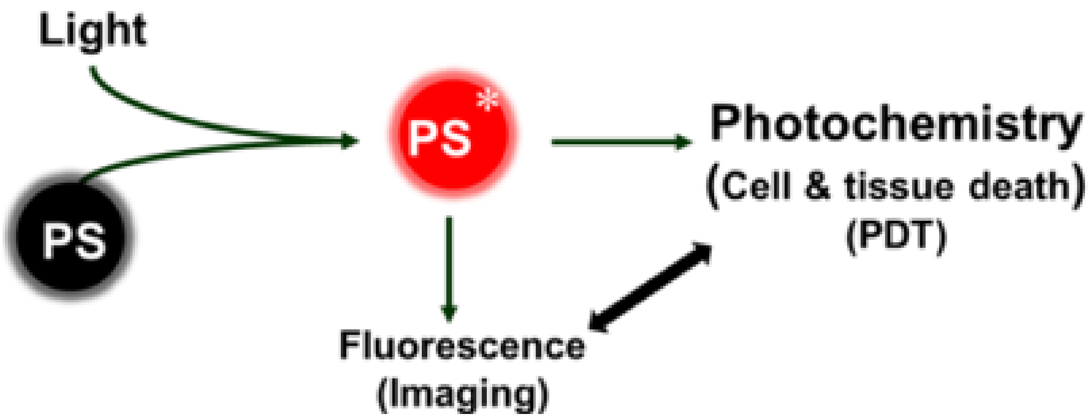
Bilayer lipid membrane as a model of photodynamic therapy processes in cancer cells

Irene Jiménez Munguía

National University of Science and Technology - MISiS

8th Regional Biophysics Conference
16th – 20th May 2018, Zreče, Slovenia

PHOTODYNAMIC THERAPY (PDT)



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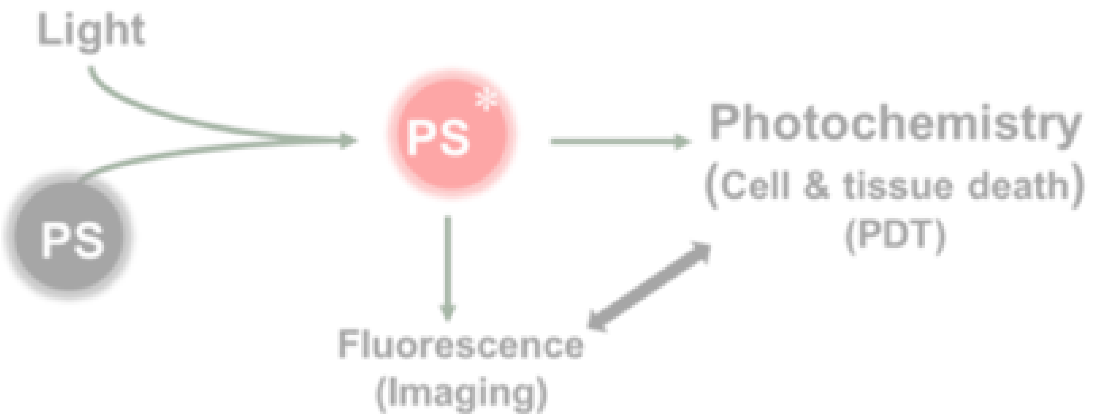

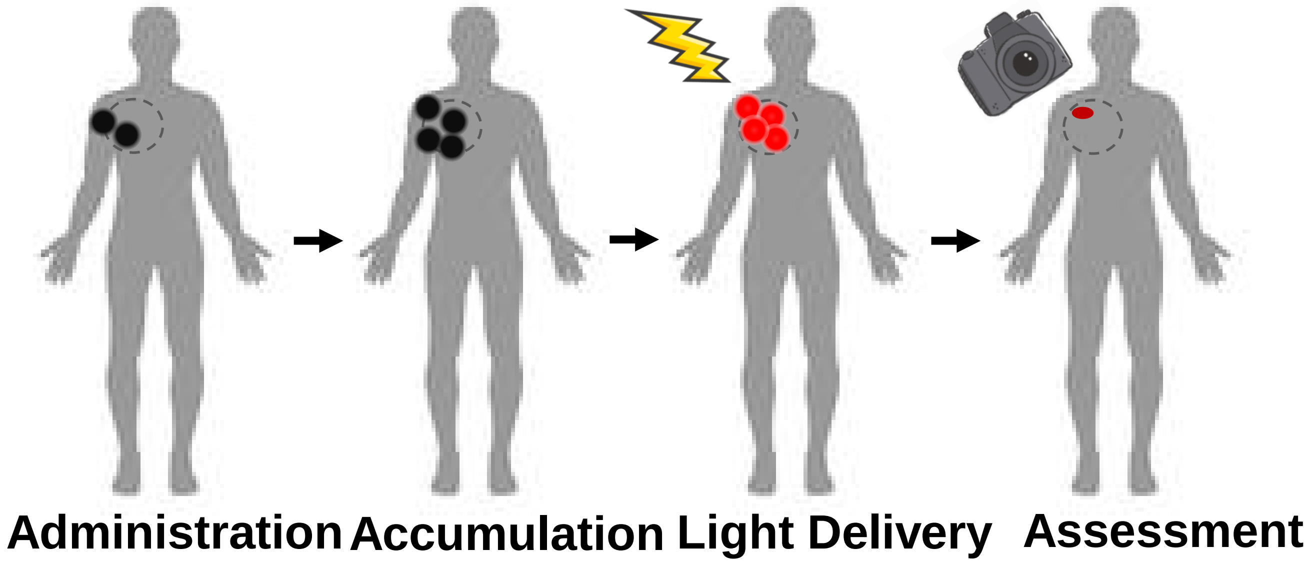

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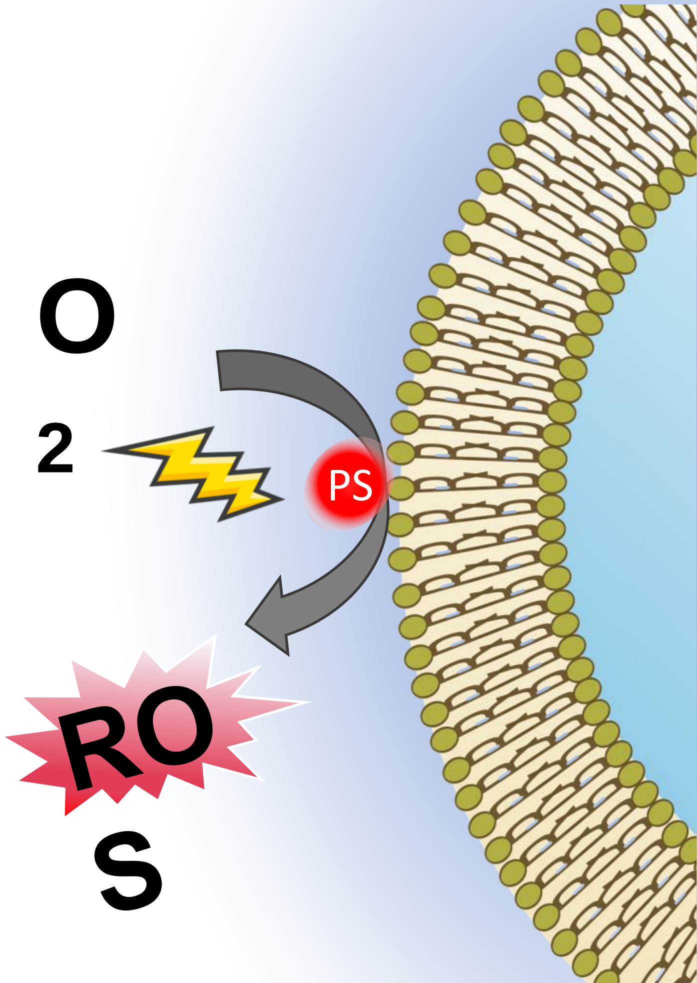

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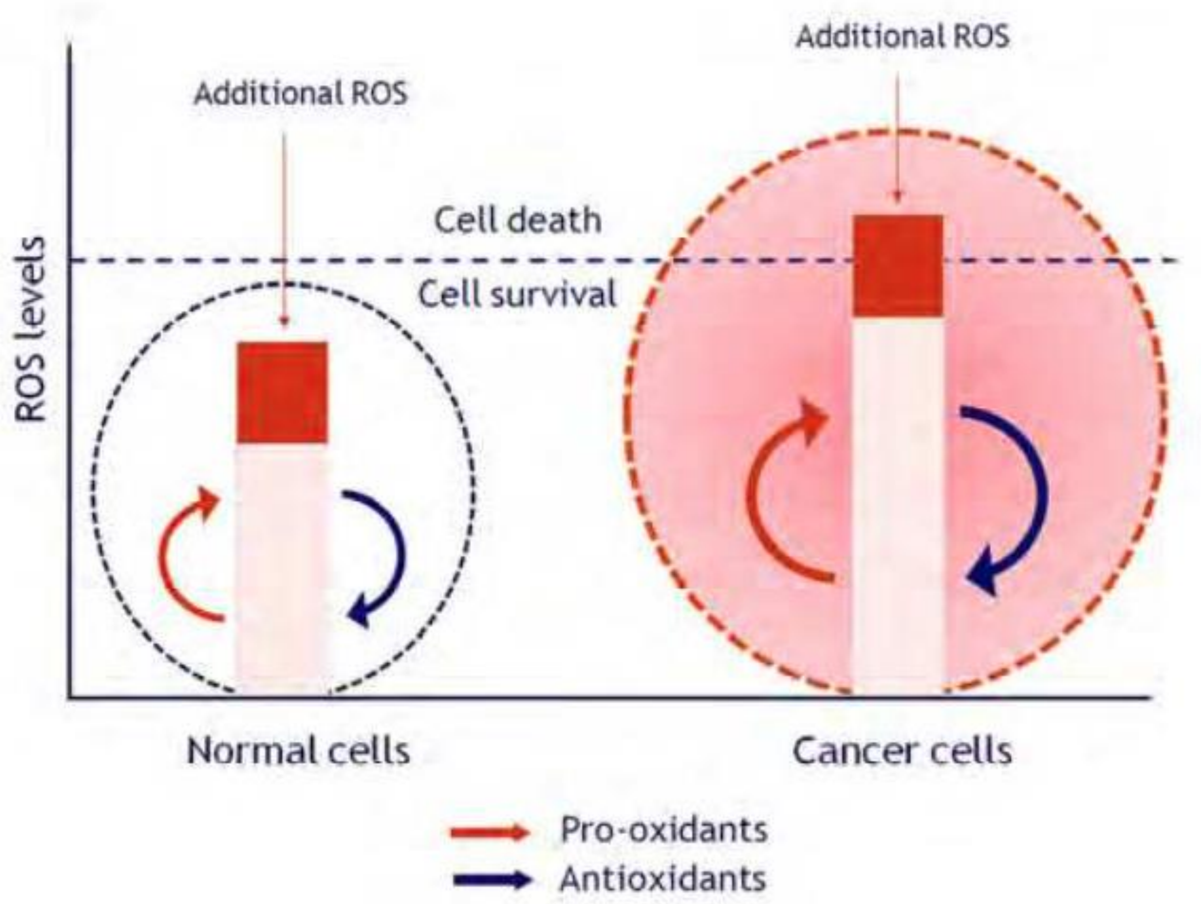
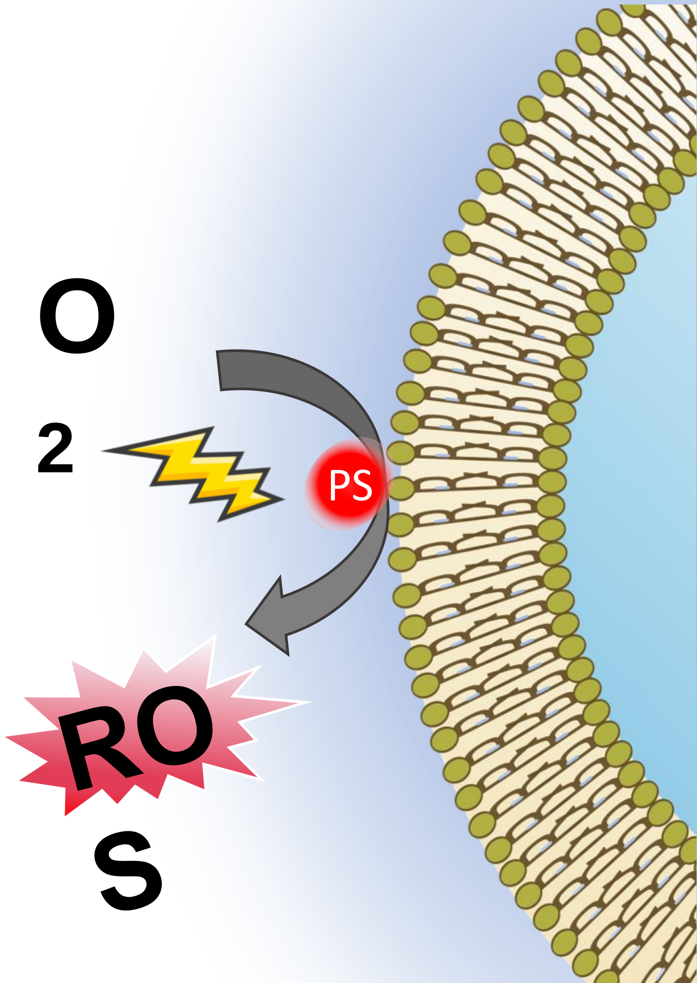


