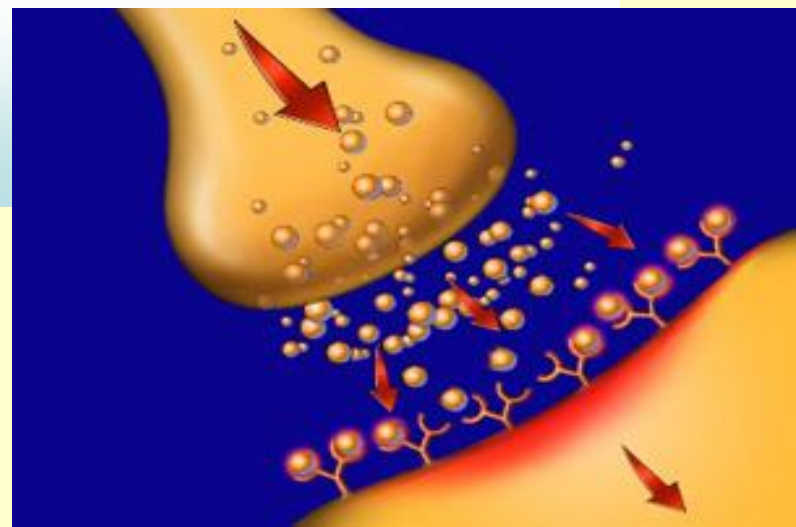
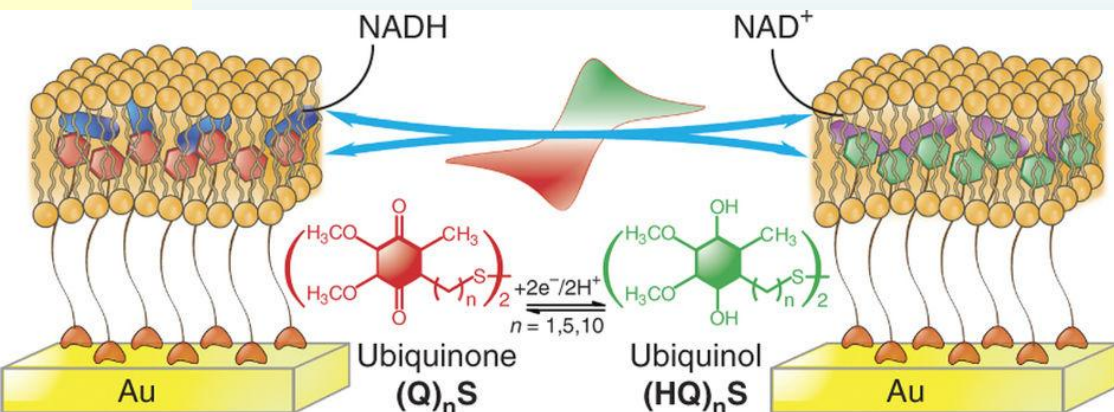
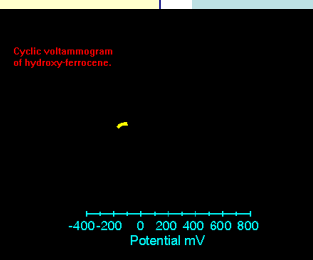
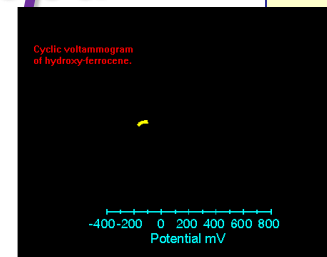
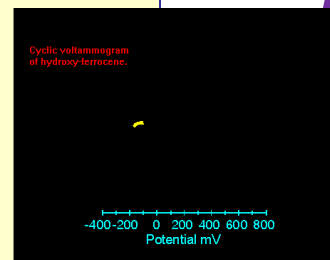


ВОЛТАМЕТРИЈА-моќна техника за детекција и испитување на својствата и механизмот на акција на некои невротрансмитери

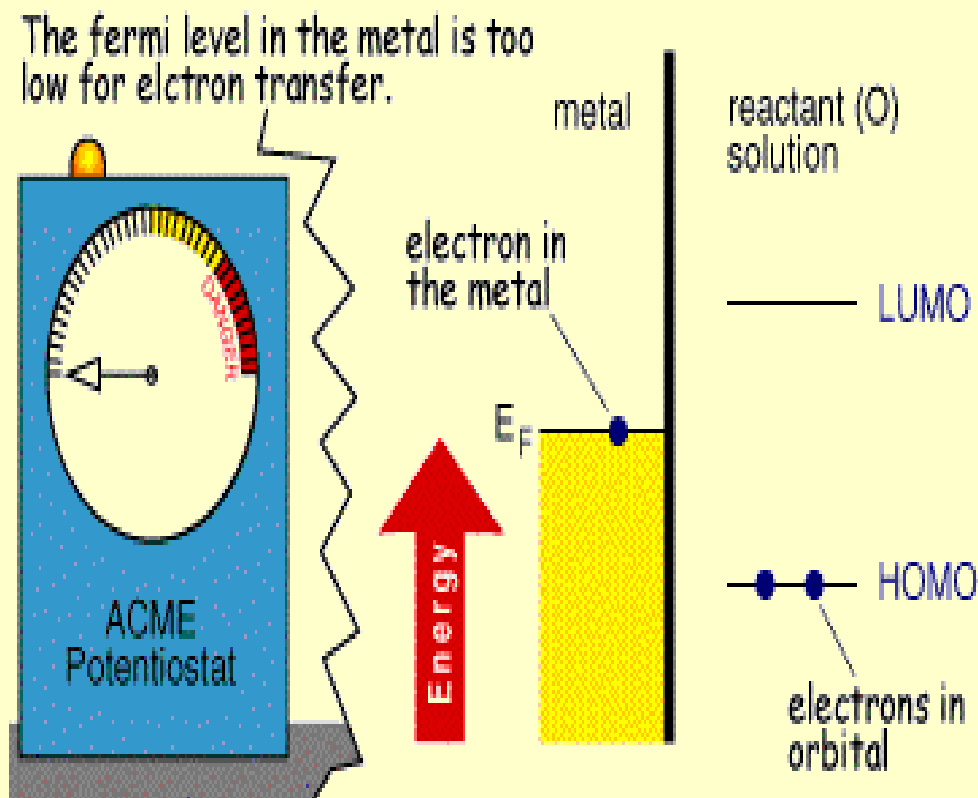
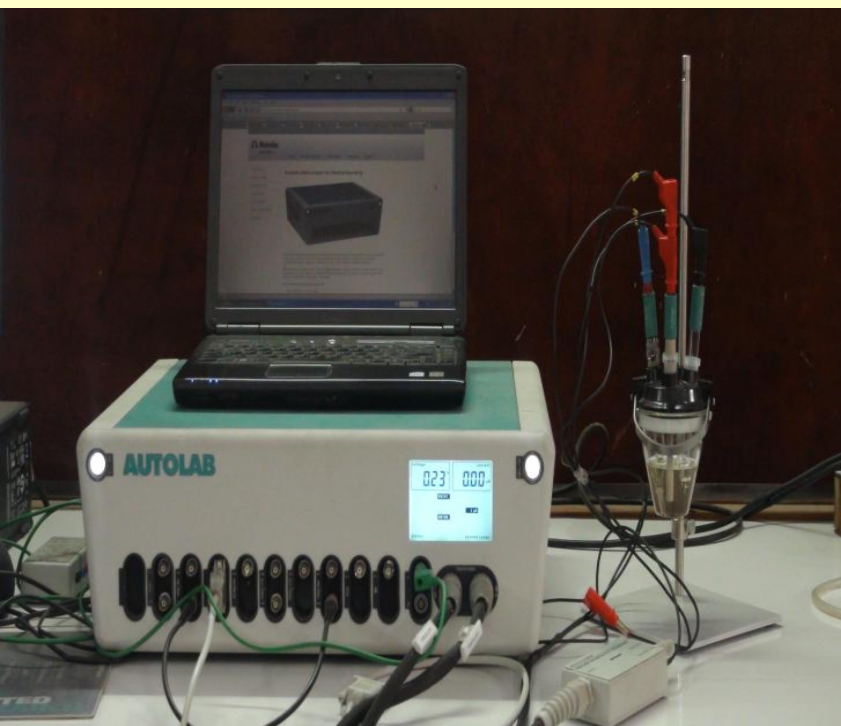
Rubin Gulaboski
СЕМИНАР НЕВРОНАУКИ

ФМН-УГД-ШТИП, 01. 11. 2017-Stip, Macedonia-

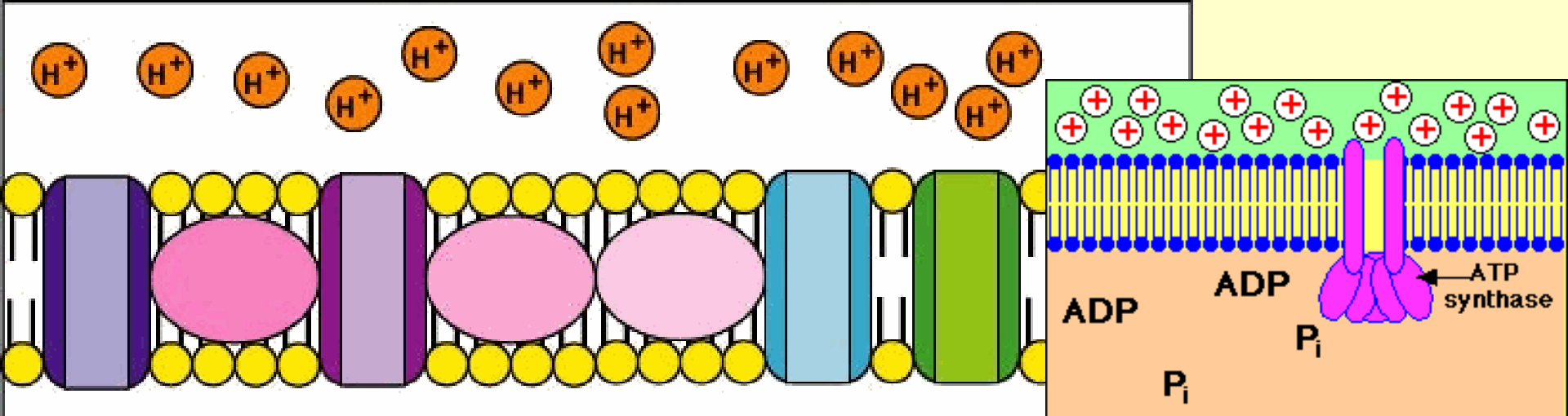
Faculty of Medical Sciences
Goce Delcev University, Stip, Macedonia



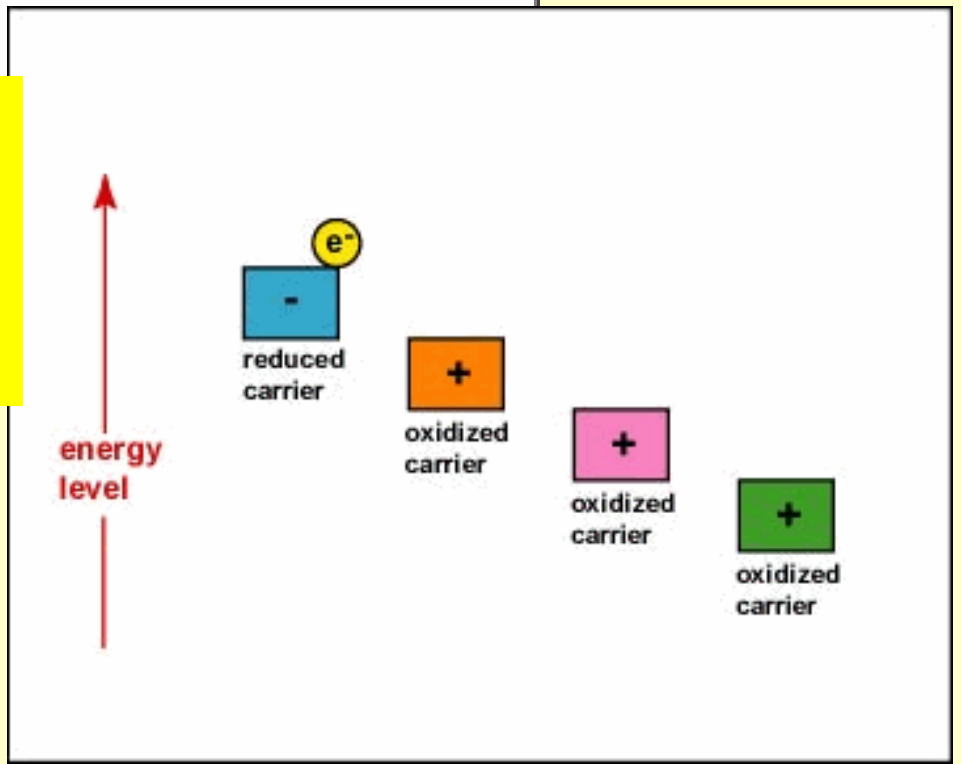
VOLTAMMETRY is a branch of **ELECTROCHEMISTRY**
*-deals wity the processes of CHARGE transfer
between two systems in contact
-FLOW of electric charge=CURRENT*

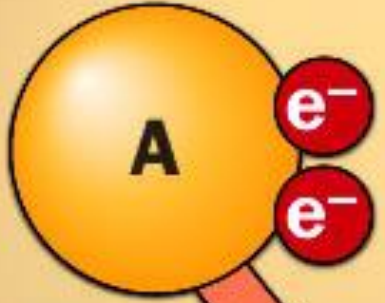


**We can say-voltammetry deals MAINLY with
Processes of oxidation and reduction**



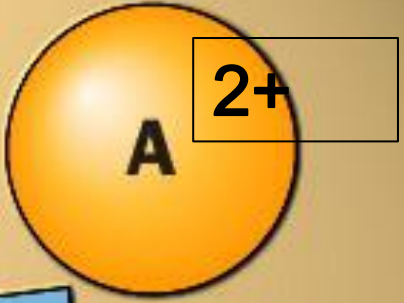
The Electron Transport Chain
 -most important
 Electrochemical process
 in living systems