Manuel de Miguel and Mario D. Cordero (2012). Oxidative Therapy Against Cancer, Oxidative Stress and Diseases, ISBN: 978-953-51-0552-7



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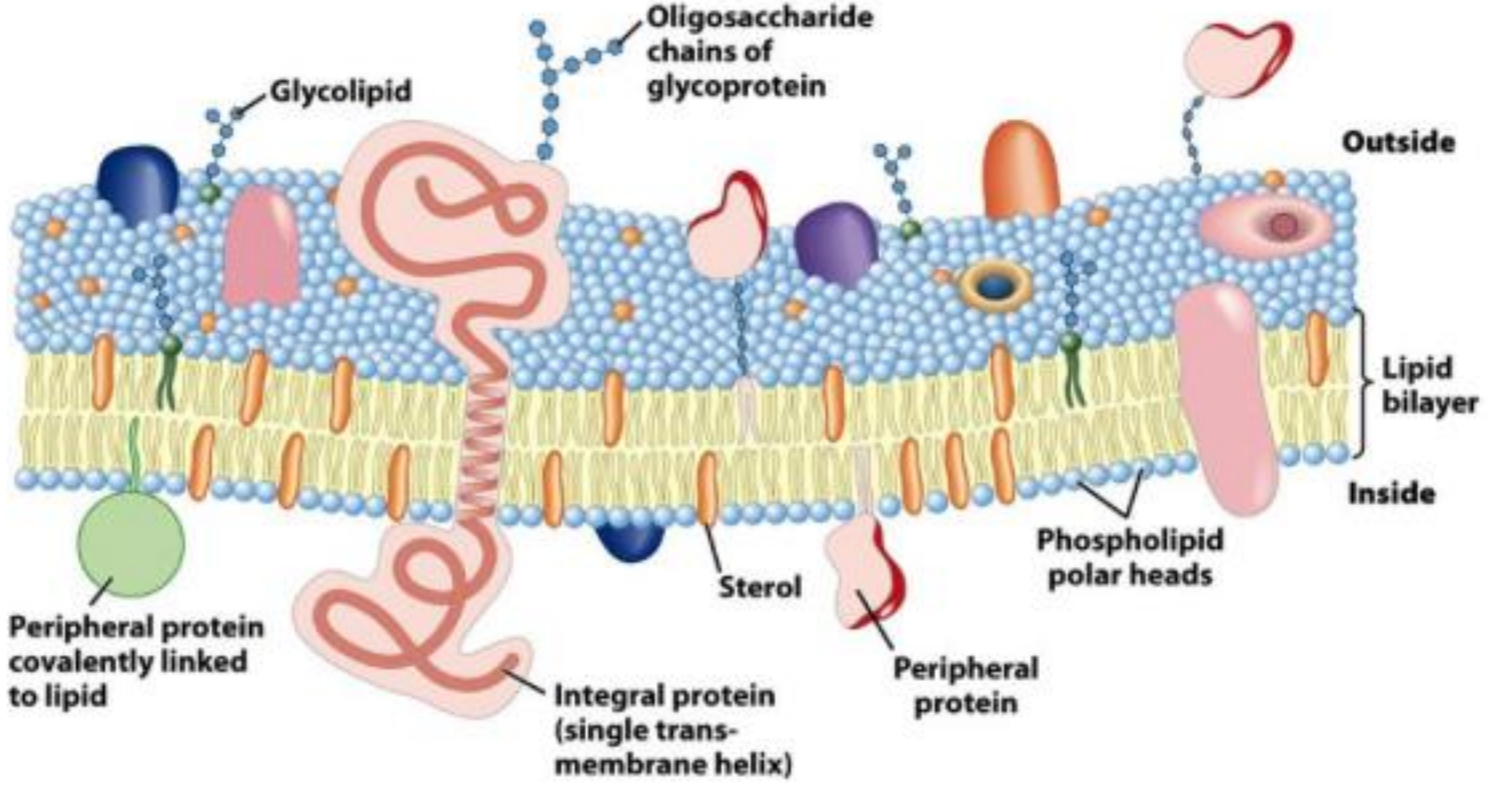
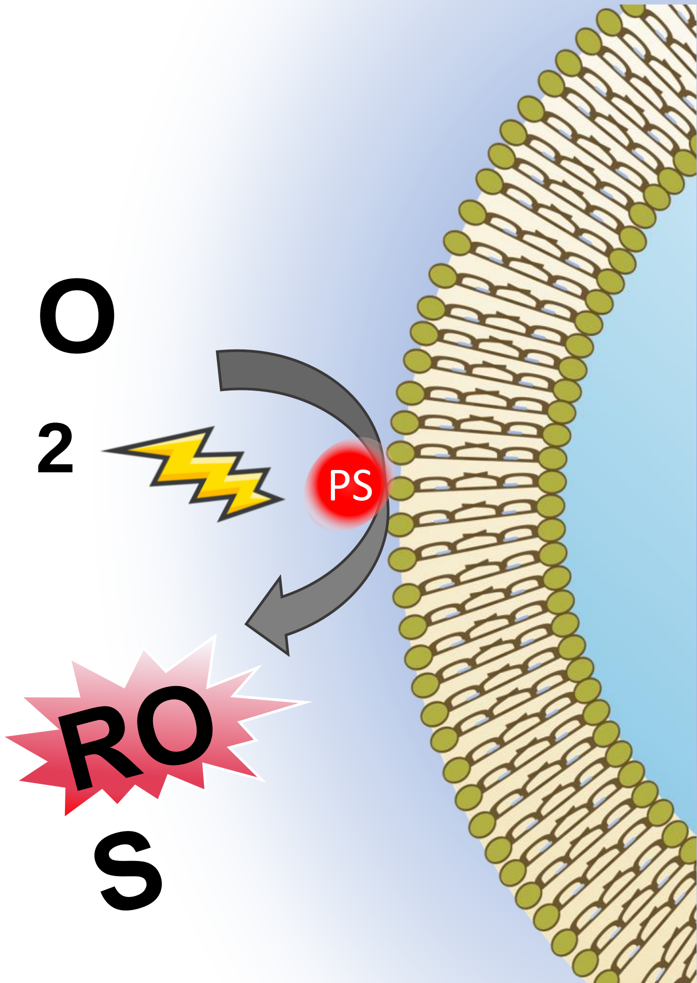
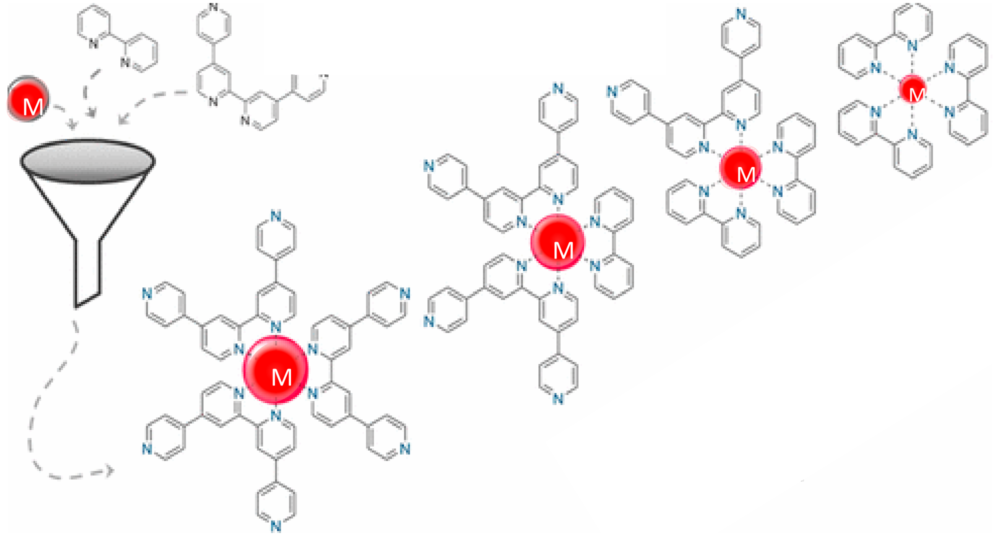


Lehninger Principles of Biochemistry, 5th edition 2008.

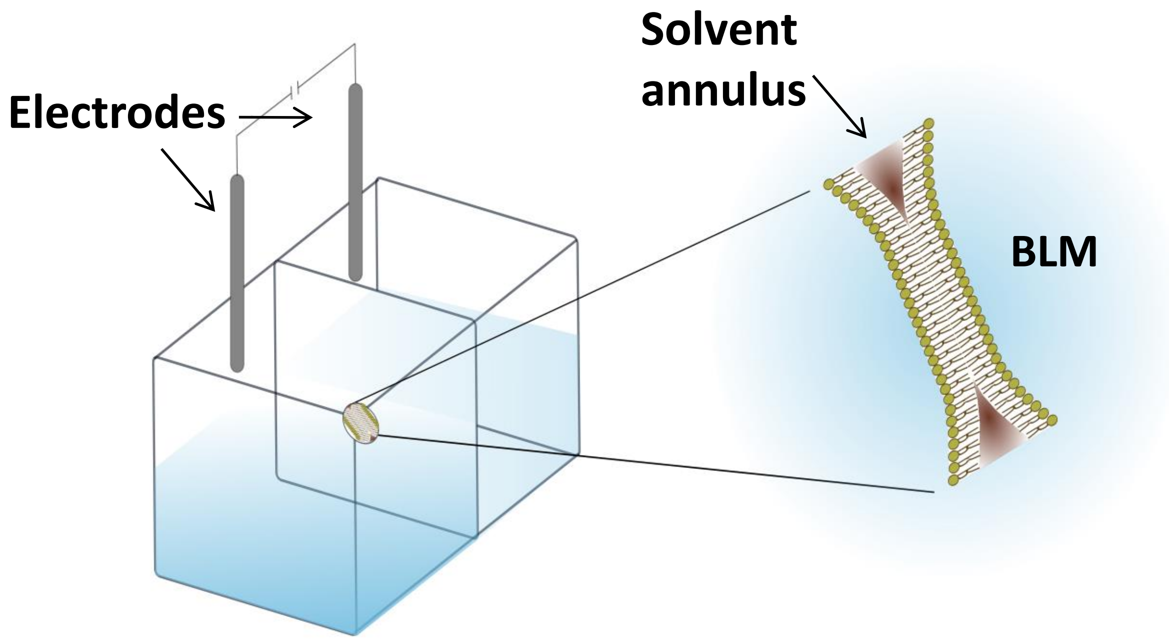


IN VITRO STUDY OF PHOTODYNAMIC THERAPY

BLM: MULLER-RUDIN METHOD



Photosensitizers



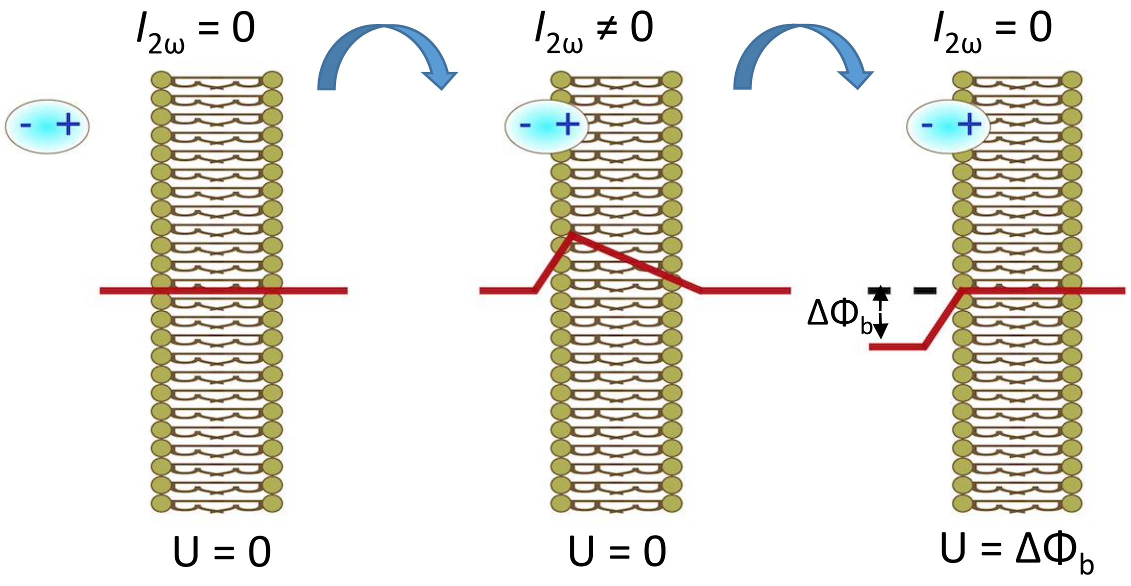
- Control conditions
- Alternative to the use of biological models

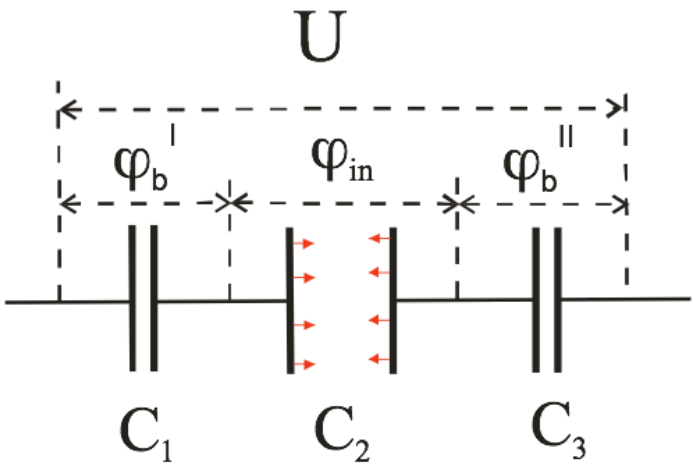
Paul Mueller, Donald O. Rudin, H. Ti Tien, and William C. Wescott
The Journal of Physical Chemistry 1963 *67* (2), 534-535

IN VITRO STUDY OF PHOTODYNAMIC THERAPY

INTRAMEMBRANE FIELD COMPENSATION METHOD (IFC)

The applied voltage = U + Vcos(ωt)





Sokolov VS, Kuz´min VG. Biofizika. 1980 Jan-Feb;25(1):170-2.

IN VITRO STUDY OF PHOTODYNAMIC THERAPY

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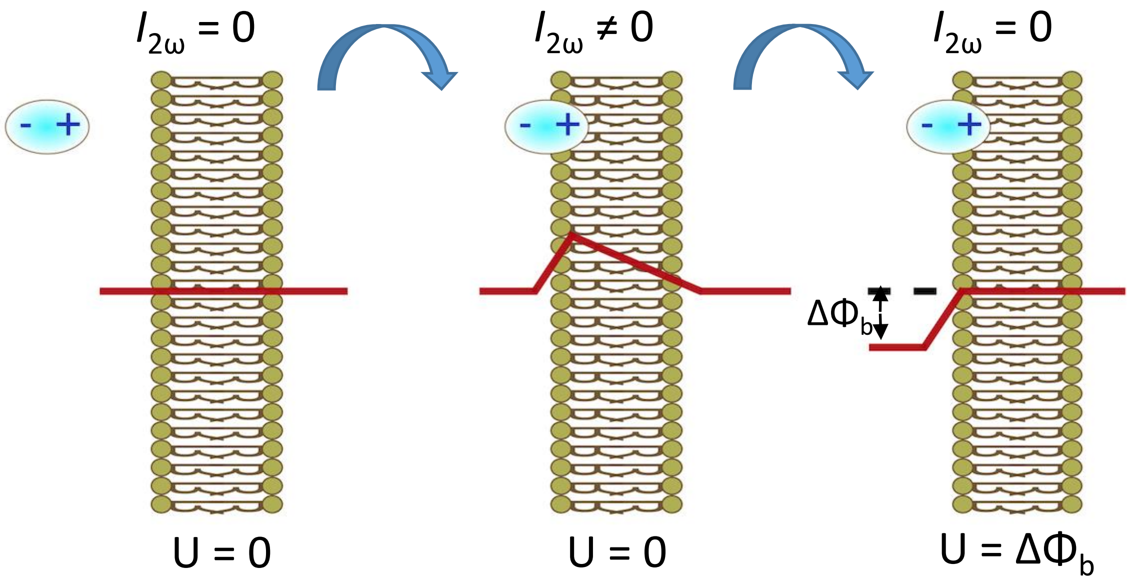


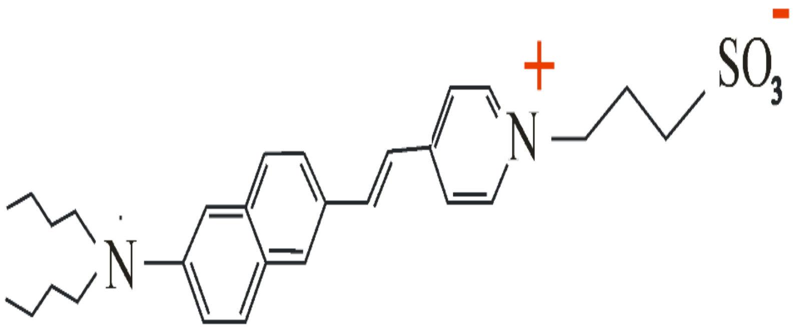
**** Ideal method for measuring boundary potentials**

Applied on the study :

- Binding of charged or dipole molecules to membrane
- Damage of target molecules in the in vitro study of PDT

IN VITRO STUDY OF PHOTODYNAMIC THERAPY

STYRIL DYES: DIPOLE MOMENT



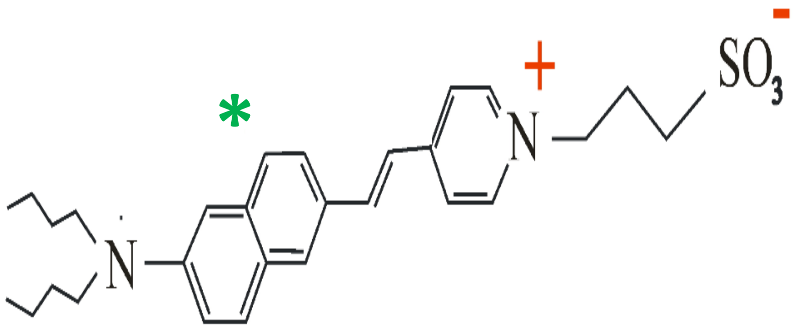
(- 4-[2-(6-(dibutylamino)-2-naphthalenyl)ethenyl)-1-(3-sulfopropyl)-pyridinium)

di-4-ANEPPS

IN VITRO STUDY OF PHOTODYNAMIC THERAPY

STYRIL DYES: DIPOLE MOMENT

*: aniline group **PROTEINS WITH AROMATIC AMINOACIDS**



(- 4-[2-(6-(dibutylamino)-2-naphthalenyl)ethenyl)-1-(3-sulfopropyl)-pyridinium)

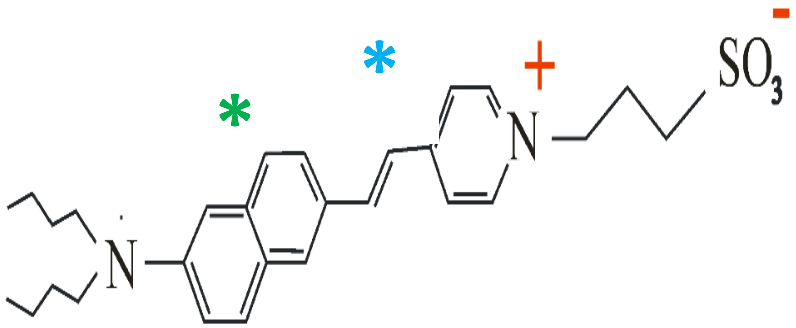
di-4-ANEPPS

IN VITRO STUDY OF PHOTODYNAMIC THERAPY

STYRIL DYES: DIPOLE MOMENT

*: aniline group **PROTEINS WITH AROMATIC AMINO ACIDS**

*: Unsaturated hydrocarbon chain **UNSATURATED LIPIDS IN MEMBRANE**



(- 4-[2-(6-(dibutylamino)-2-naphthalenyl)ethenyl)-1-(3-sulfopropyl)-pyridinium)

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IN VITRO STUDY OF PHOTODYNAMIC THERAPY

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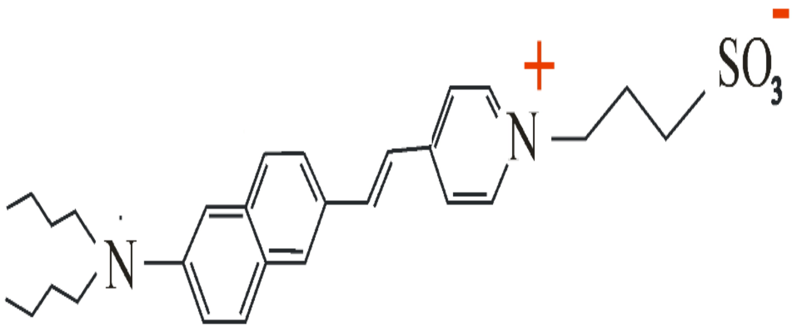

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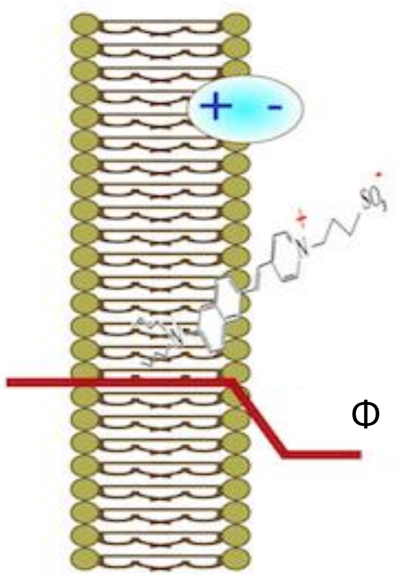

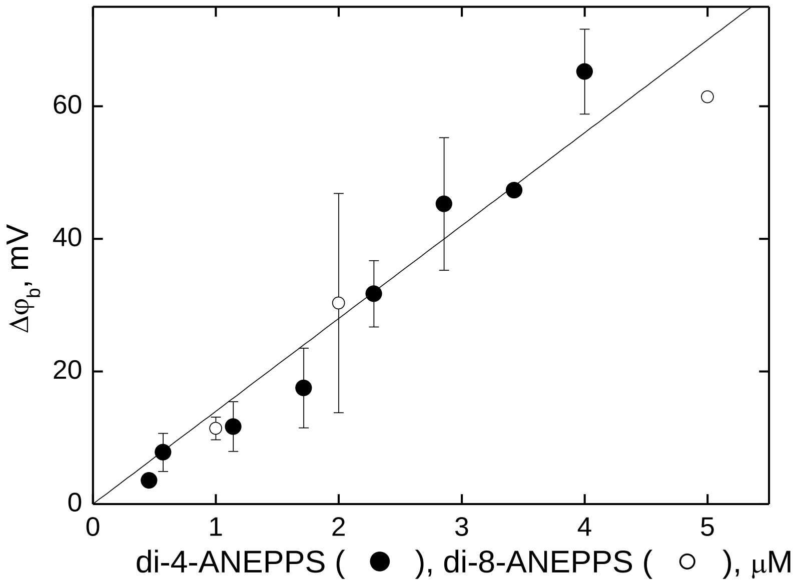

Malkov DY and Sokolov VS. Biochimia et Biophysica Acta. 1996. 197-2014.

IN VITRO STUDY OF PHOTODYNAMIC THERAPY

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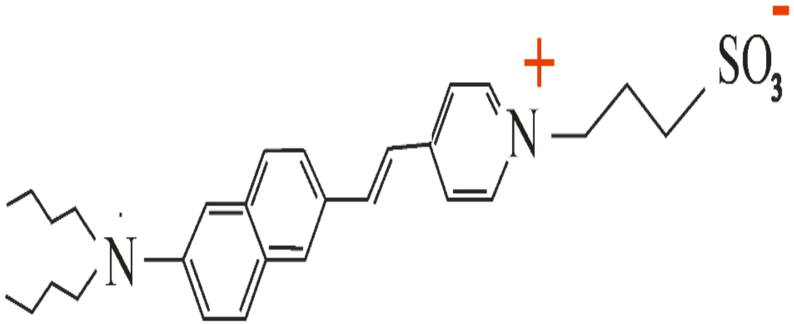


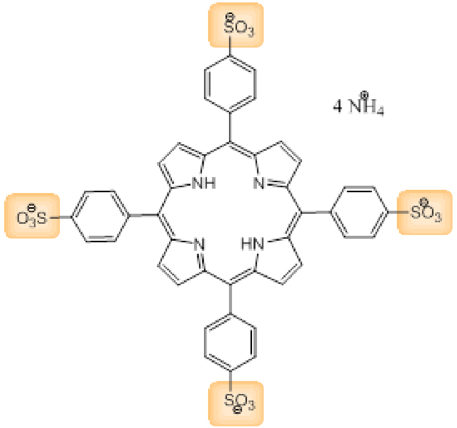
(- 4-[2-(6-(dibutylamino)-2-naphthalenyl)ethenyl)-1-(3-sulfopropyl)-pyridinium)

di-4-ANEPPS

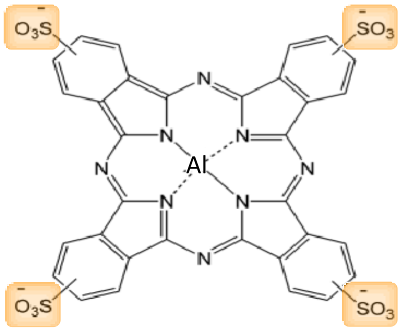
Target of SO

IN VITRO STUDY OF PHOTODYNAMIC THERAPY

STUDY OF CHARGED PHOTOSENSITIZERS



5,10,15,20-(tetra-4-sulfonatophenyl) porphyrin tetraammonium (TPPS4)