Reducing agent

Oxidation
Compound A
loses electrons

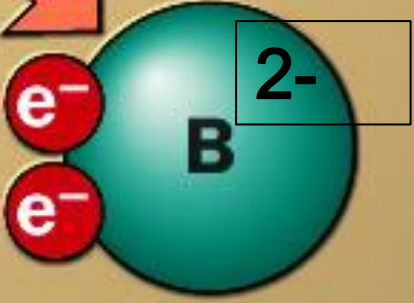


Oxidized

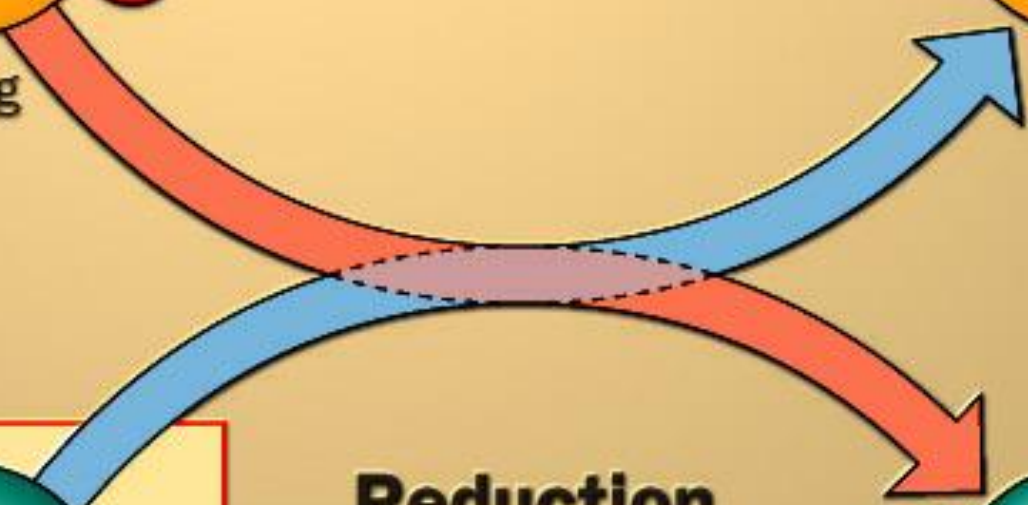


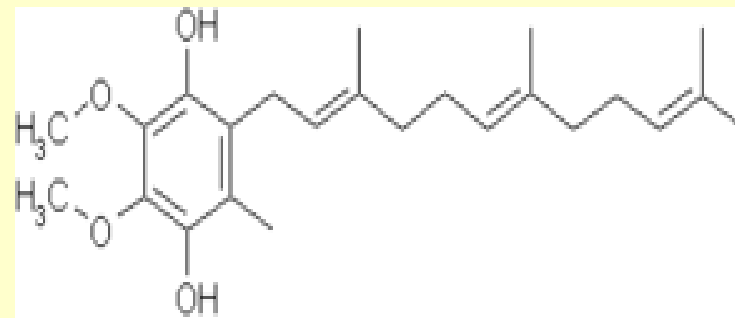
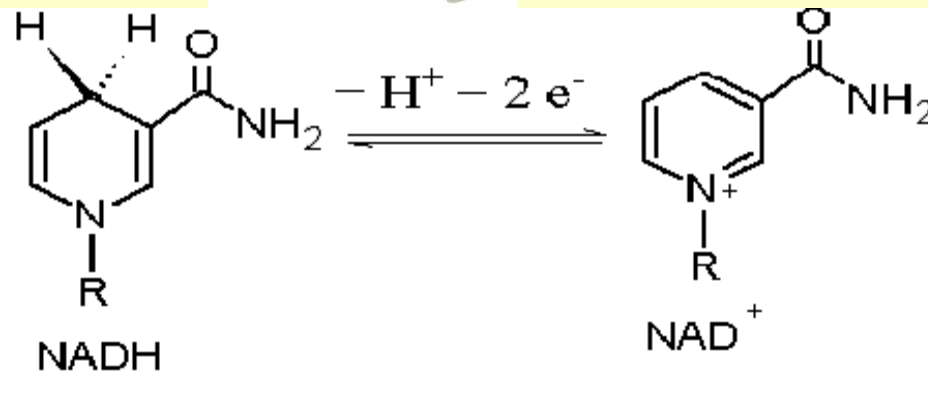
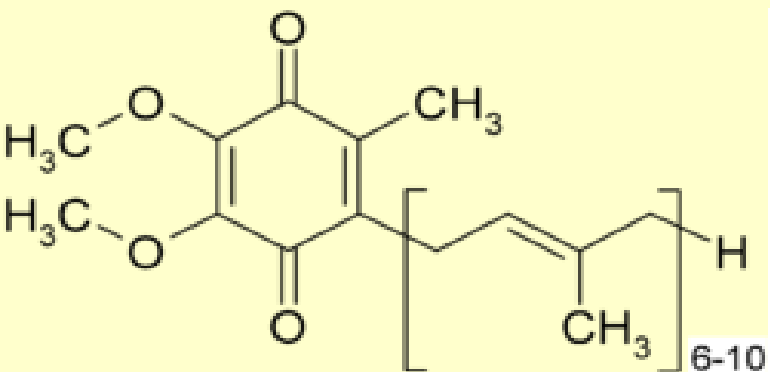
Oxidizing agent

Reduction
Compound B
gains electrons



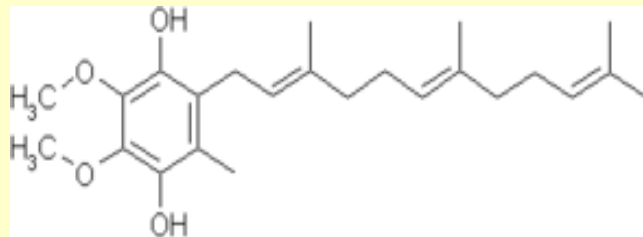
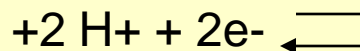
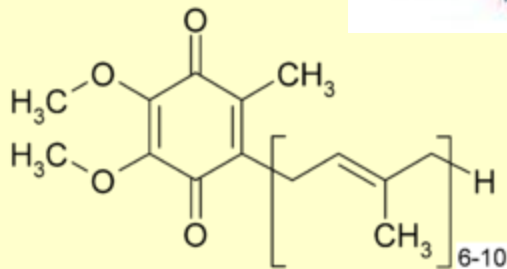
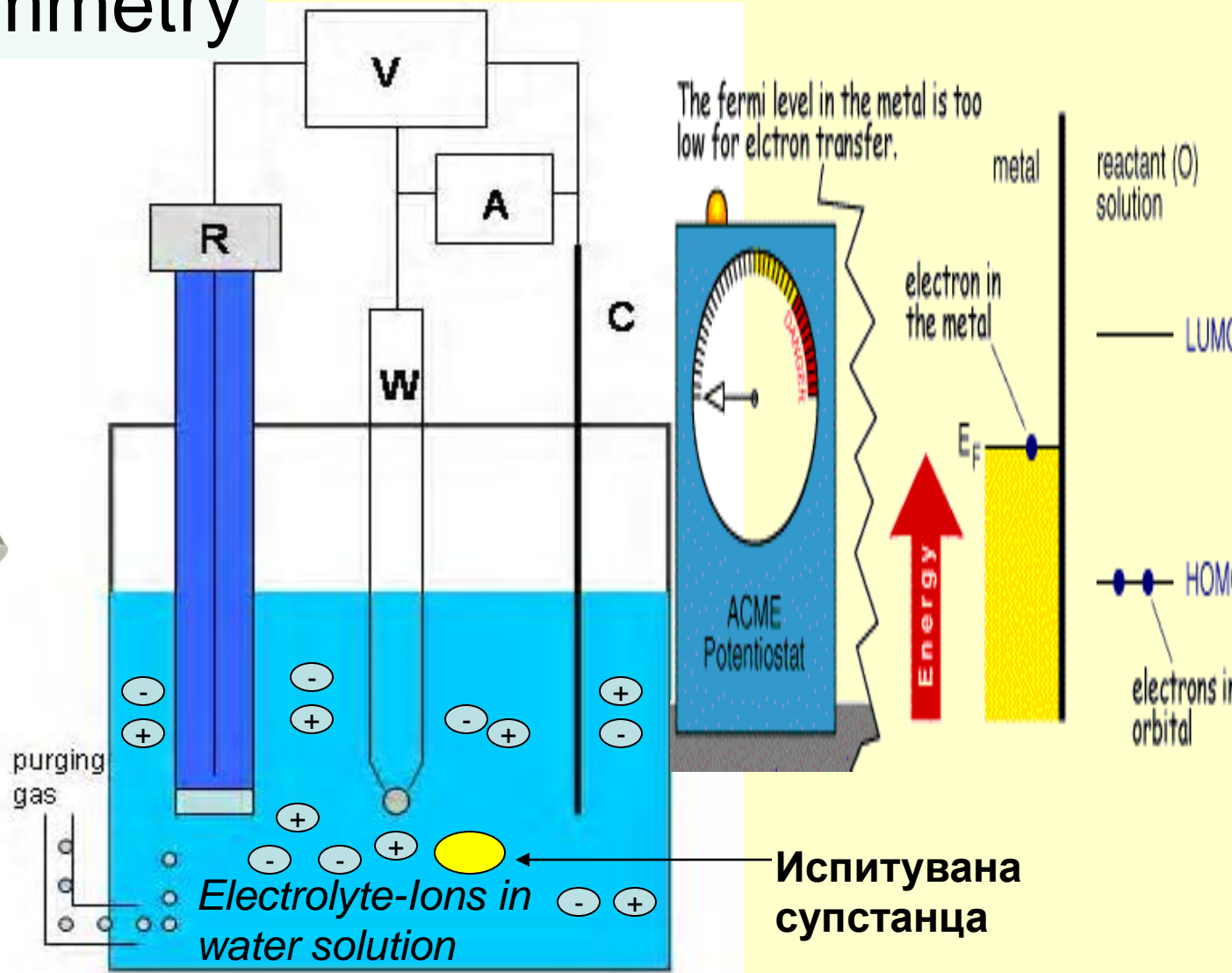
Reduced



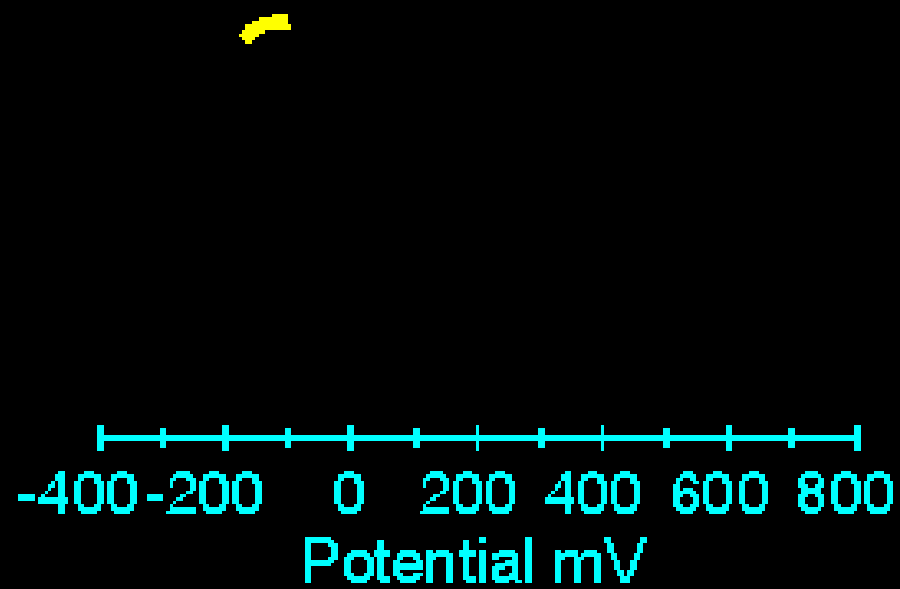


Voltammetry

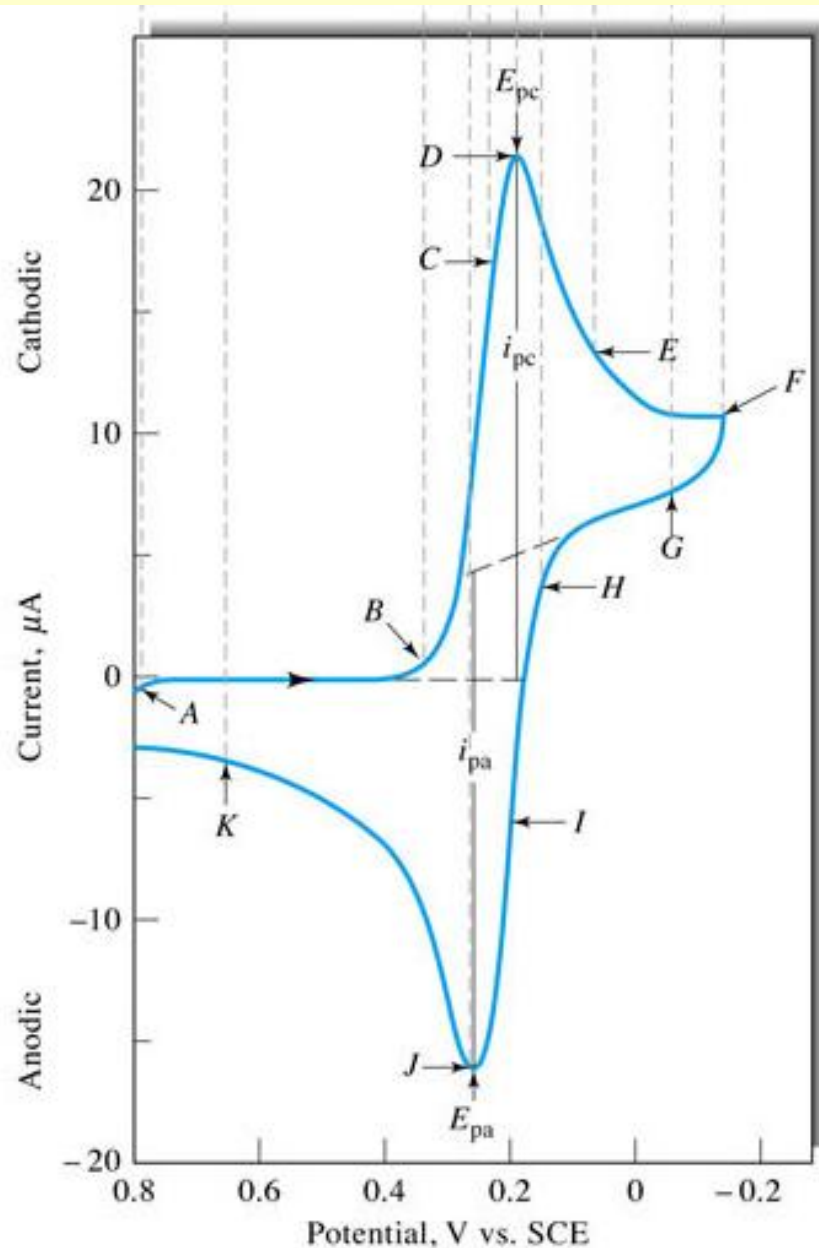
W-working electrode



**Cyclic voltammogram
of hydroxy-ferrocene.**



What do we get from cyclic voltammograms



i_{pc} i_{pa}

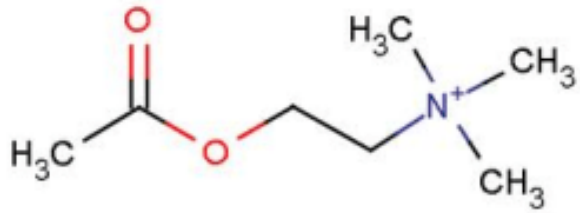
$\Delta E_p = (E_{pa} - E_{pc}) = 0.0592/n$,
 $n = \text{number of electrones exchanges}$

$E^0 = \text{mid-peak potential } E_{pa} \rightarrow E_{pc}$

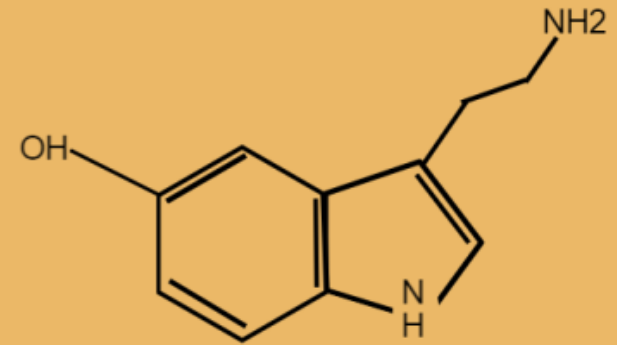
$I_p = 2.686 \times 10^5 n^{3/2} A c D^{1/2} v^{1/2}$

- **A**: electrode surface
- **c**: electroactive compound concentration
- **v**: scan rate
- **D**: diffusion coefficient

Волтаметрија на некои неутротрансмитери



Acetylcholine



SERETONIN



ДОПАМИН



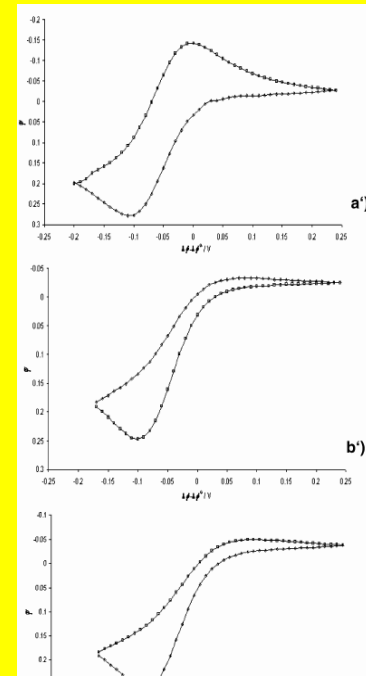
Serotonin is the main contributor to wellbeing and happiness. It also aids the sleep cycle and the digestive system. A deficit of serotonin often leads to the development of depression.