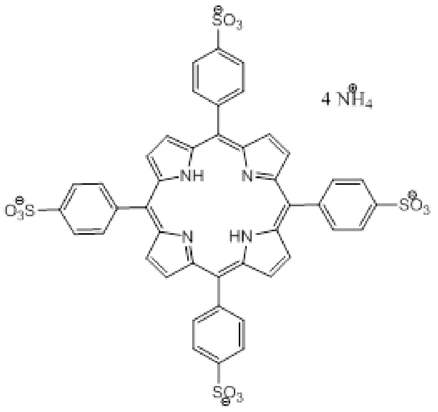
Al-phathalocyanin-Sn (AlPcSn)

IN VITRO STUDY OF PHOTODYNAMIC THERAPY

STUDY OF CHARGED PHOTOSENSITIZERS

Porphyrins:

- Naturally coloured compounds
- 4 pyrrole rings connected by methine bridges



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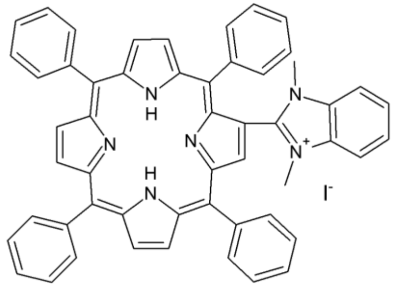
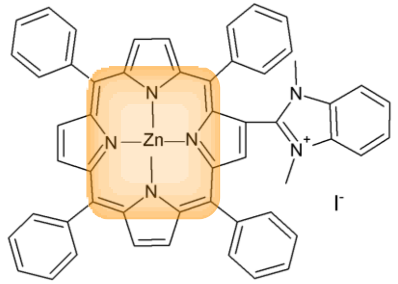
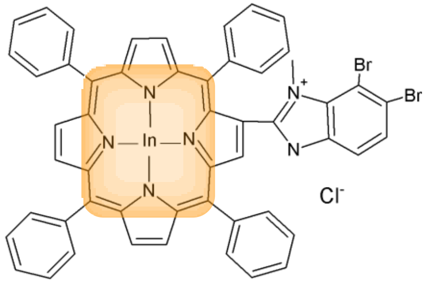
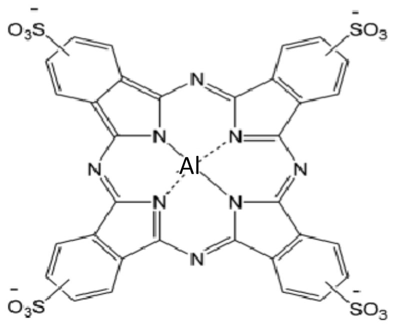






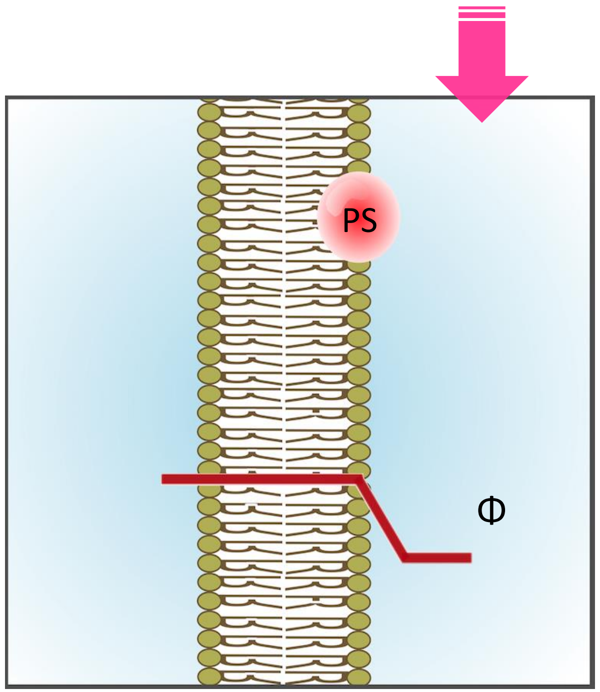


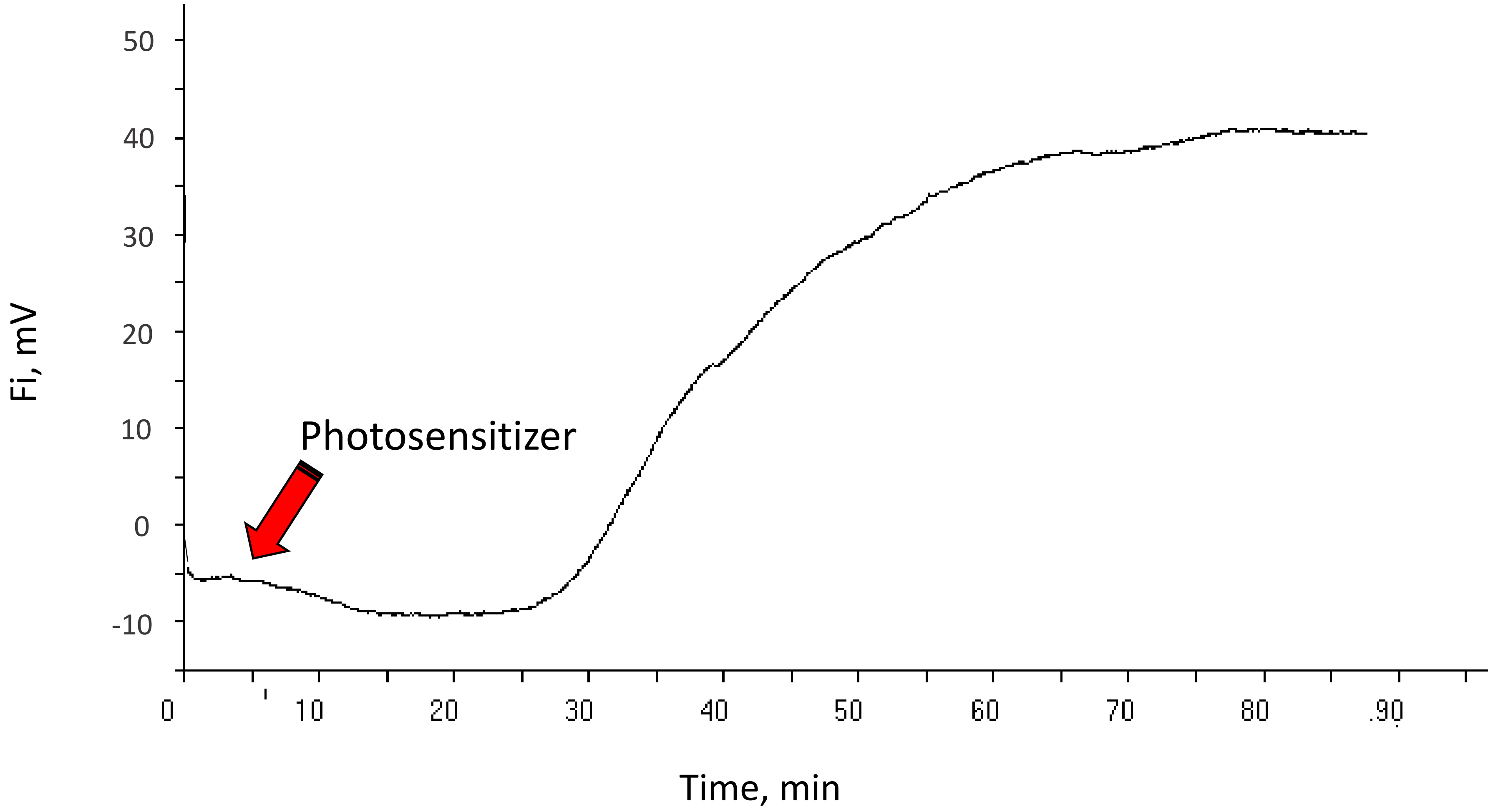
Al-phathalocyanin-Sn (AlPcSn)

OBJECTIVES

- To monitor the adsorption of 3 different porphyrins on bilayer lipid membranes (BLM) by the intramembrane field compensation (IFC) method.
- To evaluate the photodynamic efficiency of such photosensitizers by the rate of damage of molecules of di-4-ANNEPS by singlet oxygen generated under illumination of BLM.
- To compare their efficiency with a tetrasulfonated porphyrin (TPPS4) and a sulfonated aluminium phtalocyanine studied previously in our laboratory.

ADSORPTION OF PHOTOSENSITIZERS ON BLM





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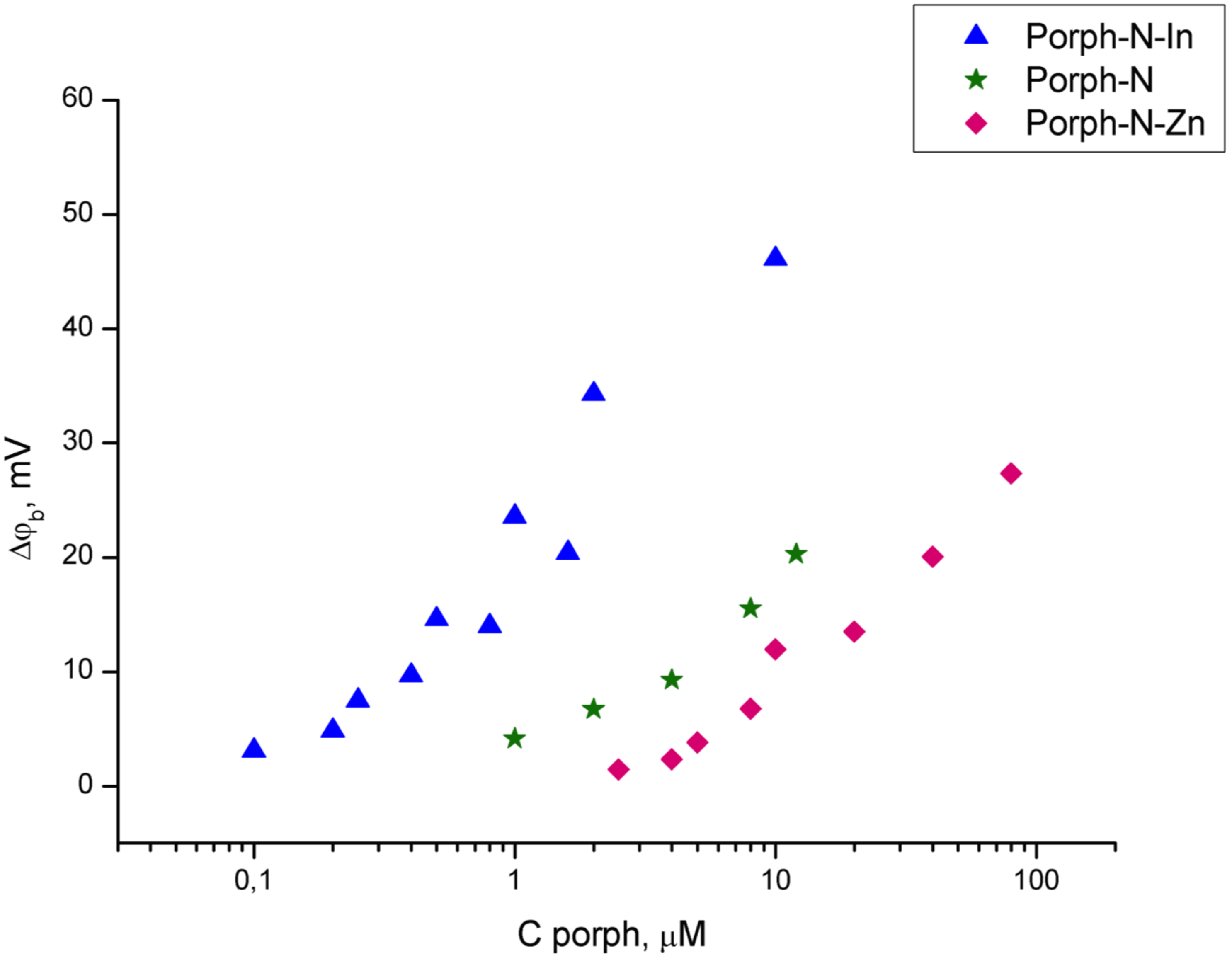