Што може да се испитува кај овие невротрансмитери со волтаметрија и на кој начин?

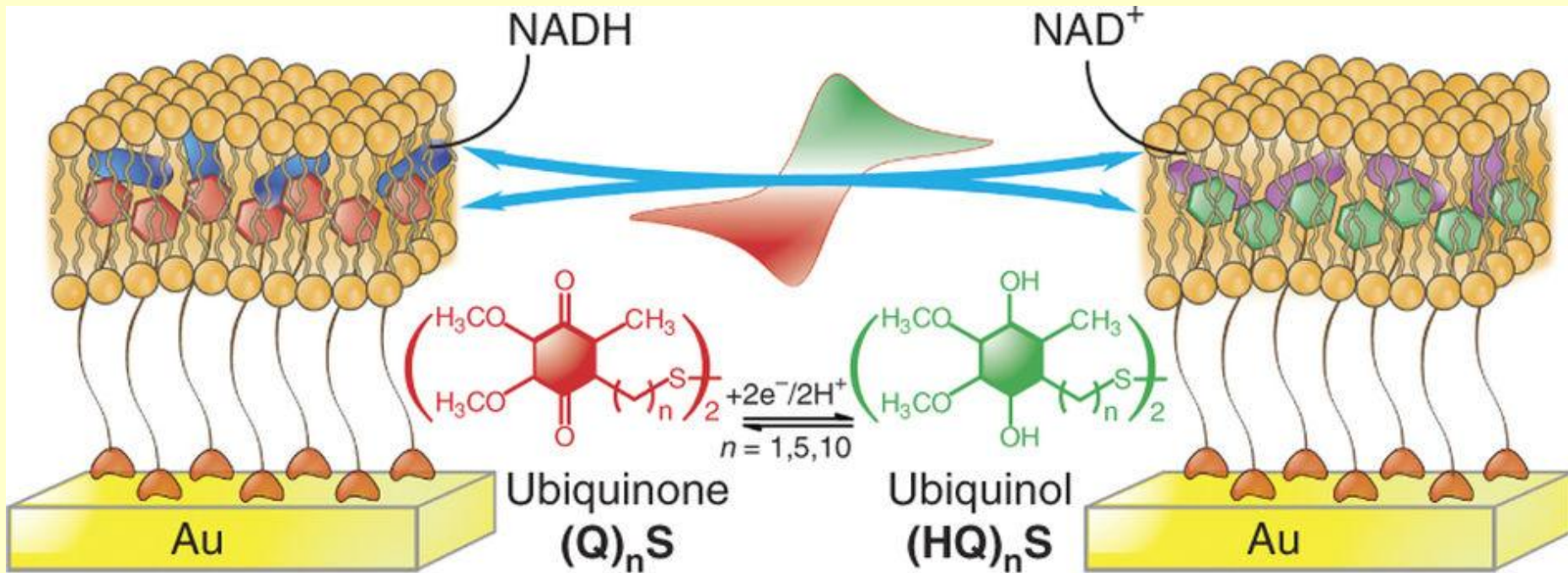
Cyclic voltammogram
of hydroxy-ferrocene.

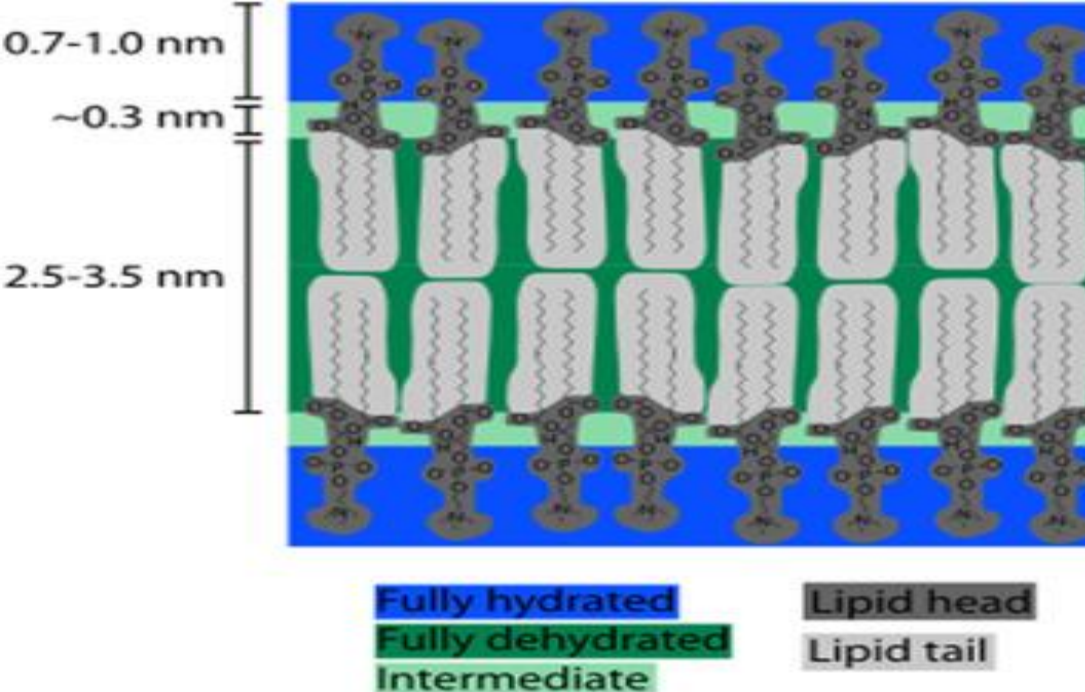
-400 -200 0 200 400 600 800
Potential mV

- нивните редокс процеси (размена на електрони)
- нивните механизми на трансфер преку мембрани
- потенцијалните интеракции со други супстанции
- брзината на дифузија
- кинетиката (брзината) на нивен трансфер или
Кинетиката на интеракциите
- можни ефекти на апсорпција, распаѓање и сл.



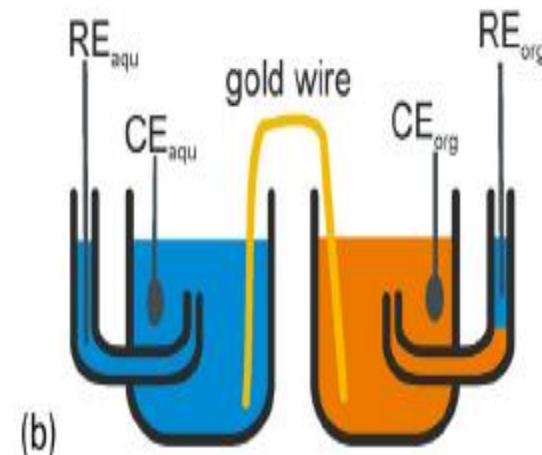
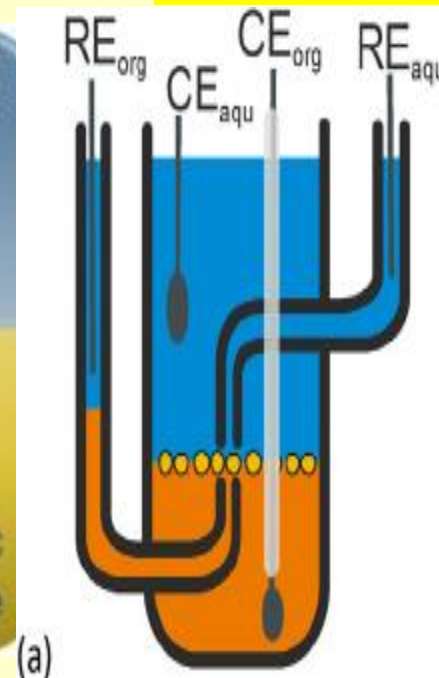
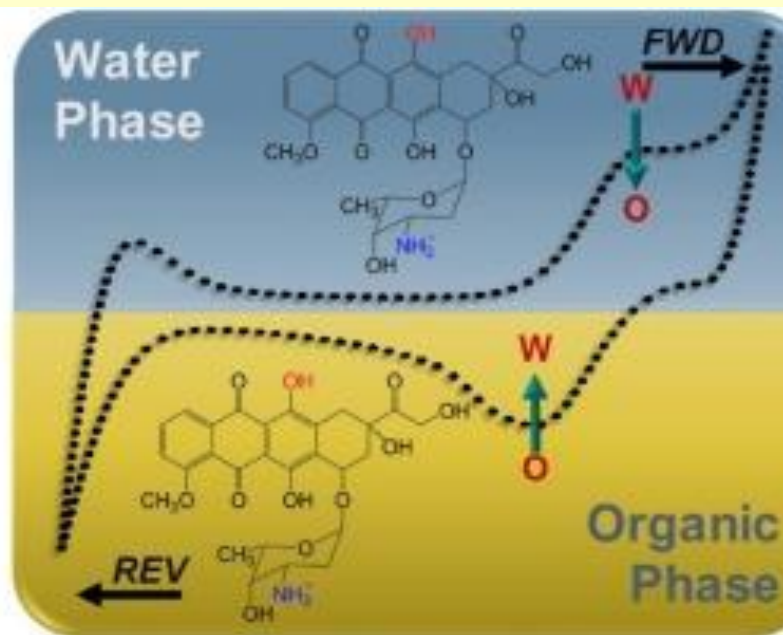
Трансфер преку Клеточни мембрани-интеракции на Невротрансмитерите со фосфолипиди...

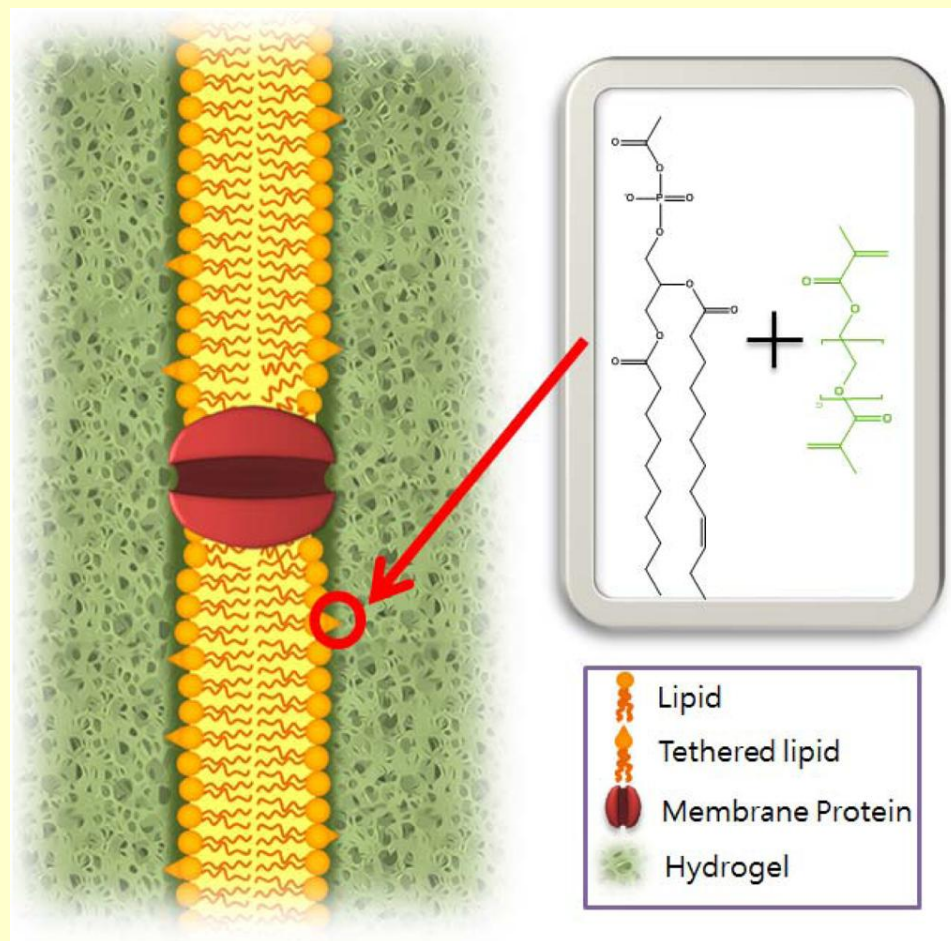
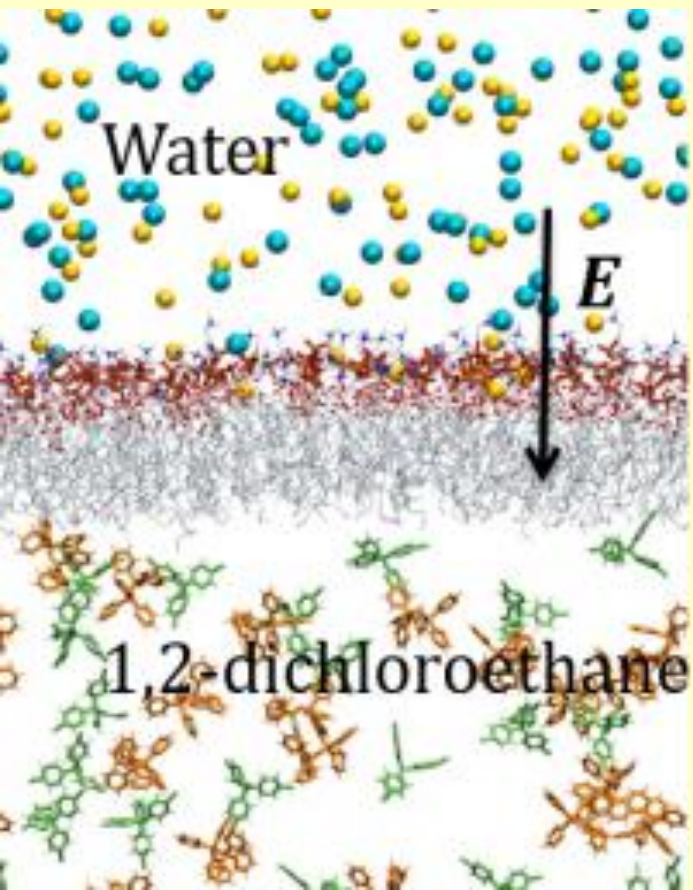


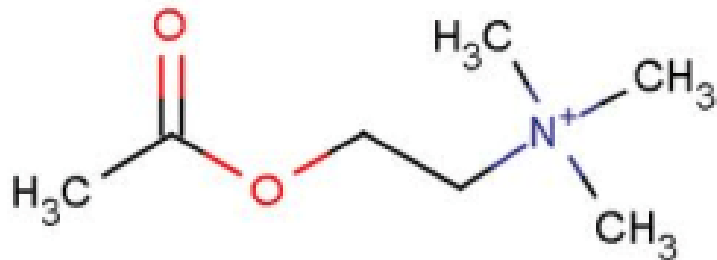


Дизајнирање на
Експеримент во кој
Фосфолипиди
Се ставаат на границата
Помеѓу две
Немешливи течности