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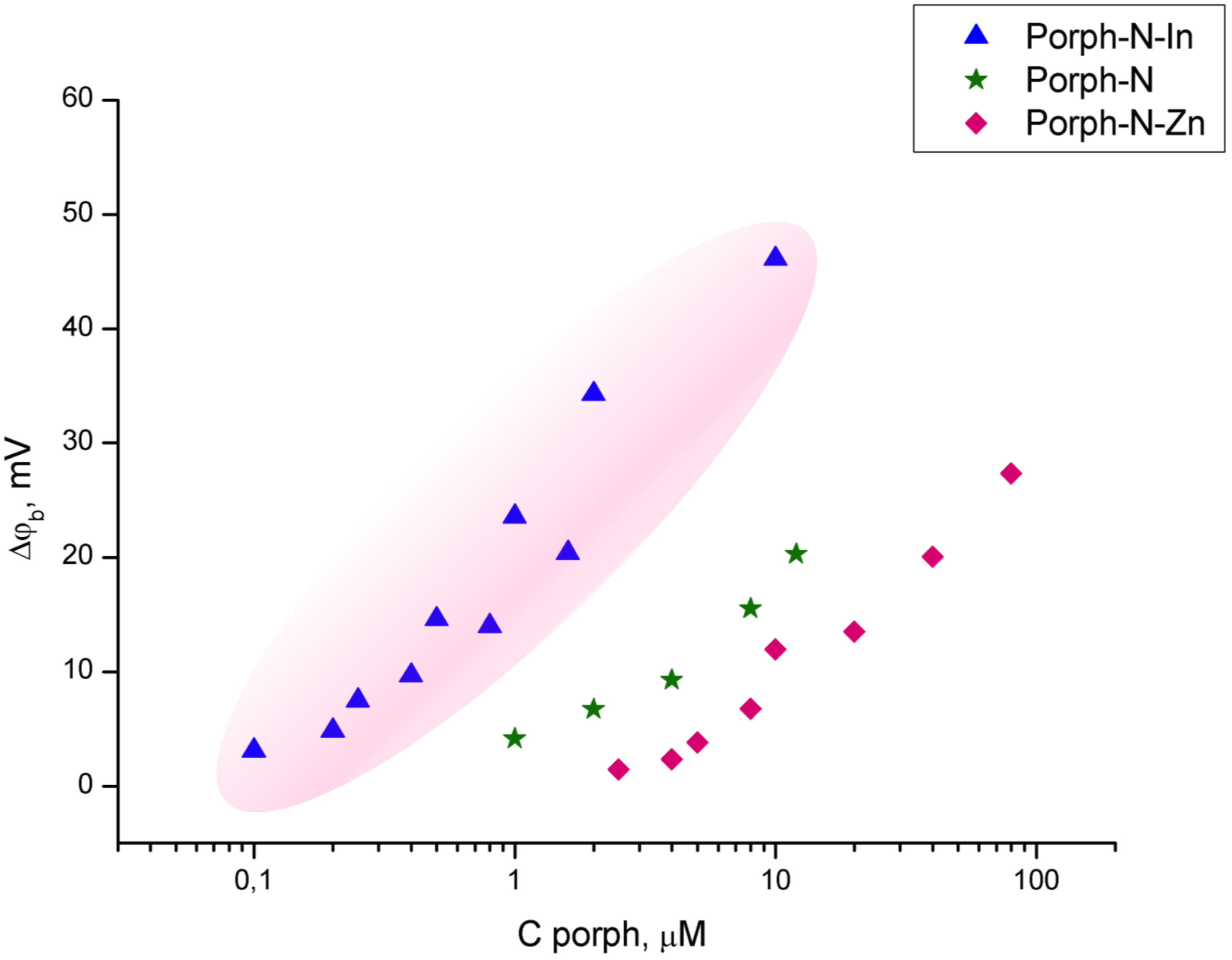

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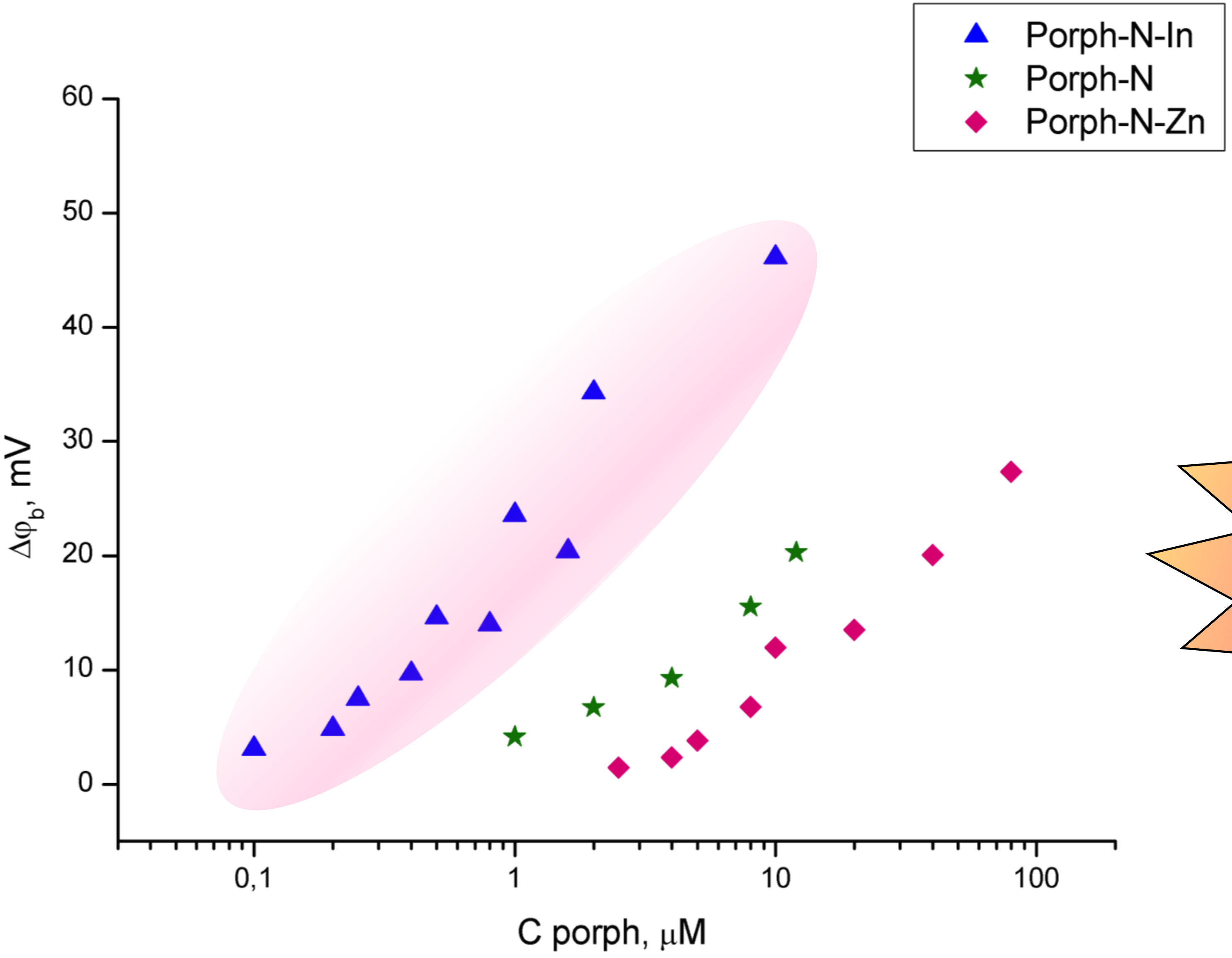
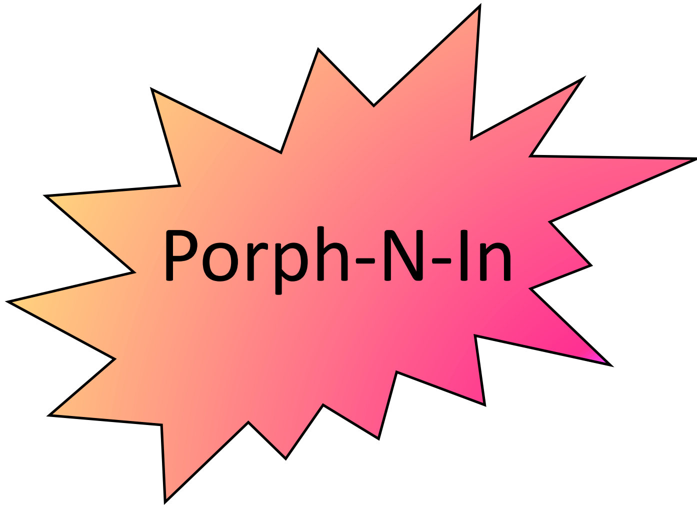
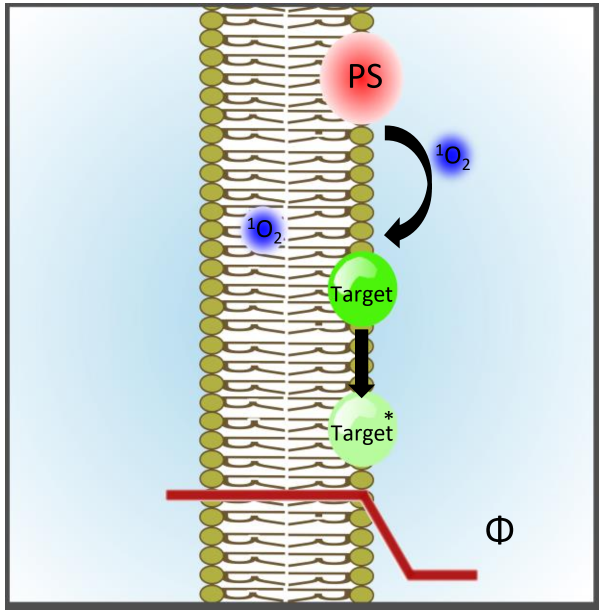


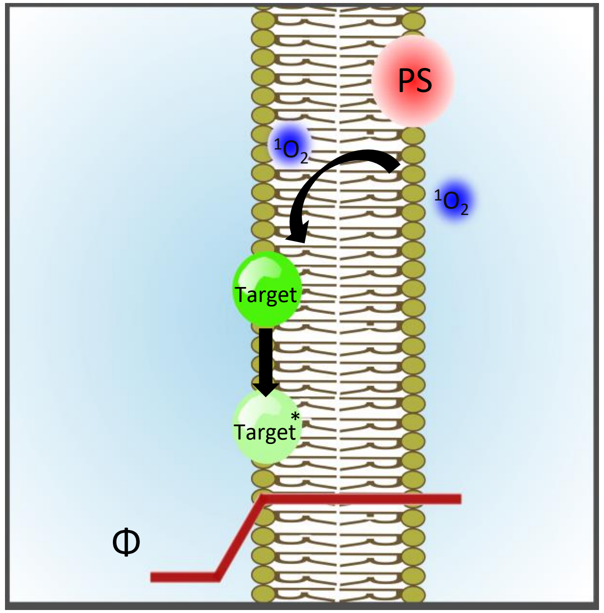


PHOTOOXIDATION OF di-4-ANEPPS BY SO

Cis- configuration



Trans- configuration



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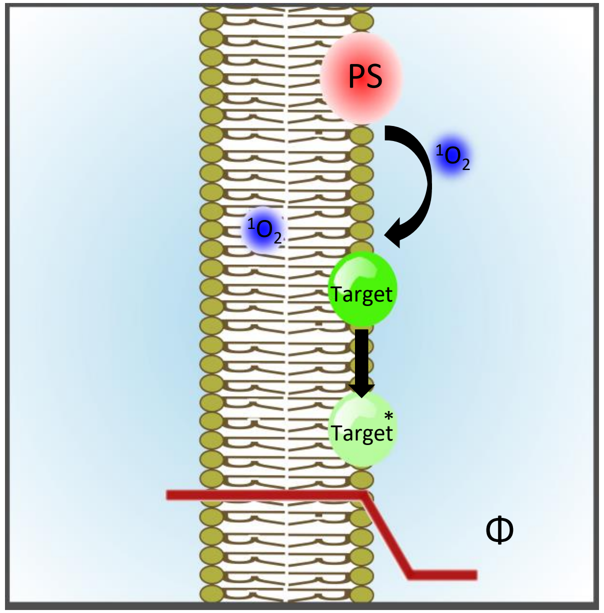

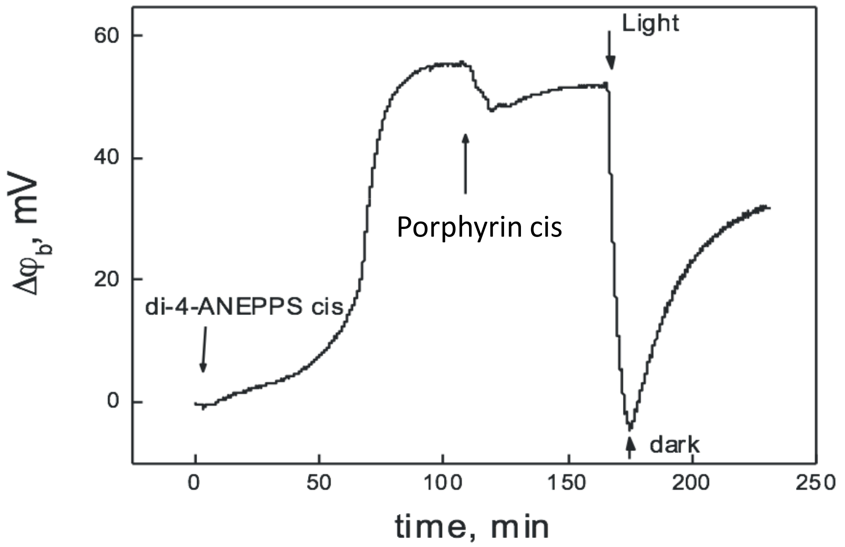

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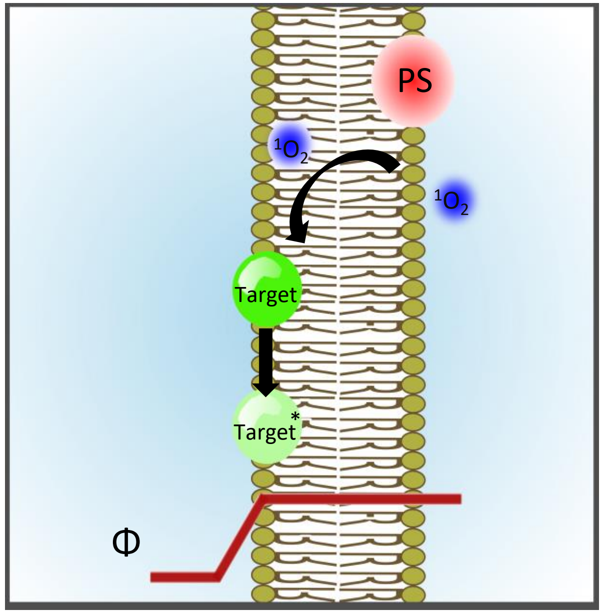