-четири електроден
систем



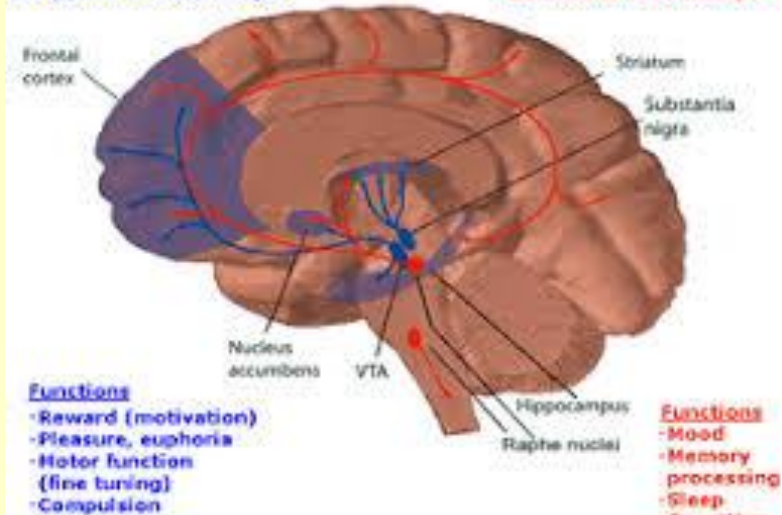




Acetylcholine

Dopamine Pathways

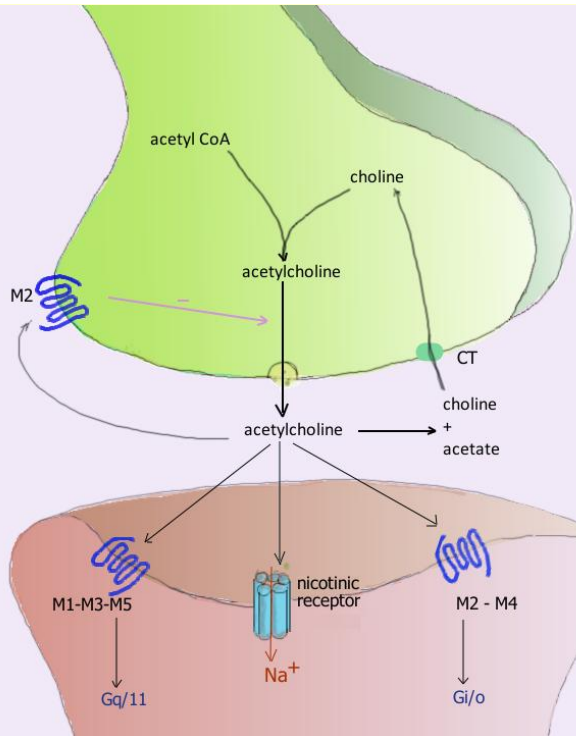
Serotonin Pathways



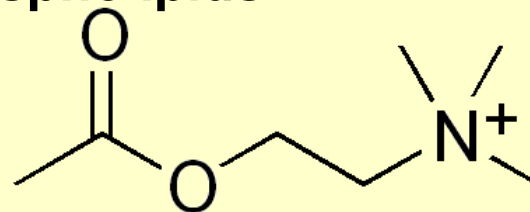
ACETYLCHOLINE

- Acetylcholine the first neurotransmitter discovered, was originally described as "vagus stuff" by Otto Loewi because of its ability to mimic the electrical stimulation of the vagus nerve. It is now known to be a neurotransmitter at all autonomic ganglia, at many autonomously innervated organs, at the neuromuscular junction, and at many synapses in the CNS.
- is a chemical that is found between the nerve synapses, or gaps, between nerve cells.

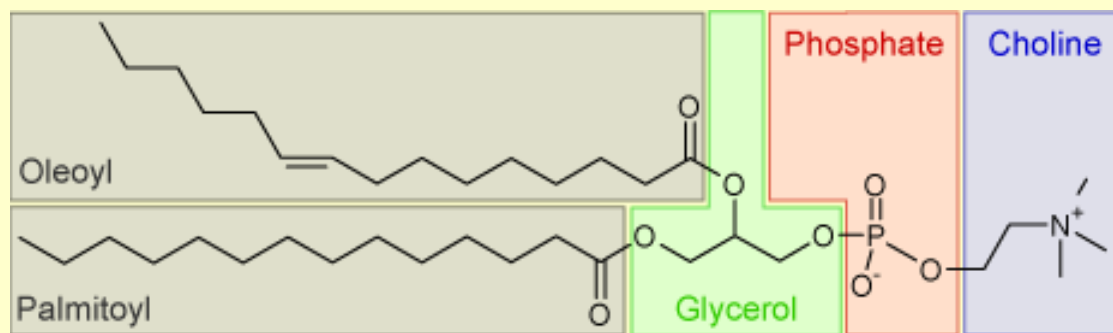
Receptors: nicotine and muscarine



-type and strengths of interactions between acetylcholine And the phospholipids



Acetylcholine



Phospholipids

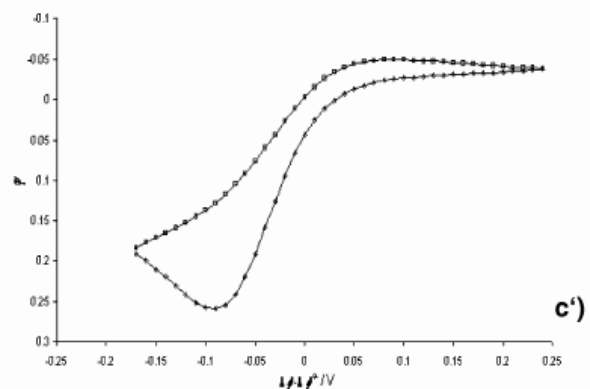
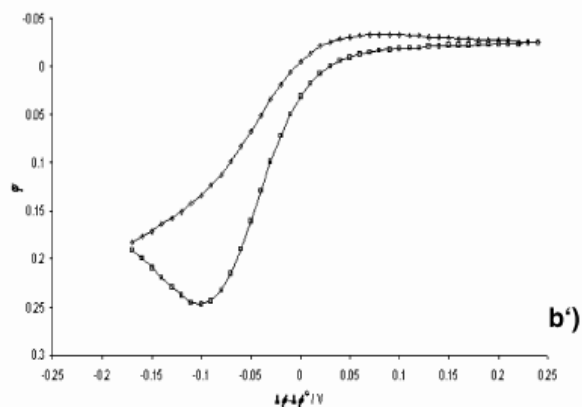
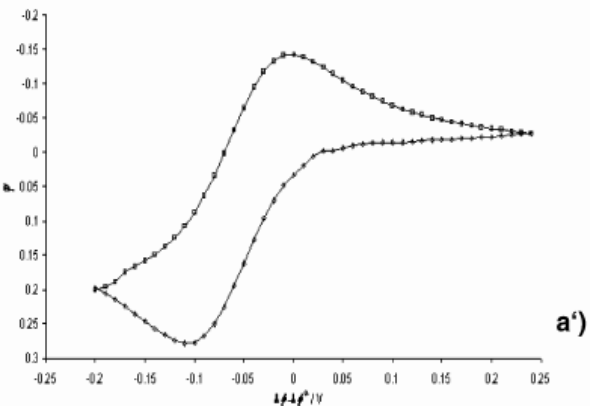
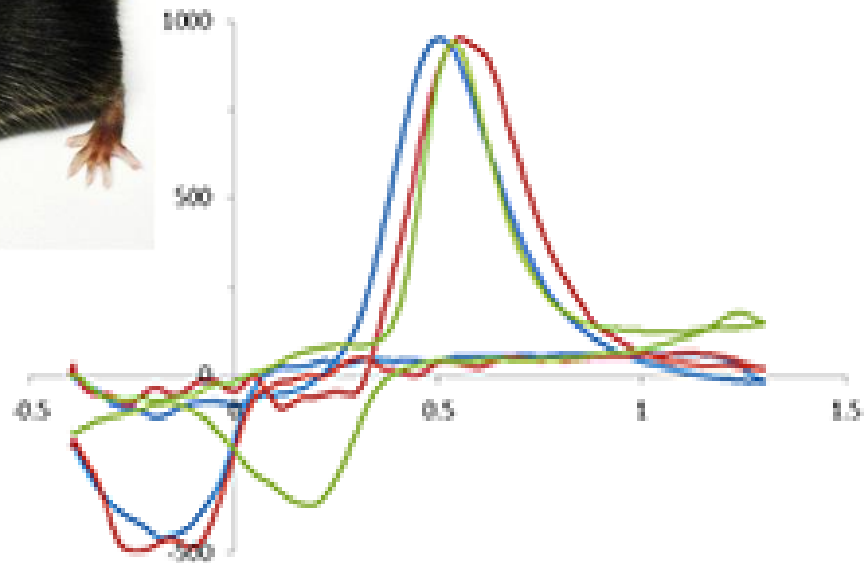
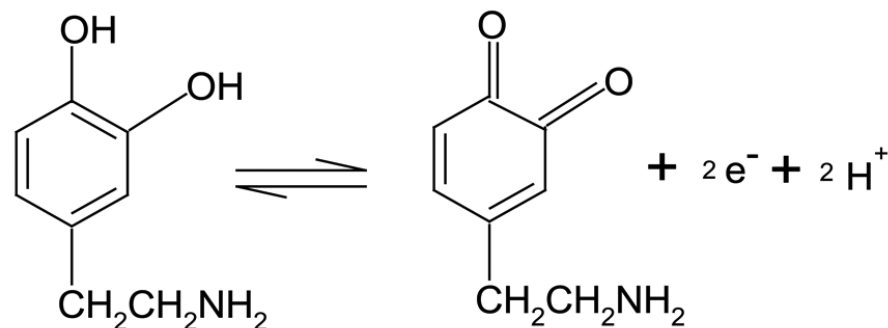
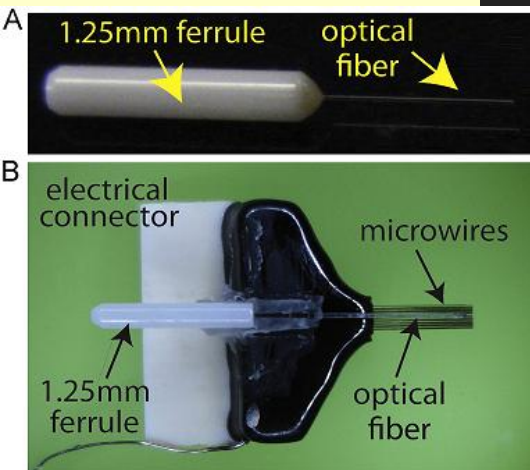
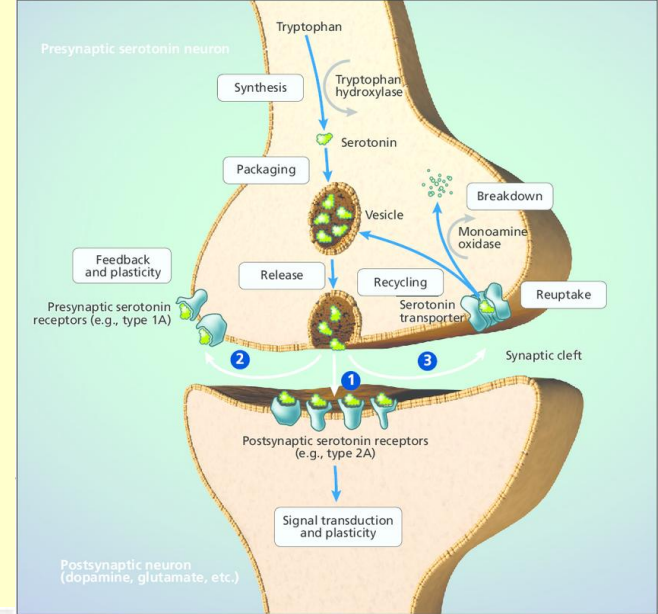
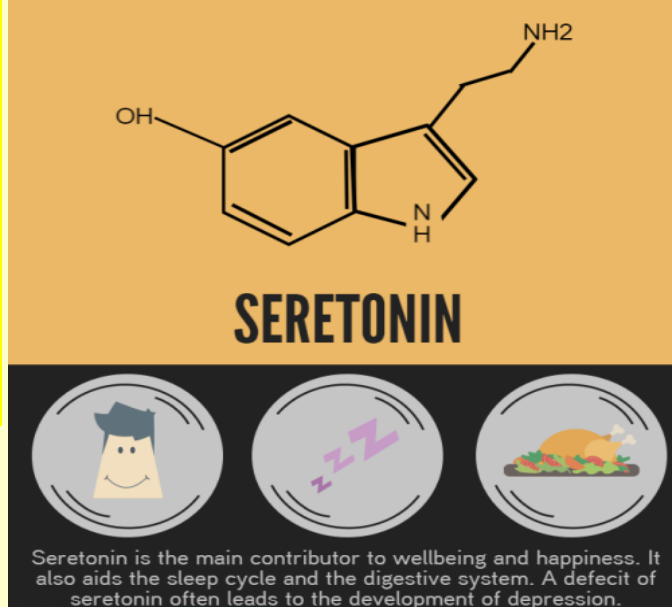


TABLE 1: Determined Kinetic Parameters of the Ion Transfer of AcH^+ from Water to DCE (k_s and α) and for the Interactions between AcH^+ and DOPC (K , ϵ , k_f , and k_b)

measuring technique	$k_s/\text{cm s}^{-1}$	α	K	ϵ/s^{-1}	k_f/s^{-1}	k_b/s^{-1}
SWV	0.0030	0.50	0.44	13.10	4.00	9.10
EIS	0.0033	0.53	0.80	13.30	5.90	7.40

In VIVO Detection of Serotonin With voltammetry





Important for motor and cognitive functions

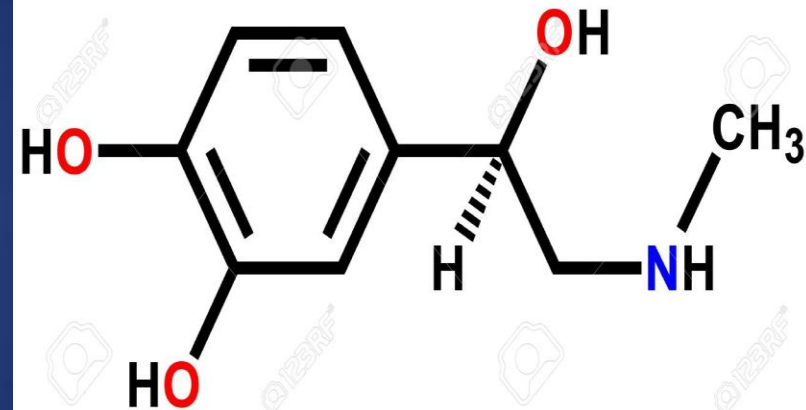
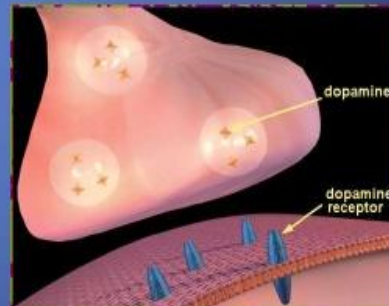
Deficits in dopamine levels cause Parkinson Disease

Regulates reward

Dopamine increases after drugs of abuse like cocaine

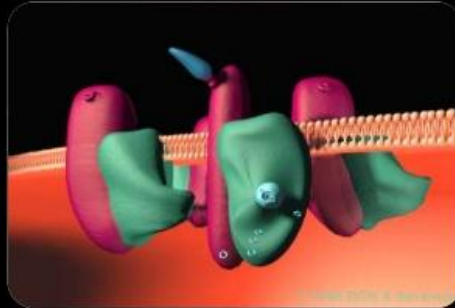
What is dopamine?