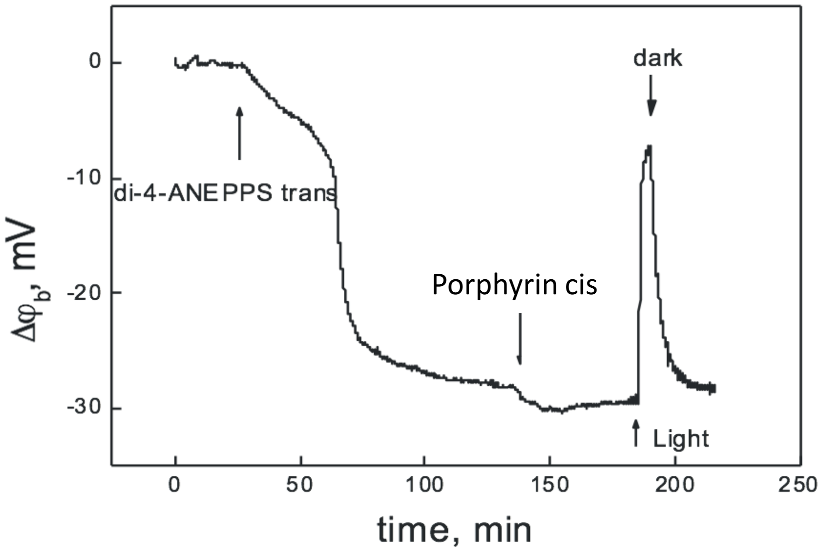

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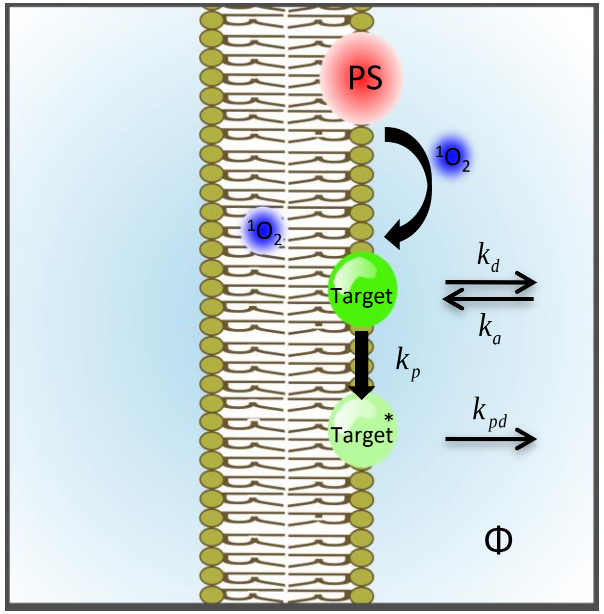

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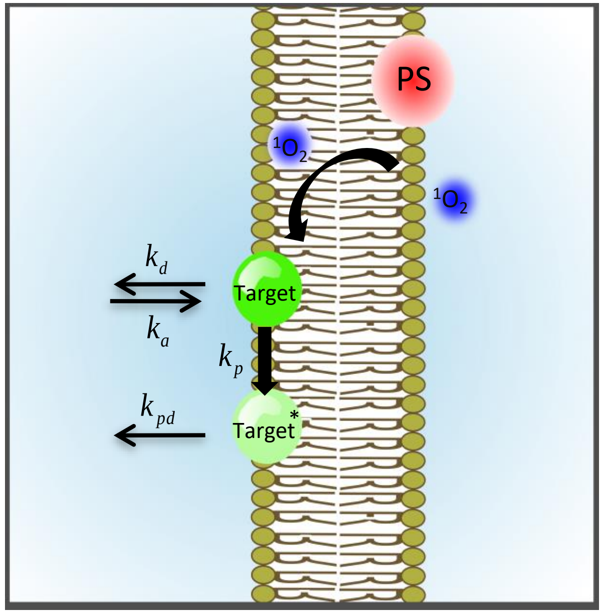
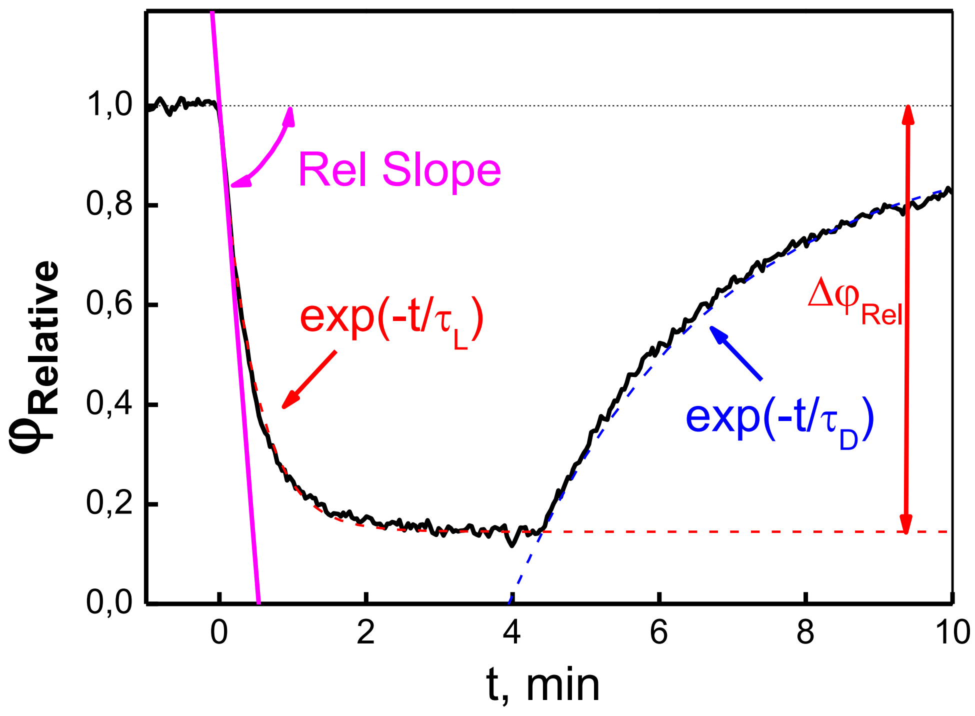
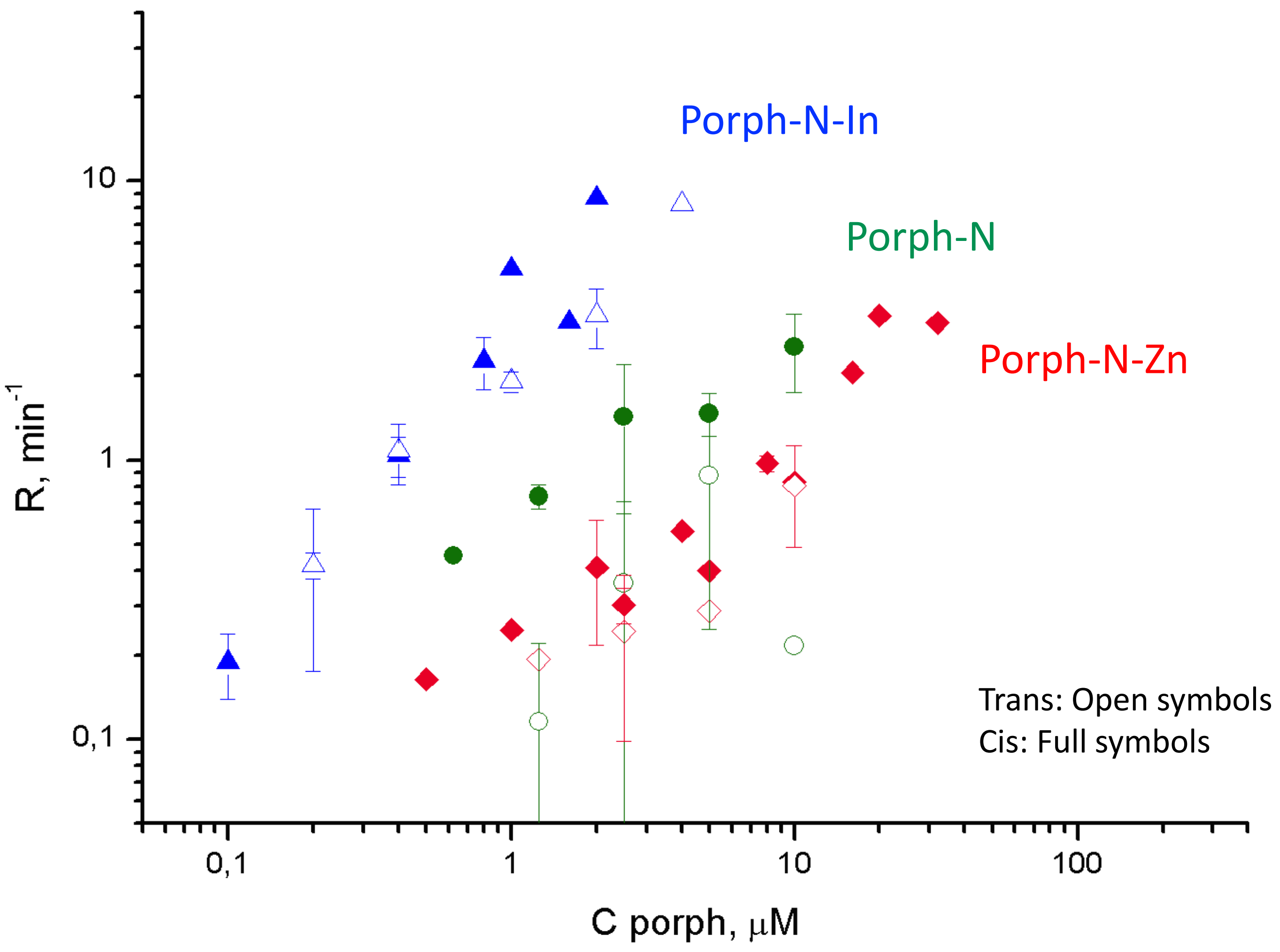




$$R = k_p[^1O_2] = \frac{1}{\tau_L} - \frac{1}{\tau_D}$$

Sokolov, V.S., Shcherbakov, A.A., Tashkin, V.Y. et al. Russ J Electrochem (2017) 53: 1171.

PHOTOOXIDATION OF di-4-ANEPPS BY SO



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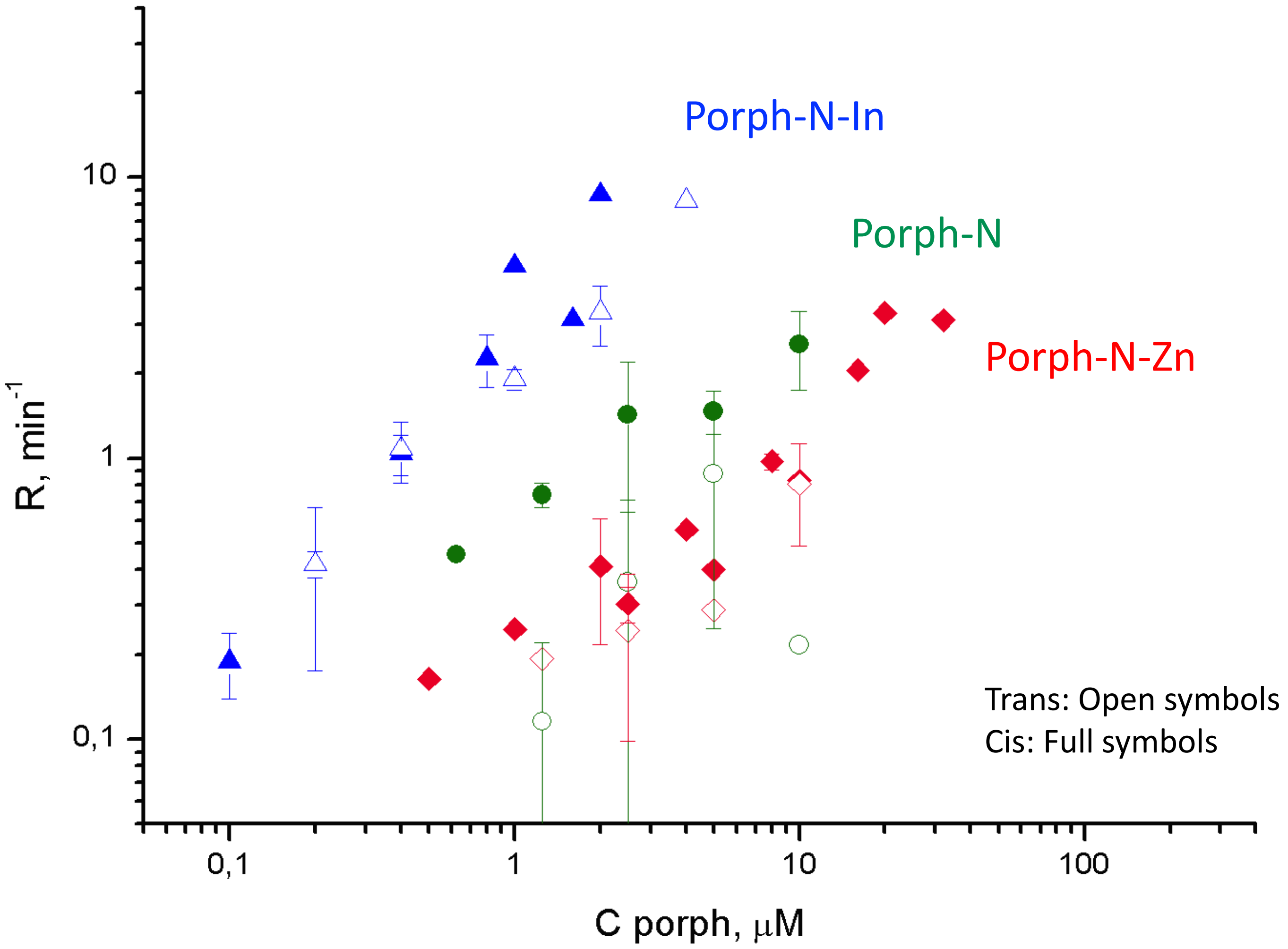

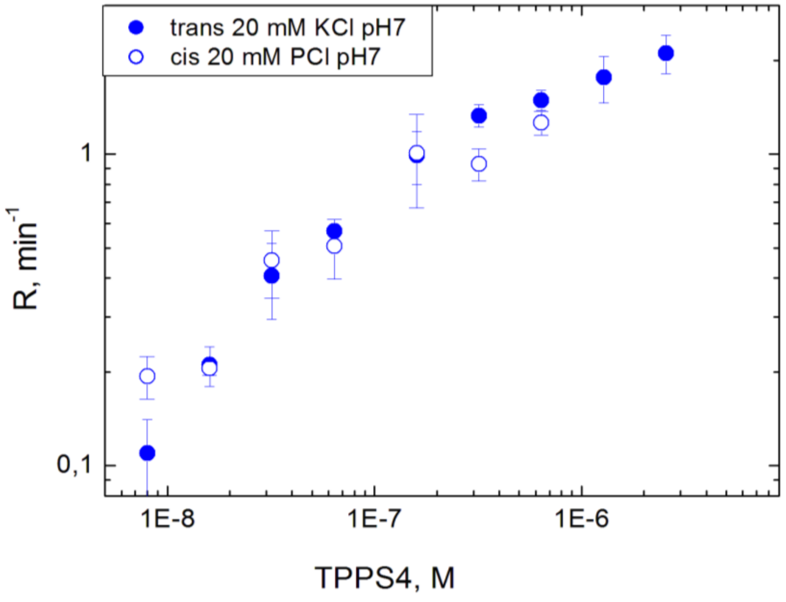

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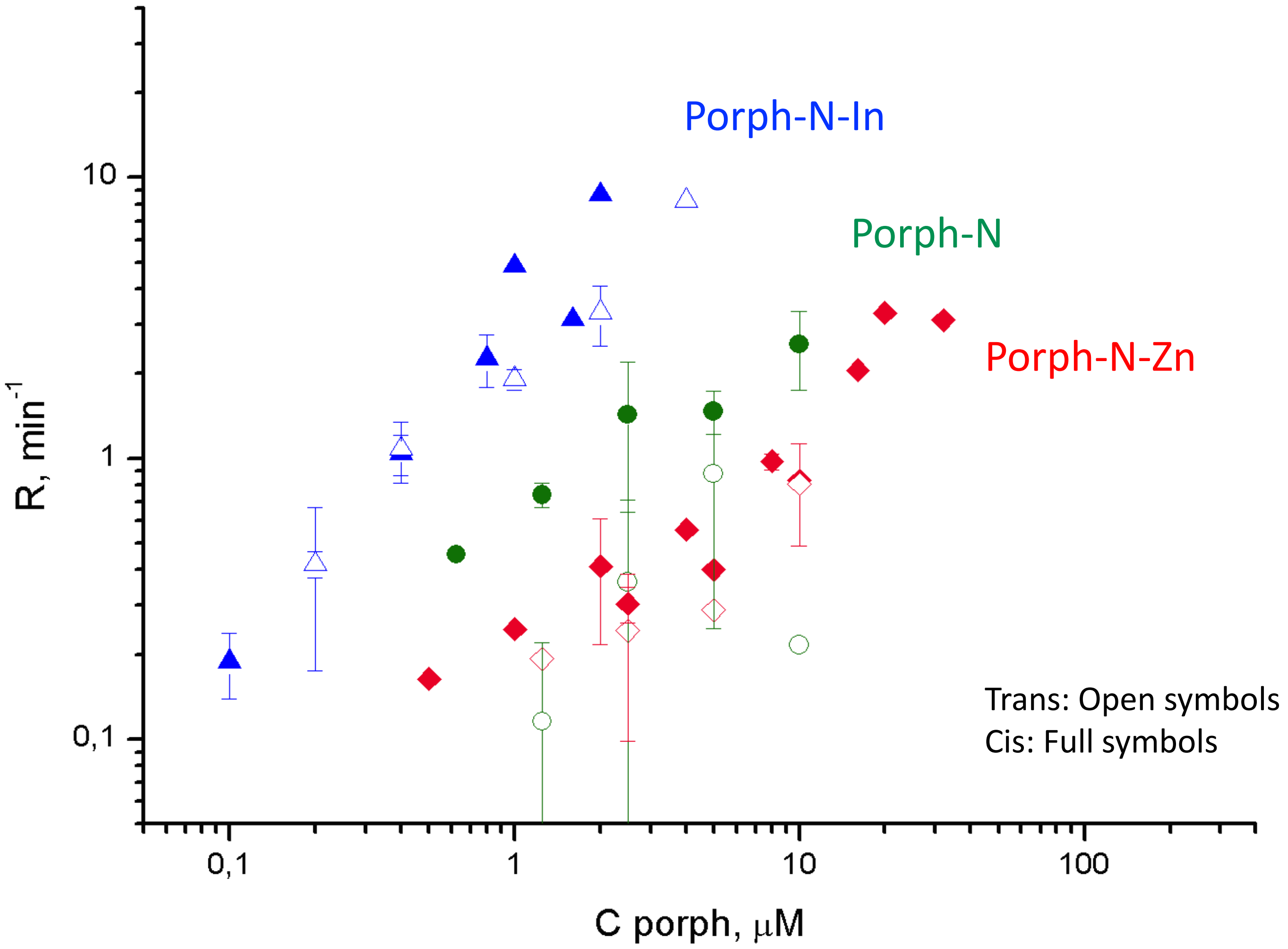
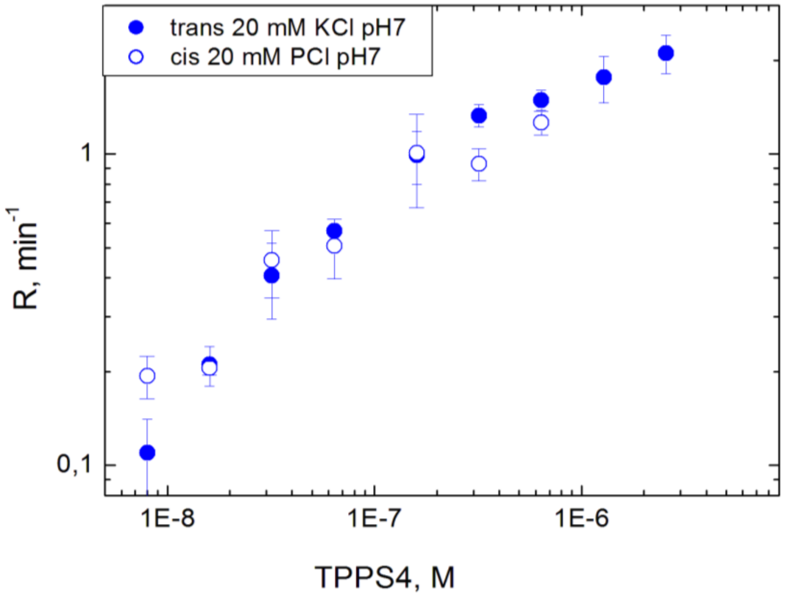
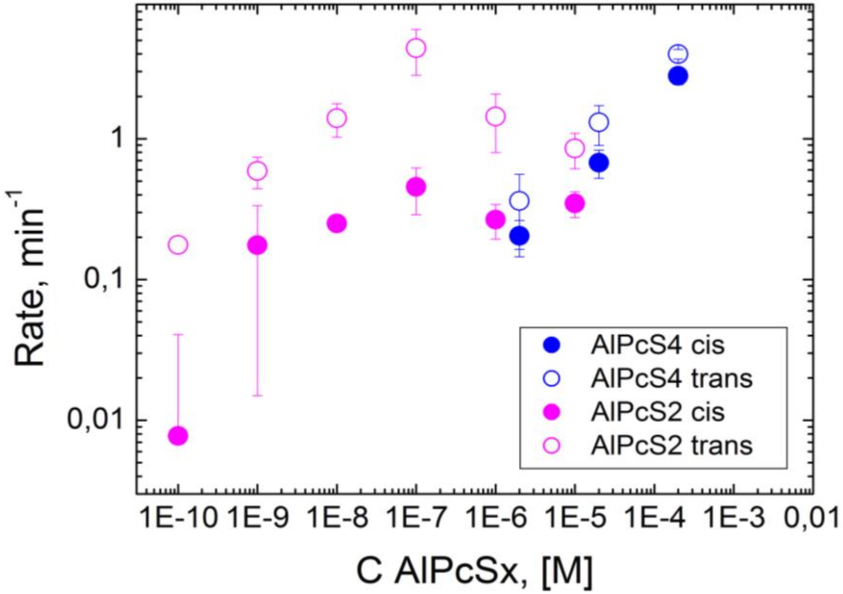


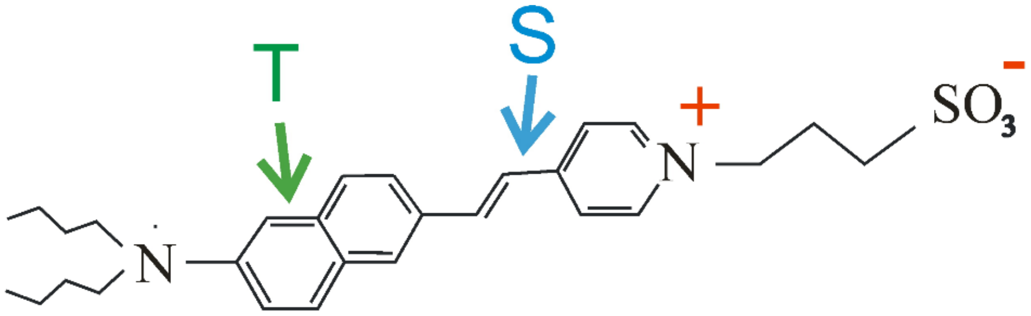


Konstantinova AN, et al. 2018. Submitted

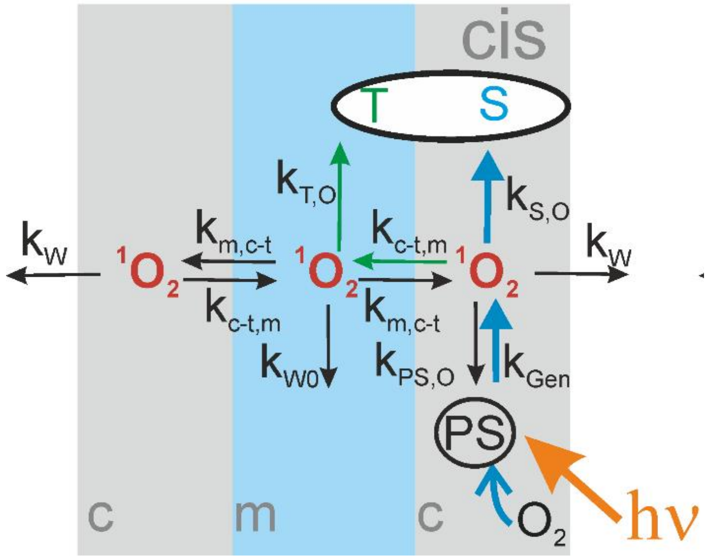


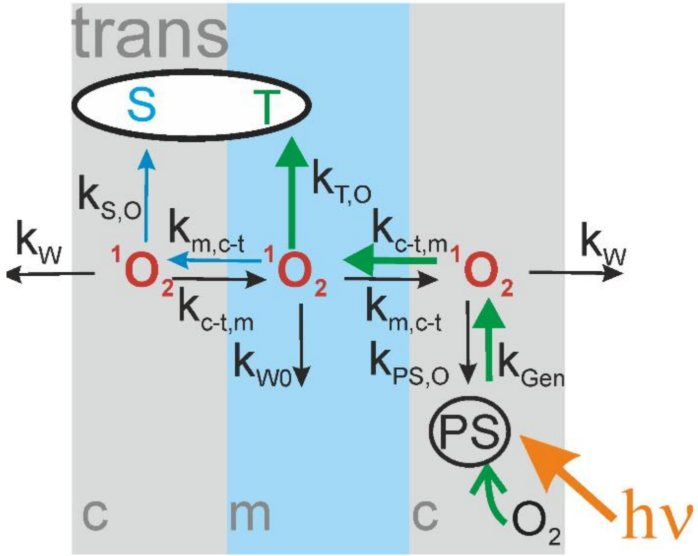
PHOTOOXIDATION OF di-4-ANEPPS BY SO PRODUCED BY $AlPcS_x$

Target molecules possess two different moieties that may serve as SO target:



* Membrane: 3-layer system





Sokolov VS, et al. 2018. Submitted

CONCLUSIONS

- All the photosensitizers used in this study showed adsorption in a concentration-dependent manner.
- Porphyrin with Indium displayed higher boundary potential in comparison with the other 2 photosensitizers.
- Rate of photooxidation of target molecule (di-4-ANEPPS) by porphyrins with metal ions was the same in both configurations (cis and trans).
- Further studies are necessary to evaluate the precise contribution of chemical structures of each compound in the photooxidation of target molecules.