- Dopamine is a neurotransmitter in the brain
- Essential component of the basal ganglia motor loop as well as the neurotransmitter responsible for controlling the exchange of information from one brain area to another
- Plays vital roles in certain behavior such as
 - Movement
 - Cognition
 - Pleasure
 - Motivation

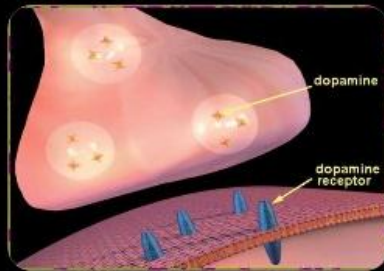


DOPAMINE RECEPTORS

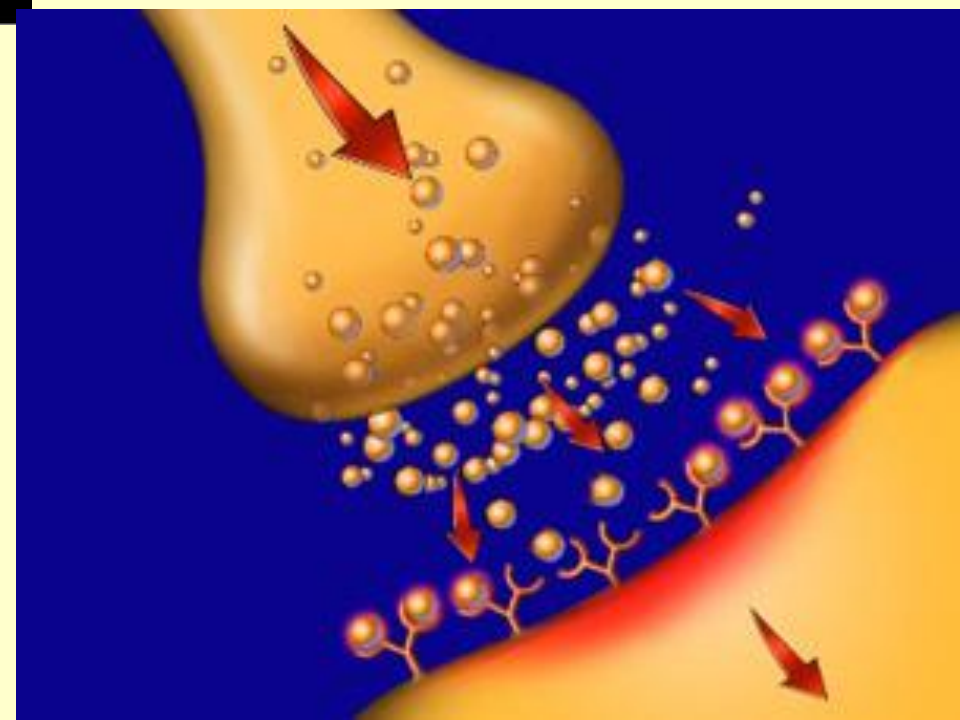
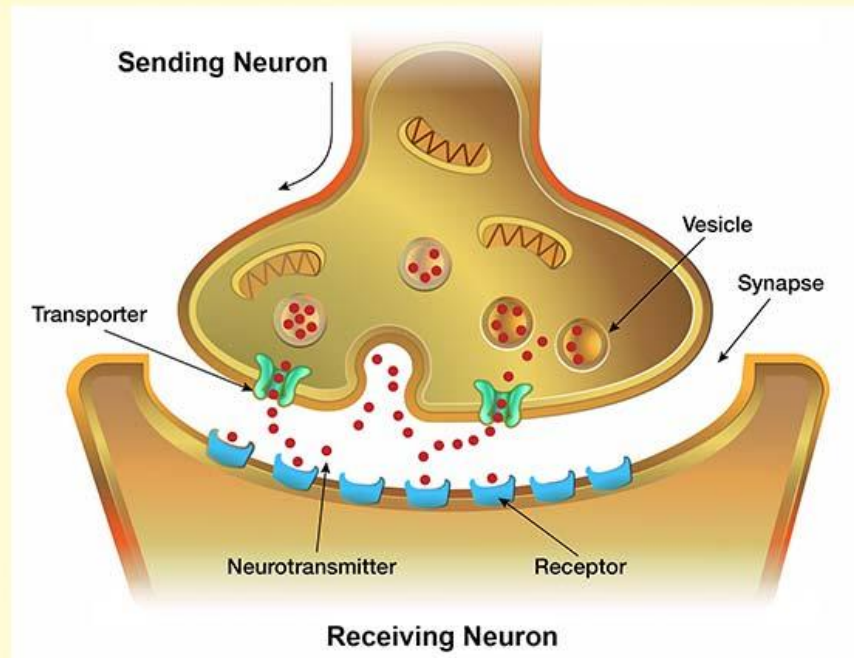
- **D₁-like family**
- D₁ and D₅ receptors
- ↑ cAMP by activating the stimulatory G protein, G_s.



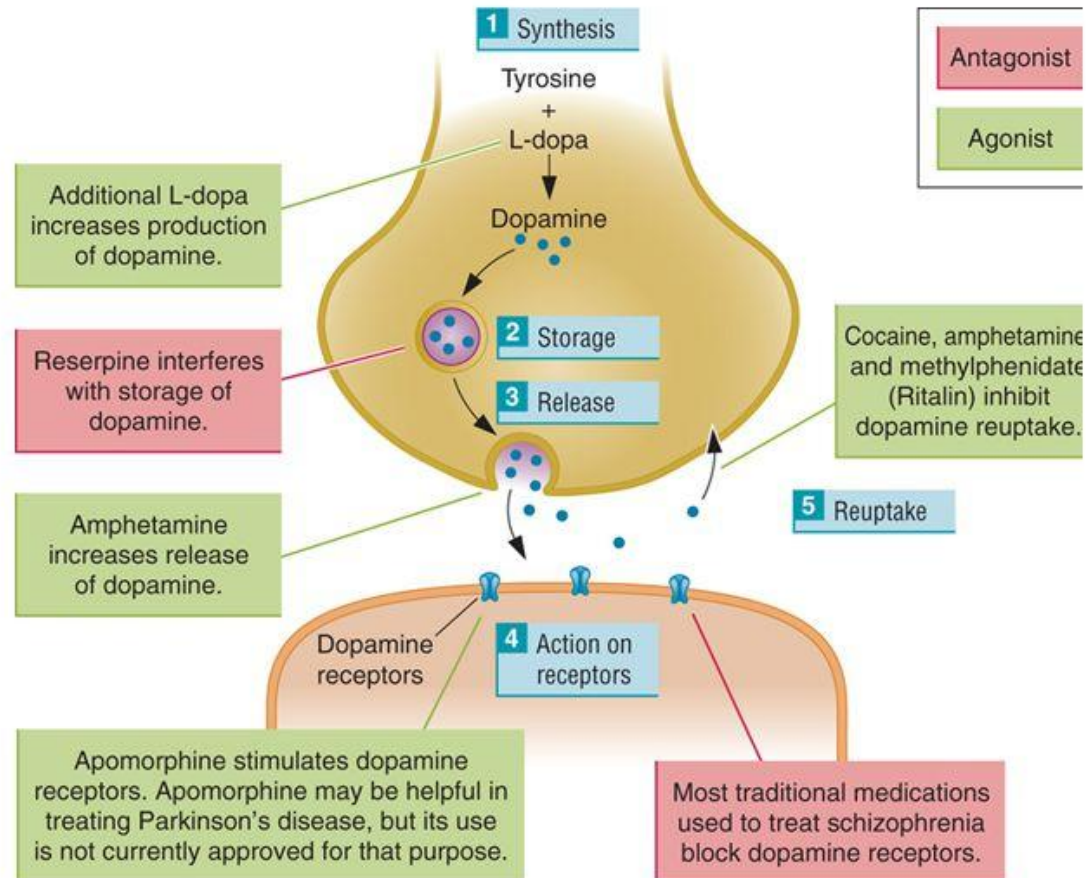
- **D₂-like family**
- D₂, D₃, and D₄ receptors
- ↓ cAMP-by activating the inhibitory G protein, G_i



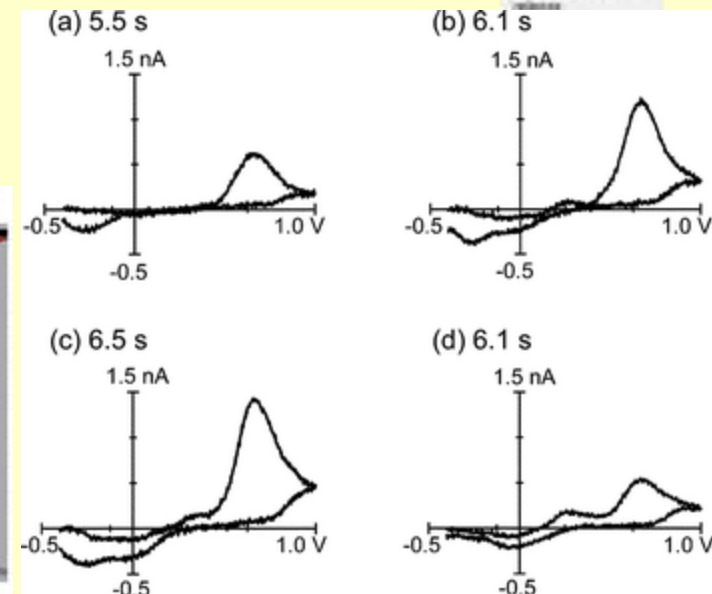
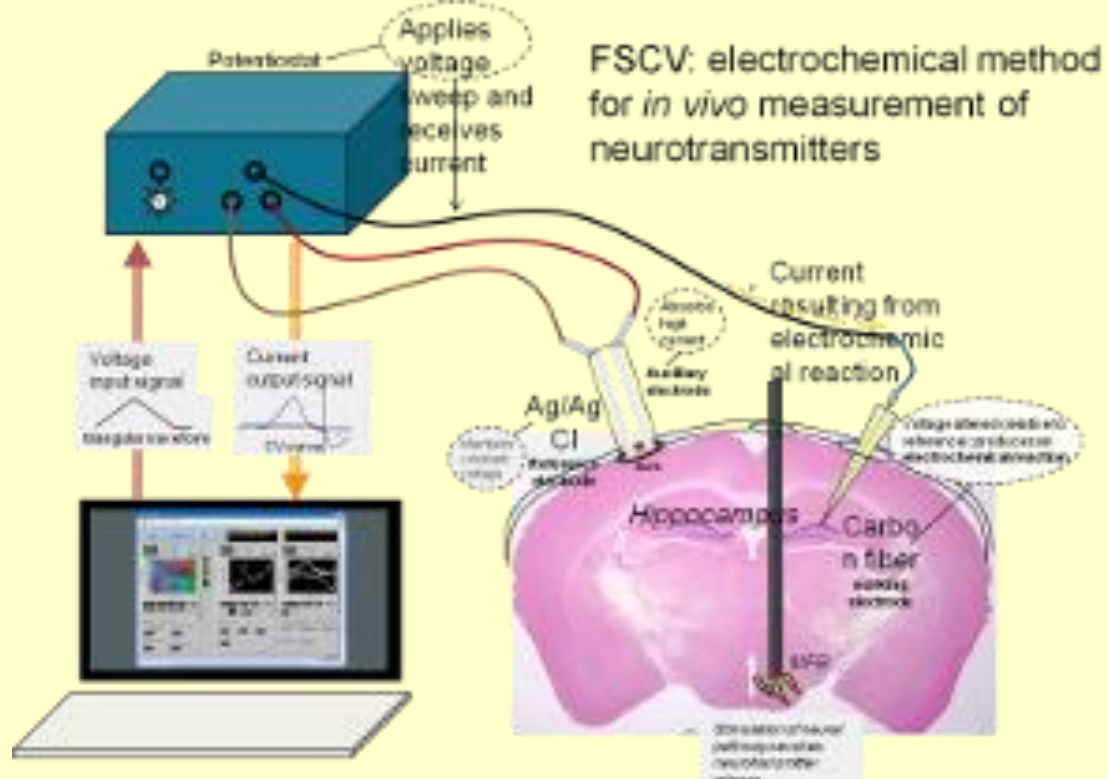
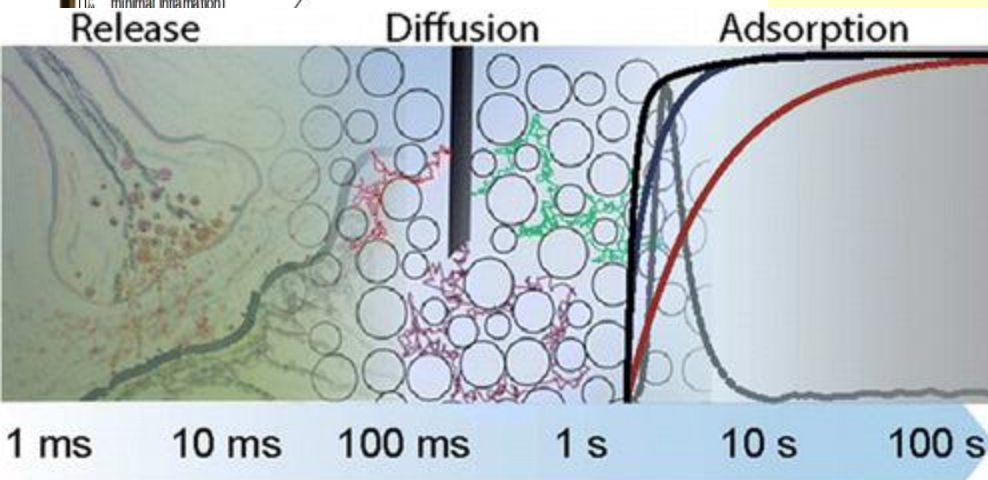
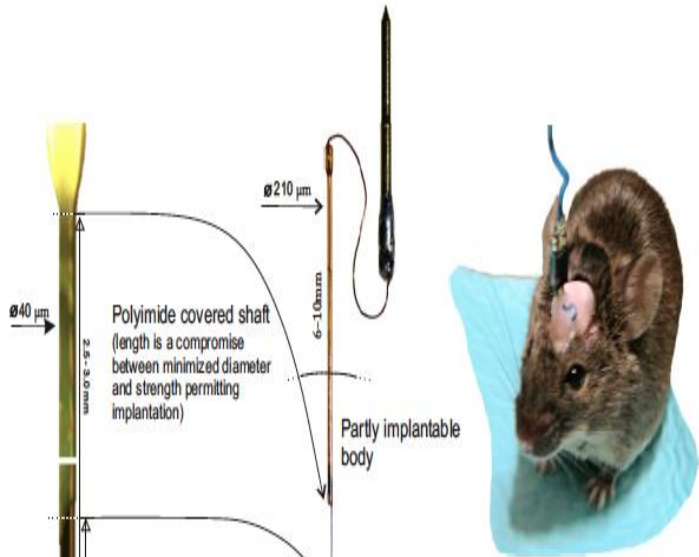
Dopamine, a "reward" neurotransmitter, can be triggered by pleasurable activities like eating and sex, and by drugs ranging from alcohol and nicotine to marijuana and cocaine. Dopamine interacts with specific dopamine receptors on "reward" neurons and the sense of pleasure begins...



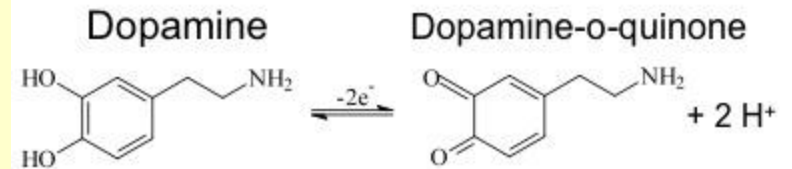
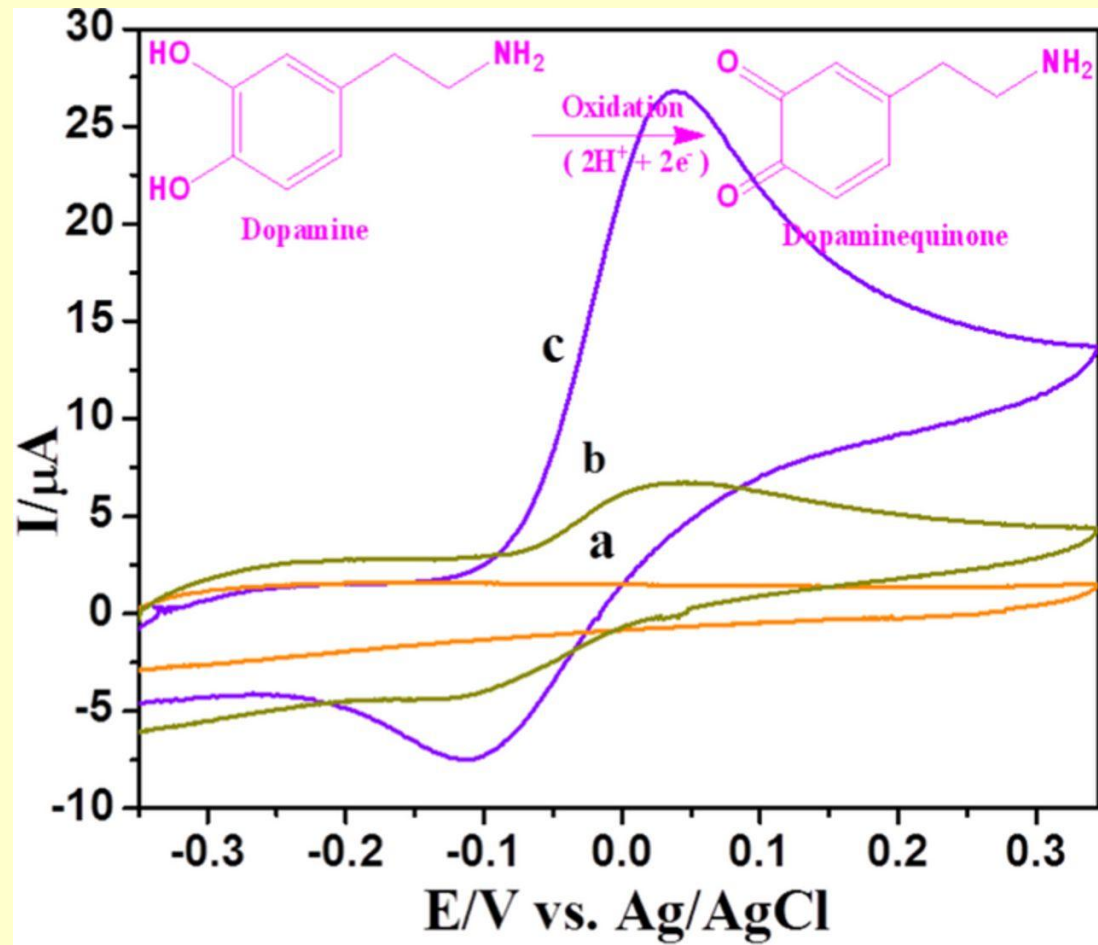
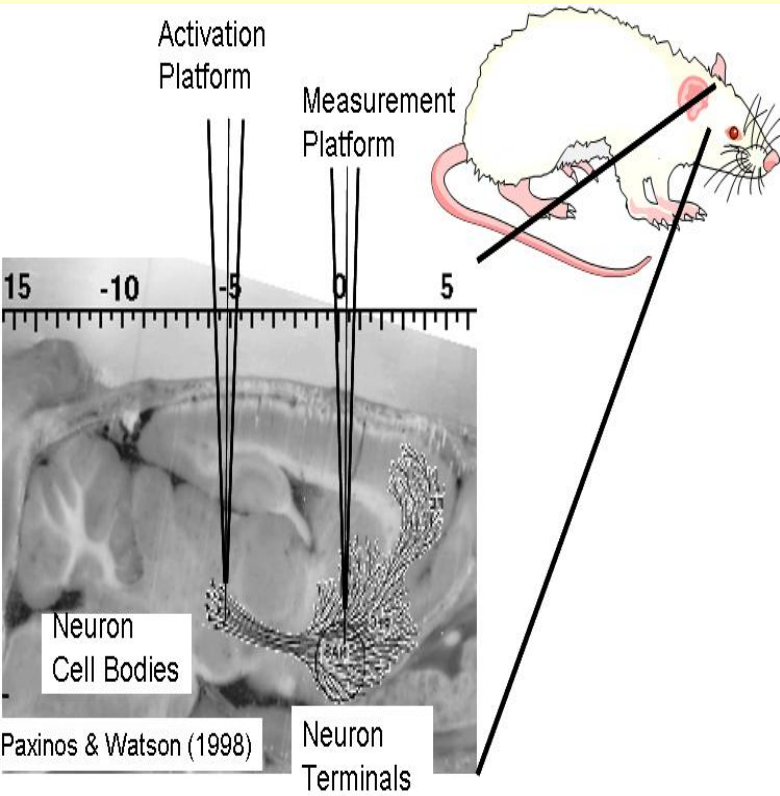
Drug Interactions at the Dopaminergic Synapse

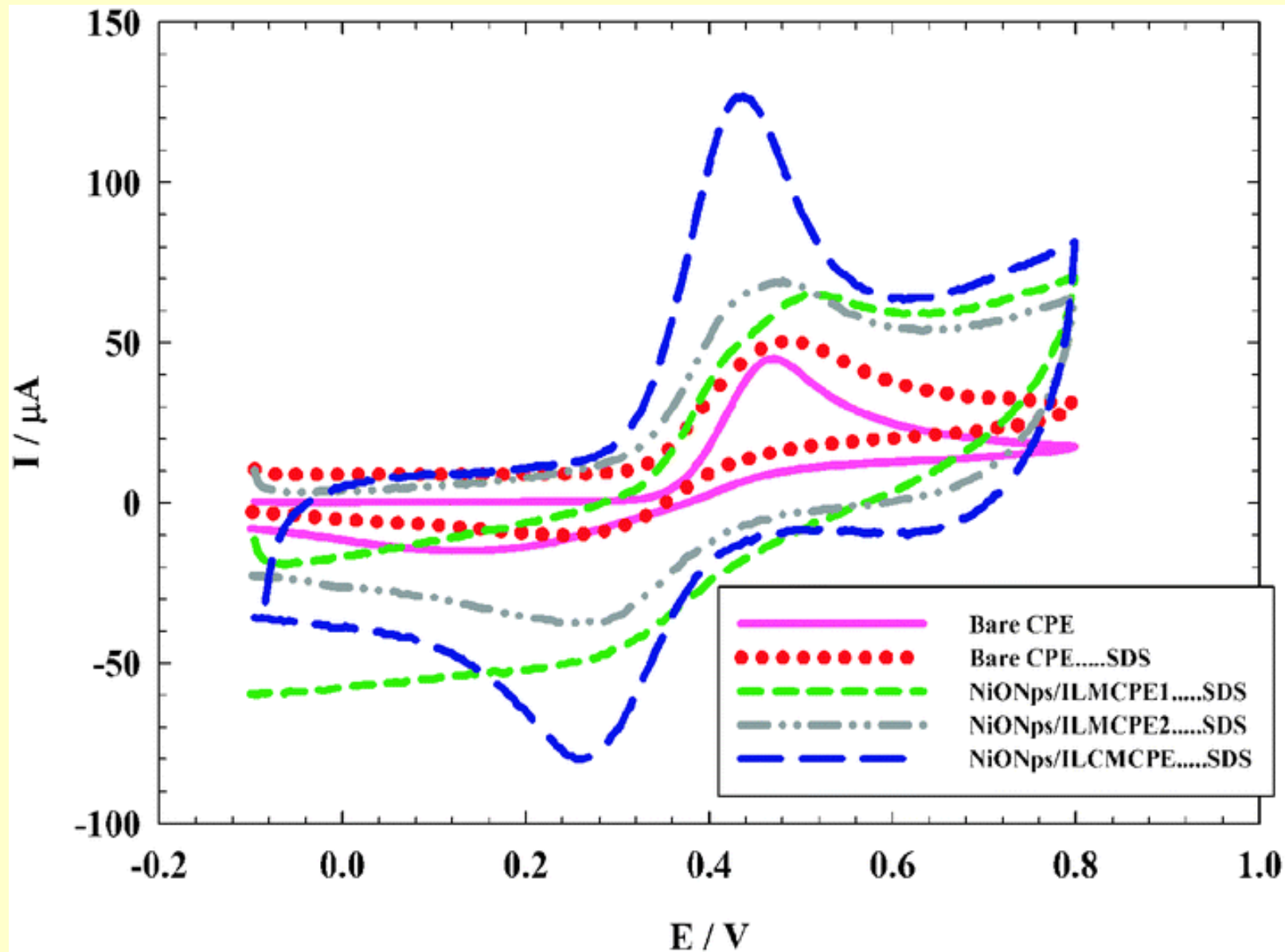


In Vivo Detection of Dopamine with Fast scan voltammetry



In-Vivo voltammetry of dopamine



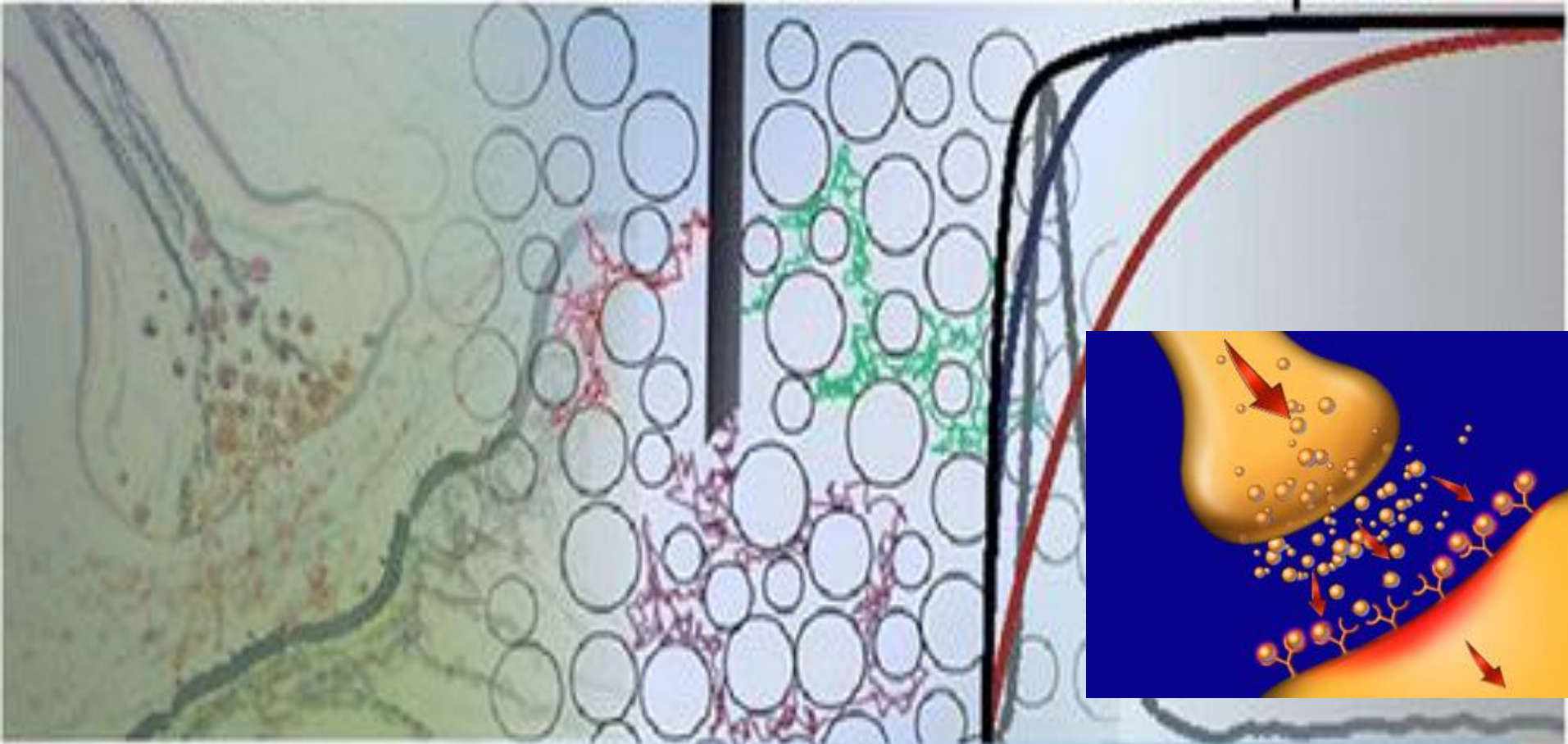


БРЗИНА НА ПРОЦЕСИ ПРИ СЕКРЕЦИЈА На ДОПАМИН

Adrenal medulla
Release

Diffusion

Adsorption



1 ms 10 ms 100 ms 1 s 10 s 100 s

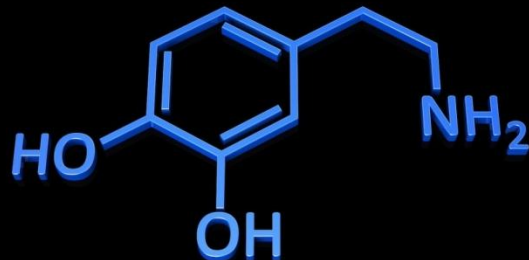
ДОПАМИН може да реагира со
ПРООКСИДАНТИ и **Лекови** со прооксидантни својства