ACKNOWLEDGMENTS

Kirill Birin

Yulia Gorbunova

Valery Sokolov

Sergey Akimov

Oleg Batishchev

A.N. Frumkin Institute of Physical Chemistry and Electrochemistry

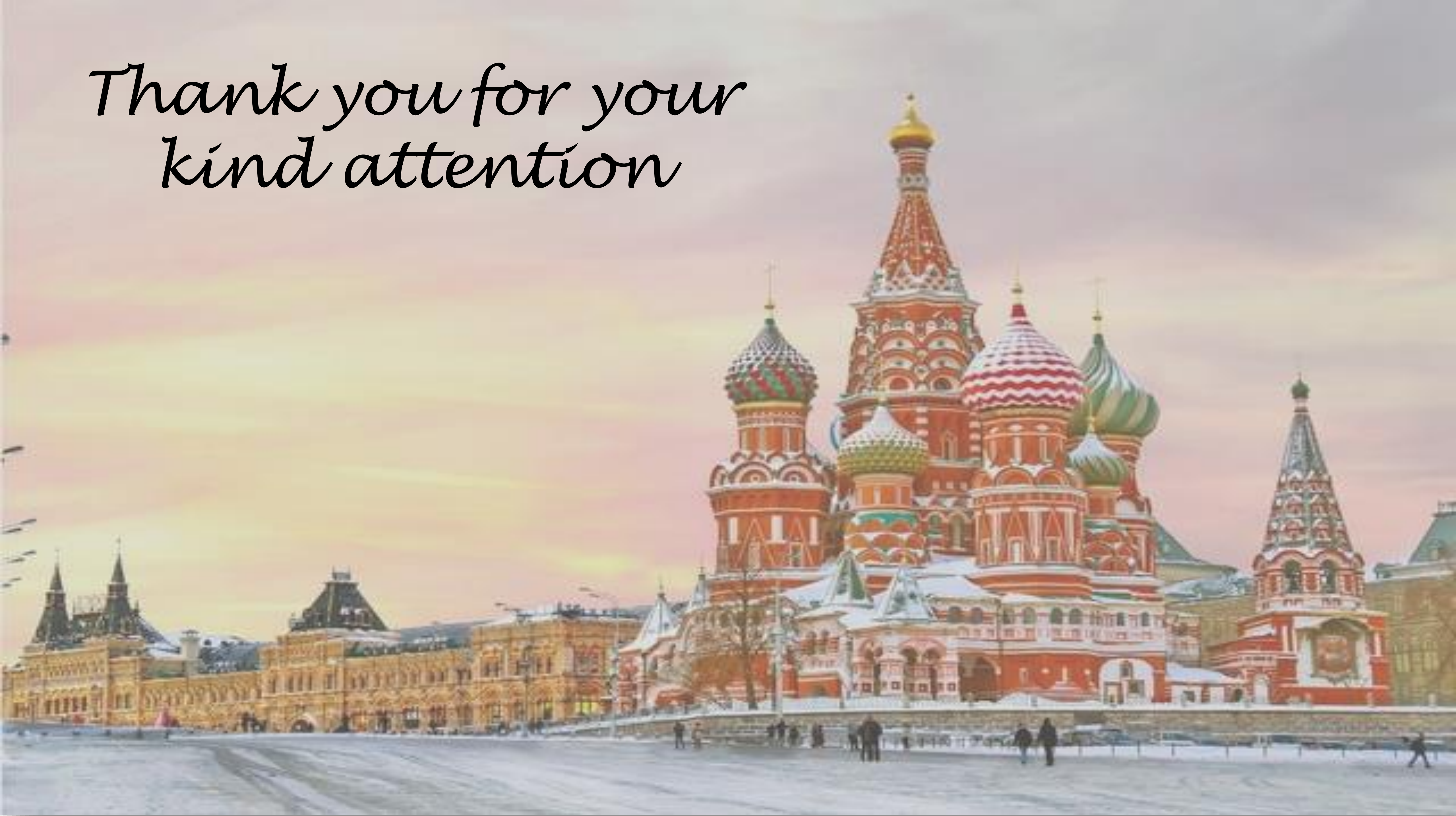
N.S. Kurnakov Institute of General and Inorganic Chemistry

RSF | Russian Science Foundation

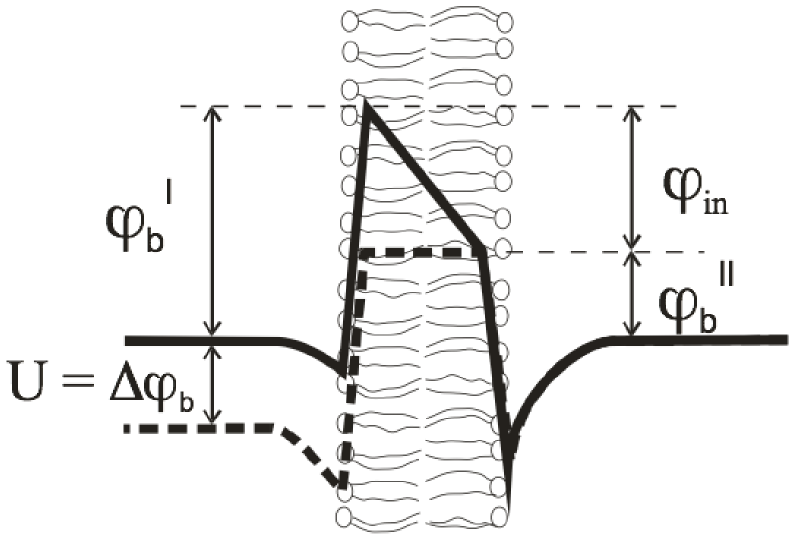
MISIS National University of Science and Technology

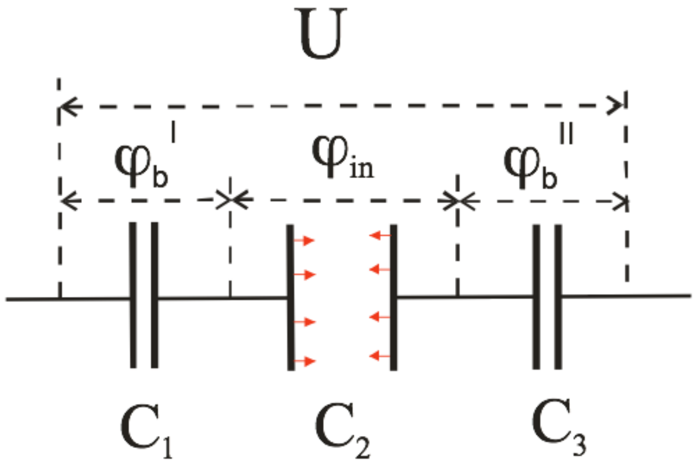
Russian Academy of Sciences

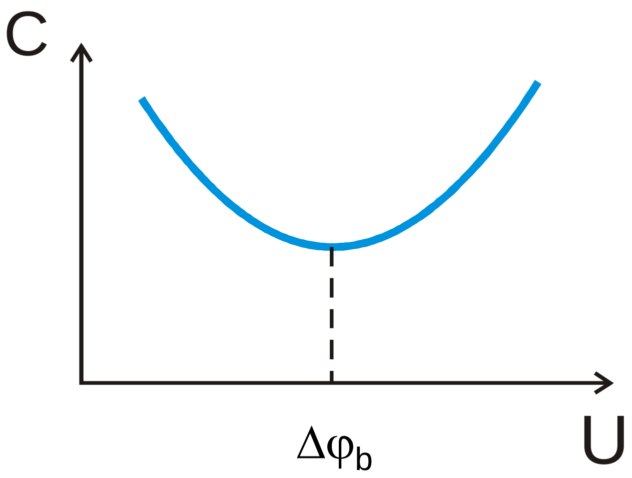
Thank you for your kind attention



How to measure the boundary potential by IFC?







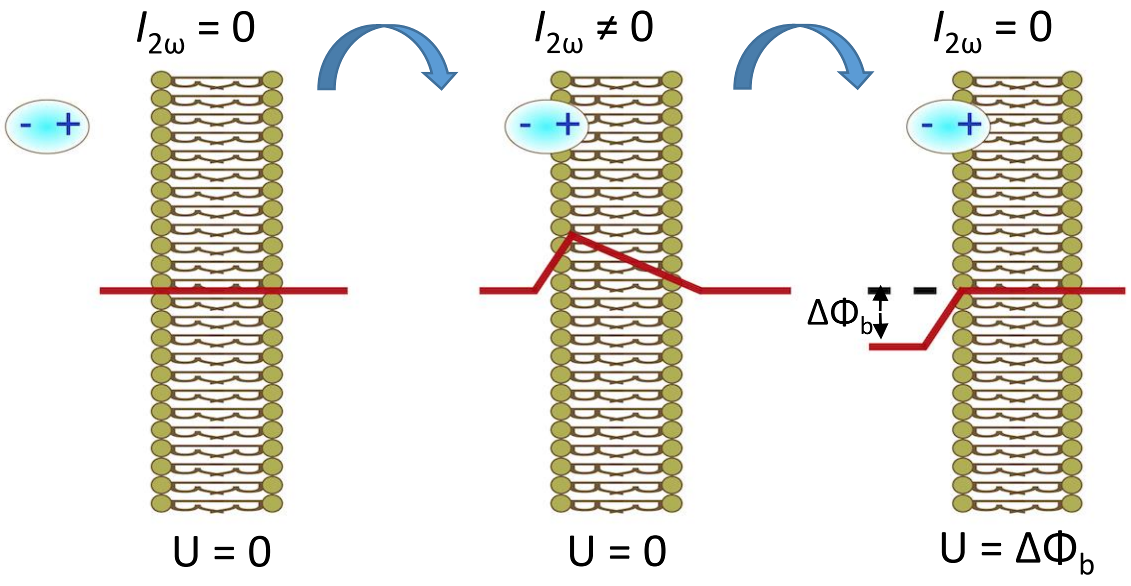
$$C = C_0\left[1 + \alpha(U - \Delta\varphi_b)^2\right]$$

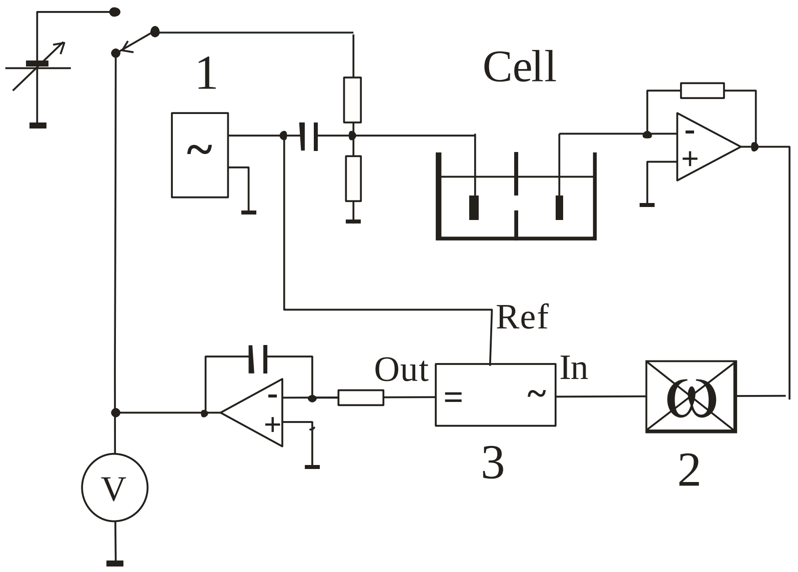
$$U = U_0 + V\cos(\omega t)$$

$$I_{2\omega} = 3\alpha C_0 \omega V^2 (U_0 - \Delta\varphi_b)$$

Inner field compensation: realization

The applied voltage = U + Vcos(ωt)





Sokolov VS, Kuz´min VG. Biofizika. 1980 Jan-Feb;25(1):170-2.