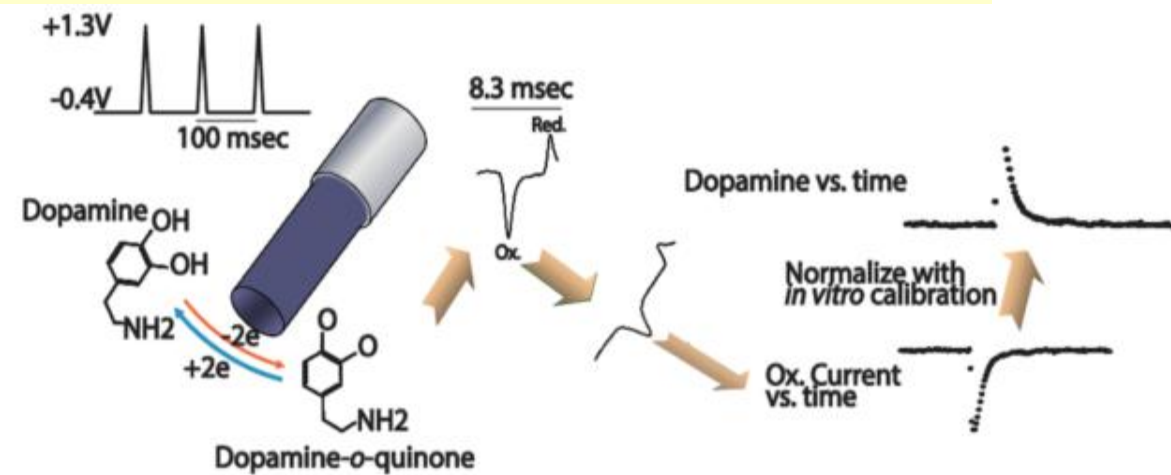
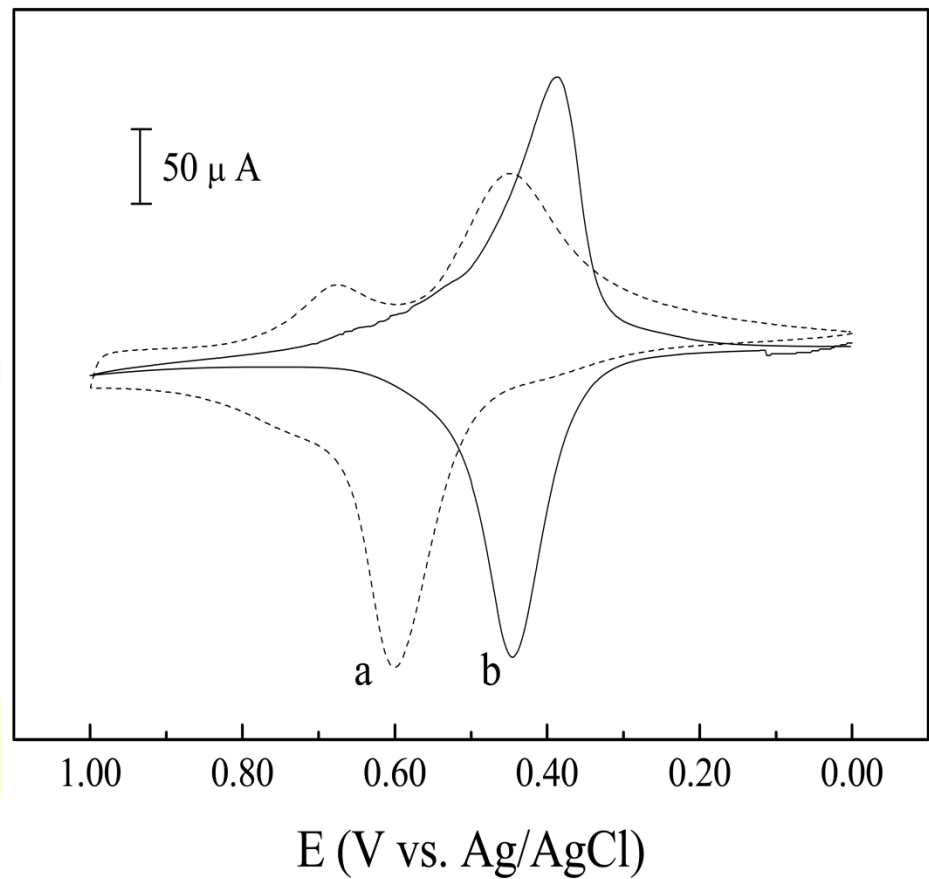
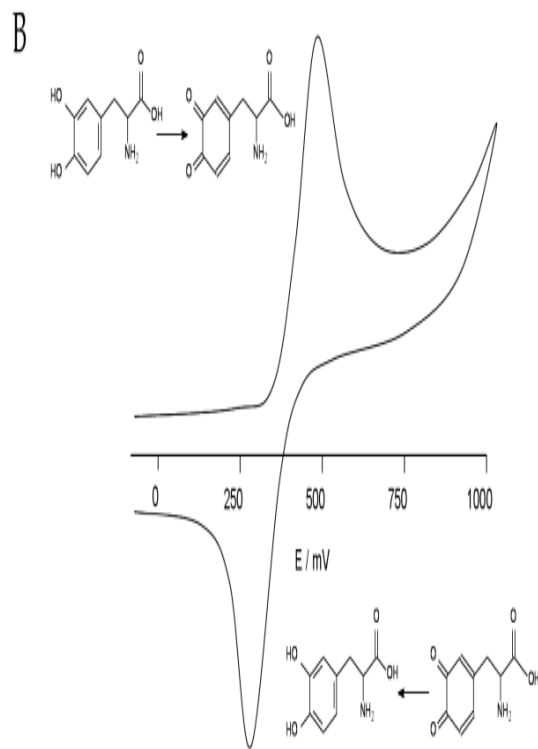
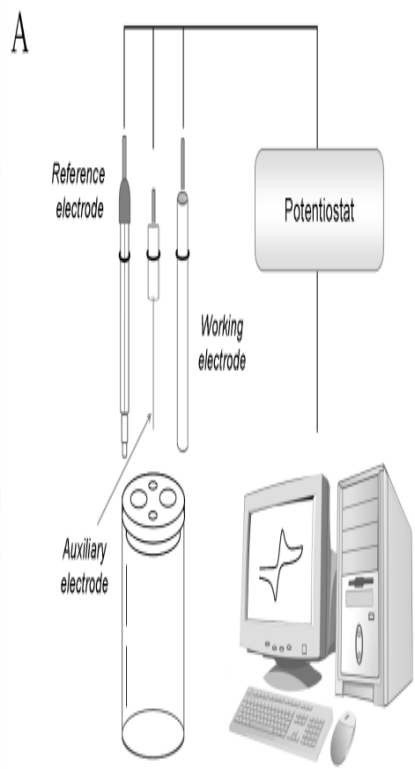
Водороден Пероксид: **Супероксид Радикал:**
Хидроксид радикал

Метални јони: Fe^{3+} ; Cu^{2+} ; Mo^{6+} ; Mn^{4+} ;

Параацетамол-индуцира креирање на слободни радикали

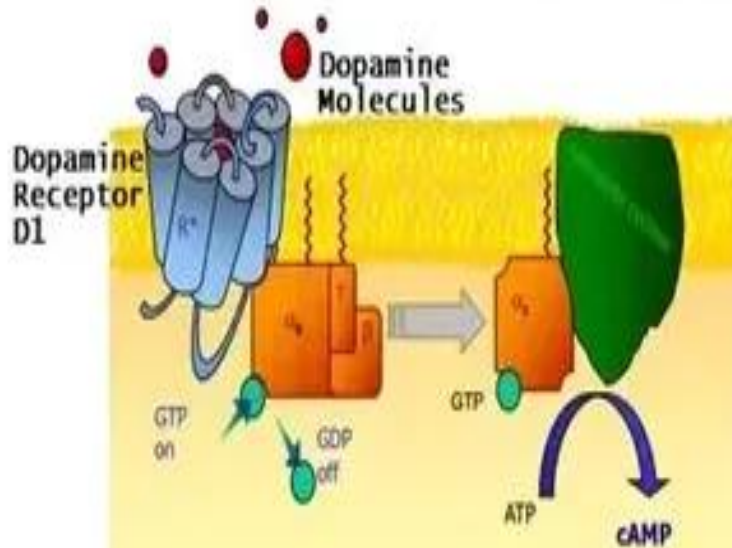
-Покрај тоа, допамин МОЖЕ да комплексира и некои Катјони на металните јони од земноалкални метали!!!



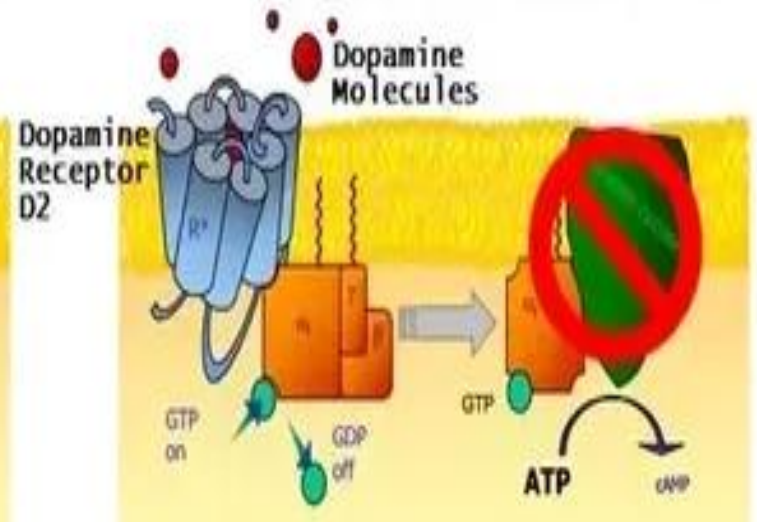


Рецептори за допамин се G-протеински комплекси

D1-like Dopamine Receptors

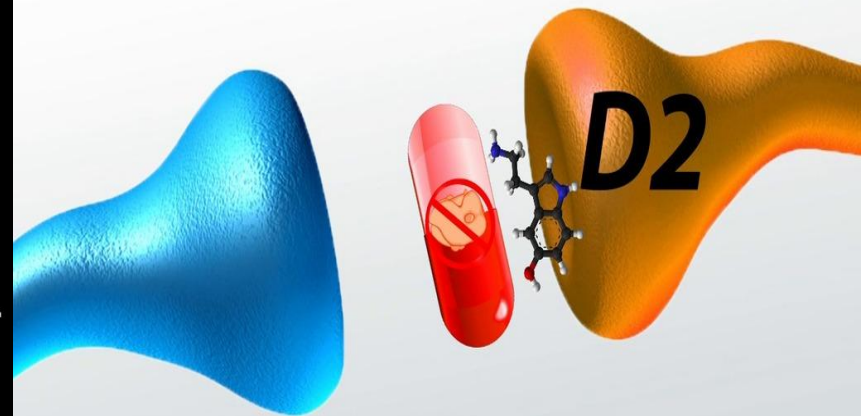
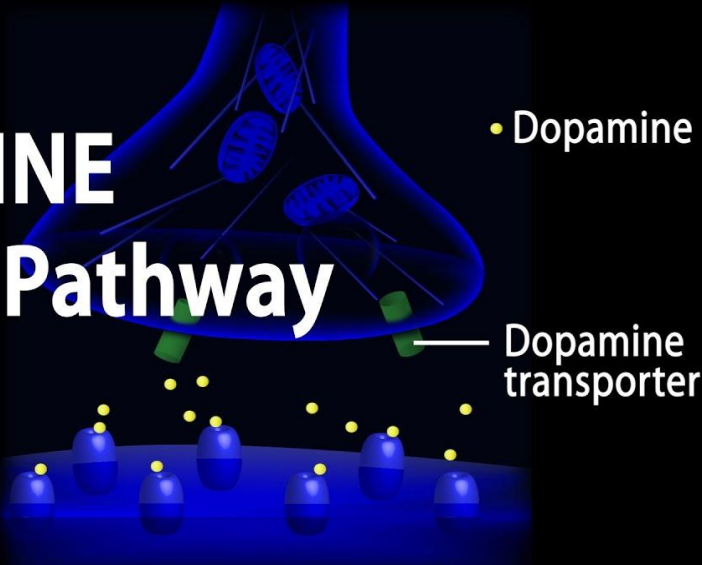


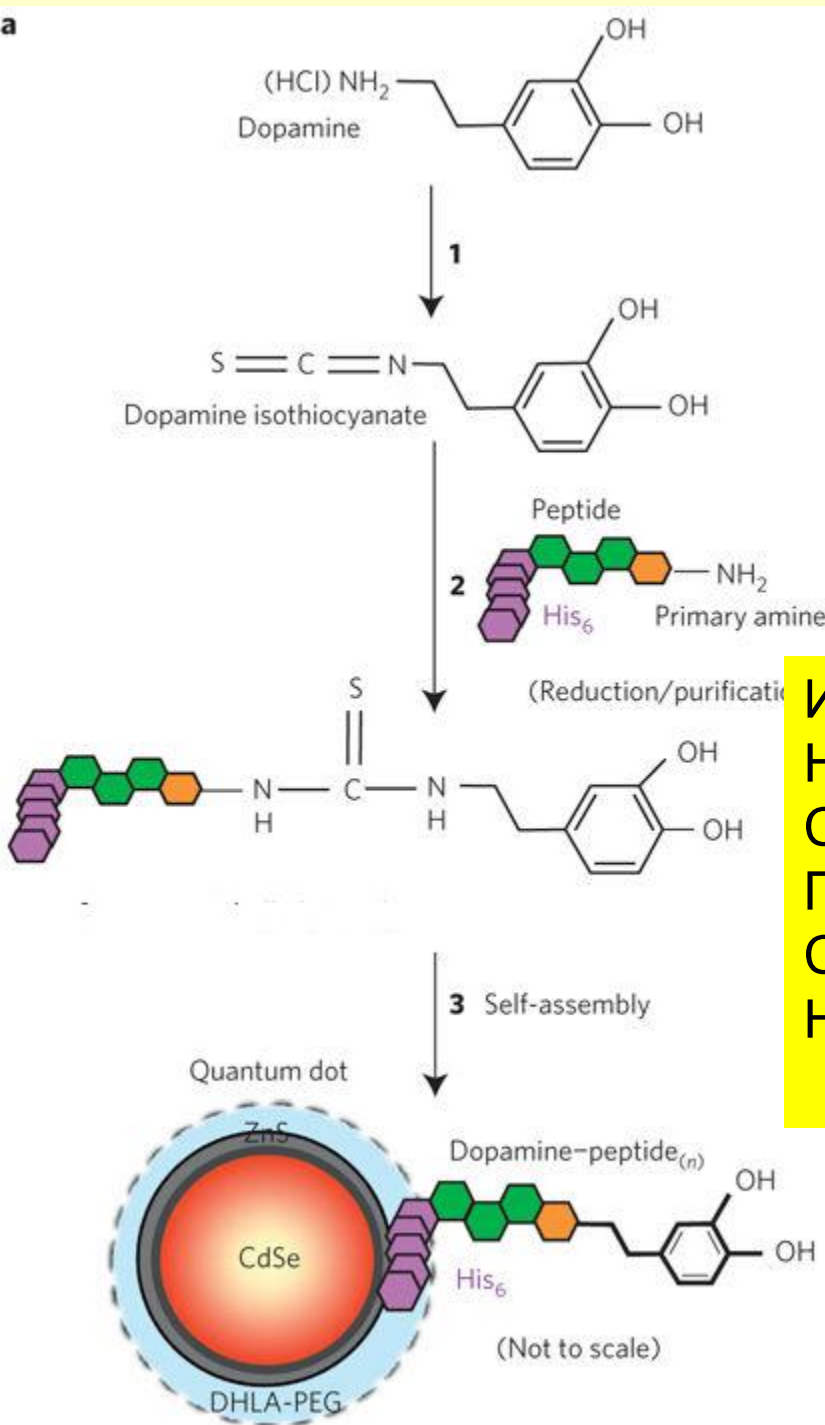
D2-like Dopamine Receptors



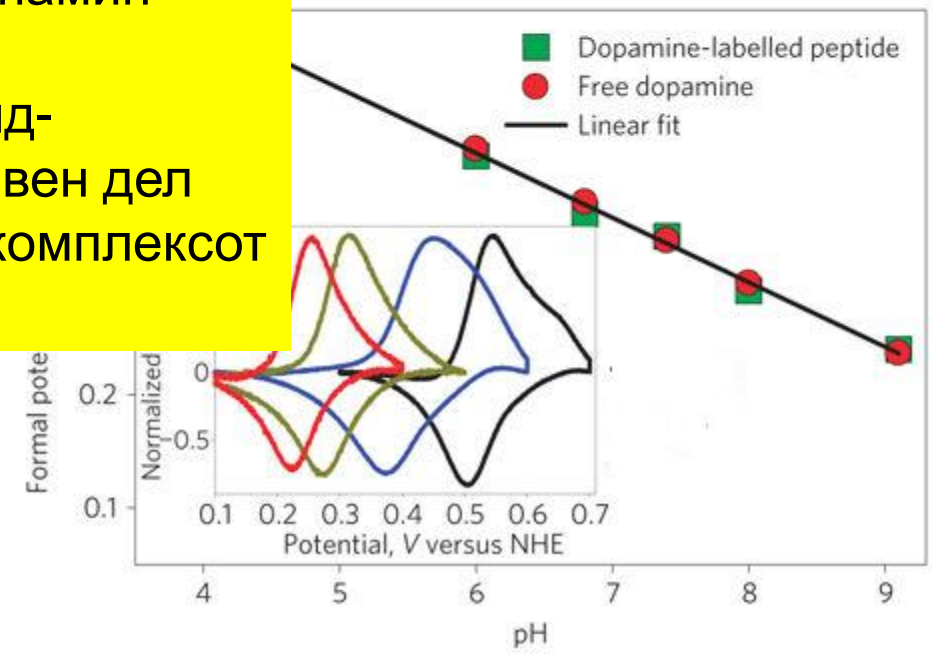
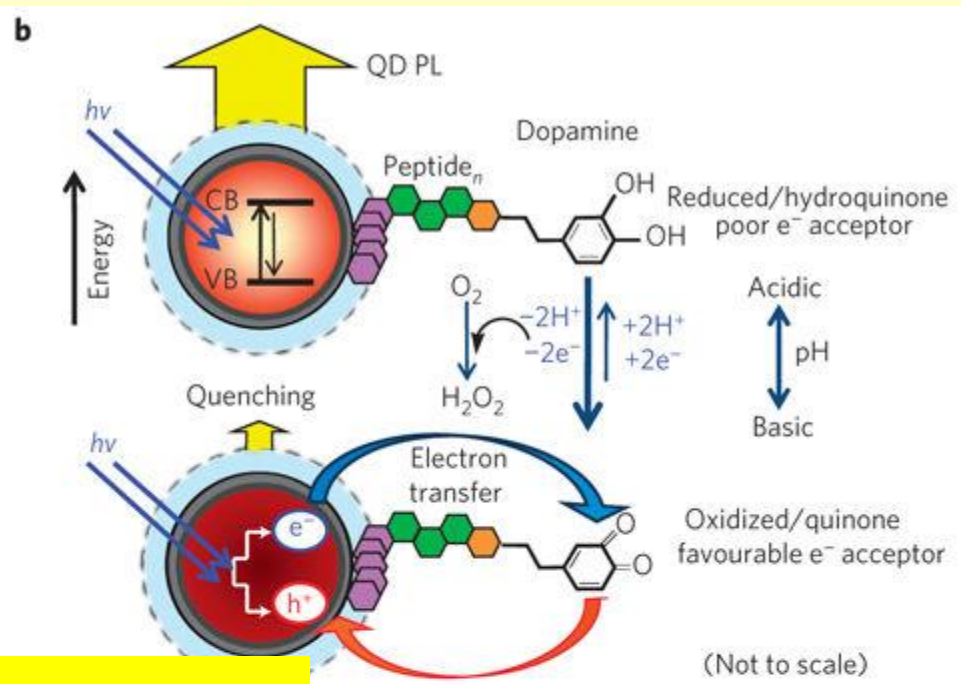
HOW ANTIPSYCHOTICS WORK

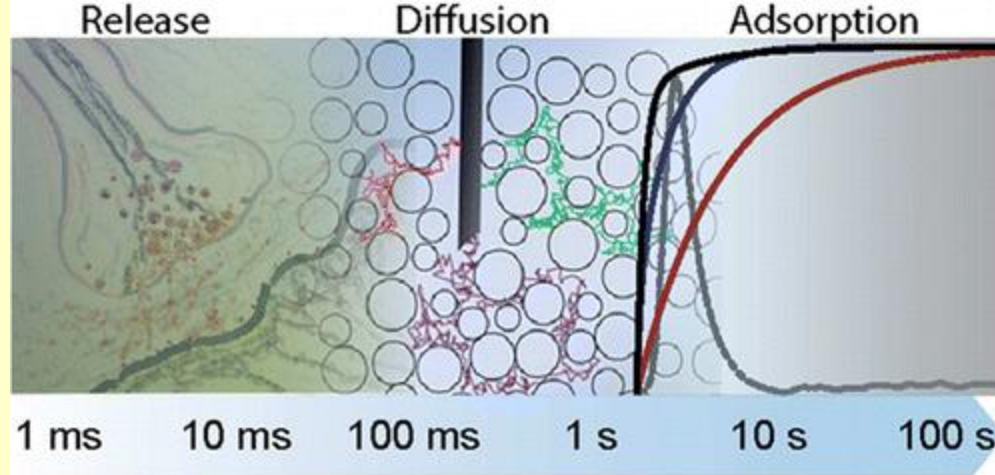
DOPAMINE Reward Pathway





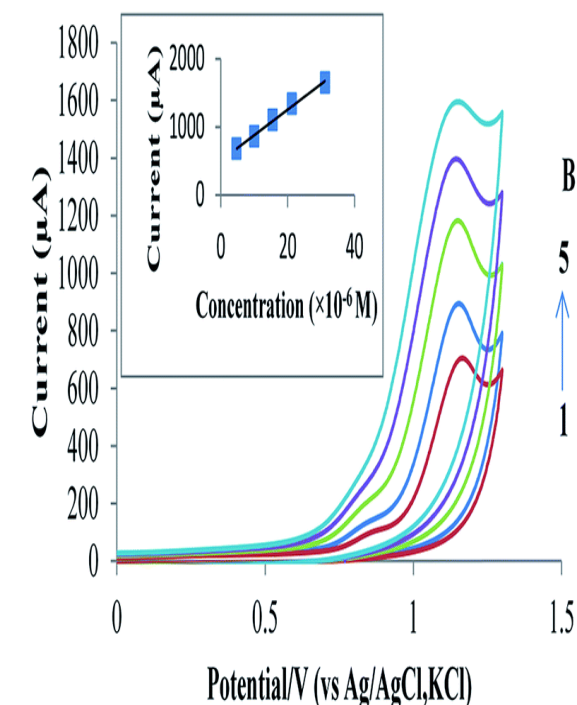
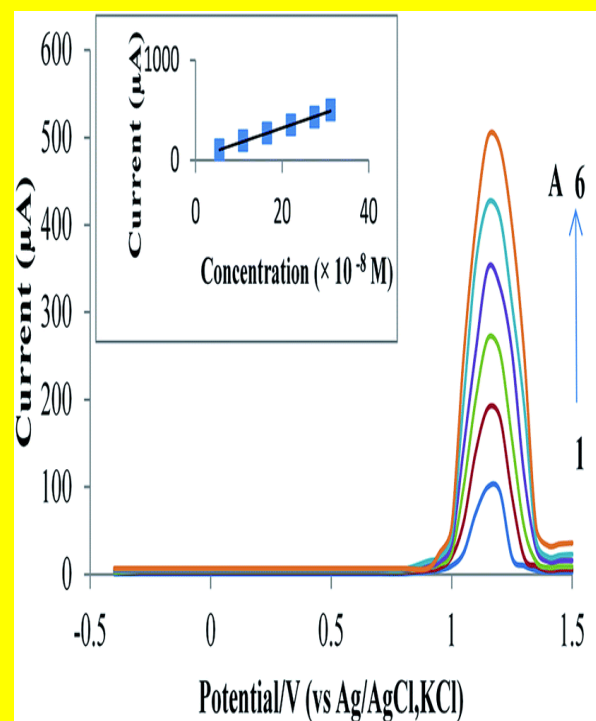
Интеракции
 На допамин
 Со
 Пептид-
 Составен дел
 На Г-комплексот

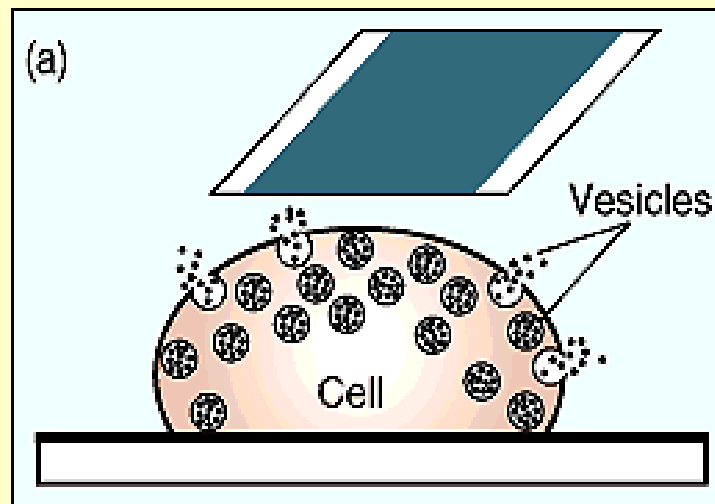




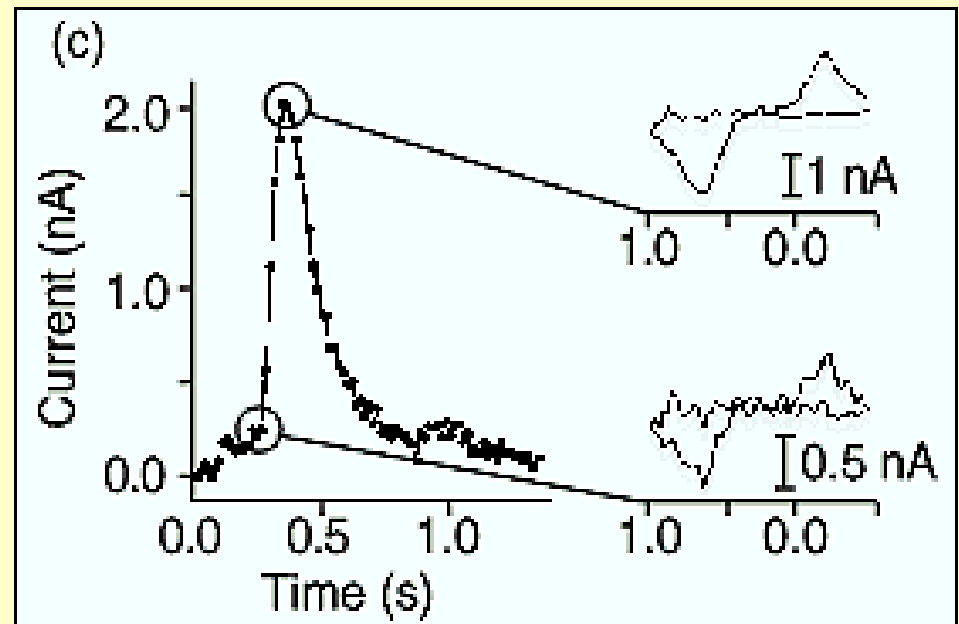
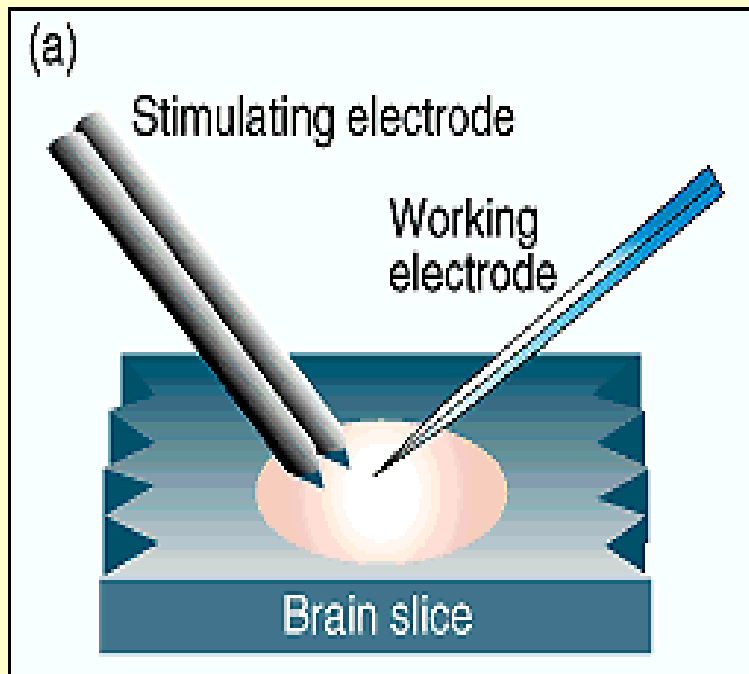
Кинетички параметри ($k_c/\text{mol}^{-1}\text{Ls}^{-1}$) на реакции на ДОПАМИН (во физиолошки услови-pH од 7.40) со...

- H₂O₂----- 0.0000025
- OH⁻ -----0.440!!!**
- O^{·2-} -----0.050
- Fe³⁺ -----0.080**
- Cu²⁺ -----0.005
- Mo⁶⁺ -----0.10!!**
- Прашок од Aluminium-**
- за запрашување**
- Ацо Рембрант....?**





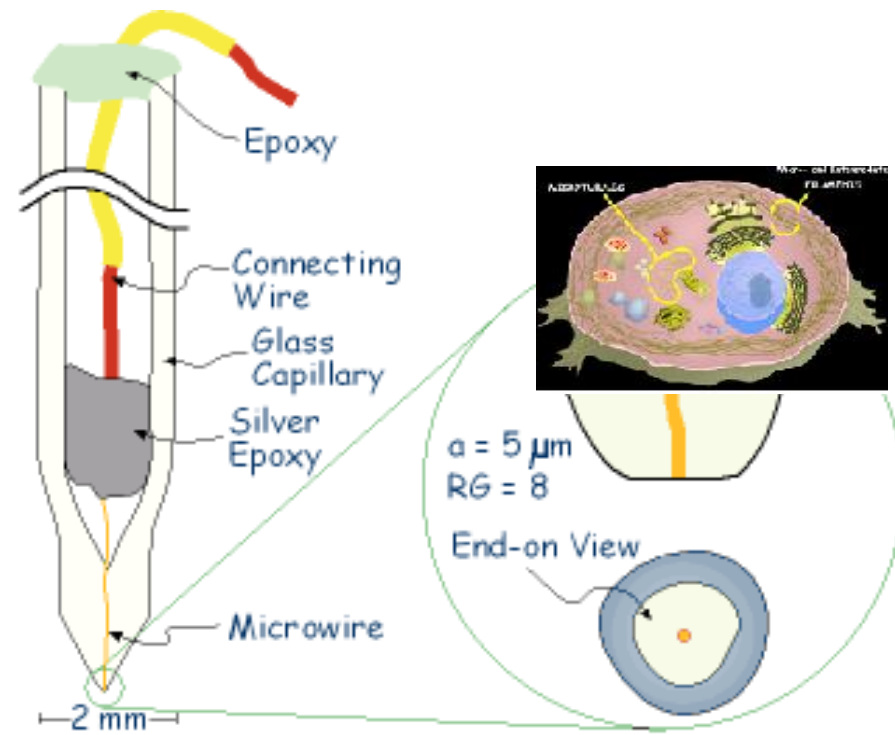
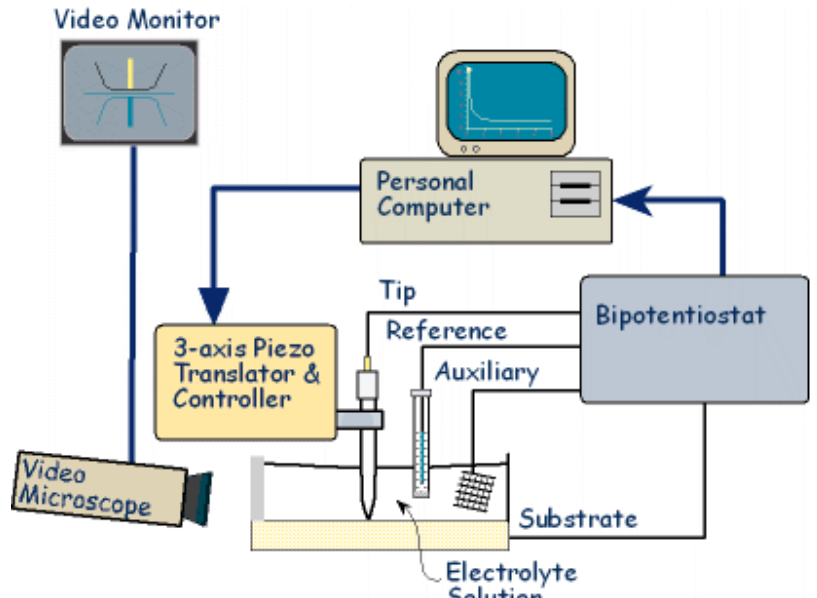
IN-VIVO voltammetric determination of catecholamine



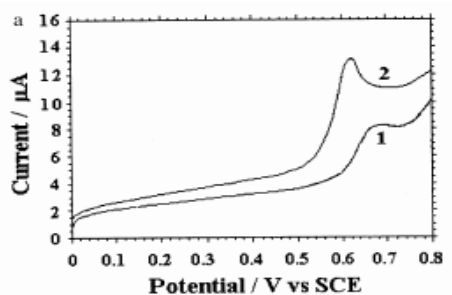
Voltammetry in service of the Scanning Electrochemical Microscopy



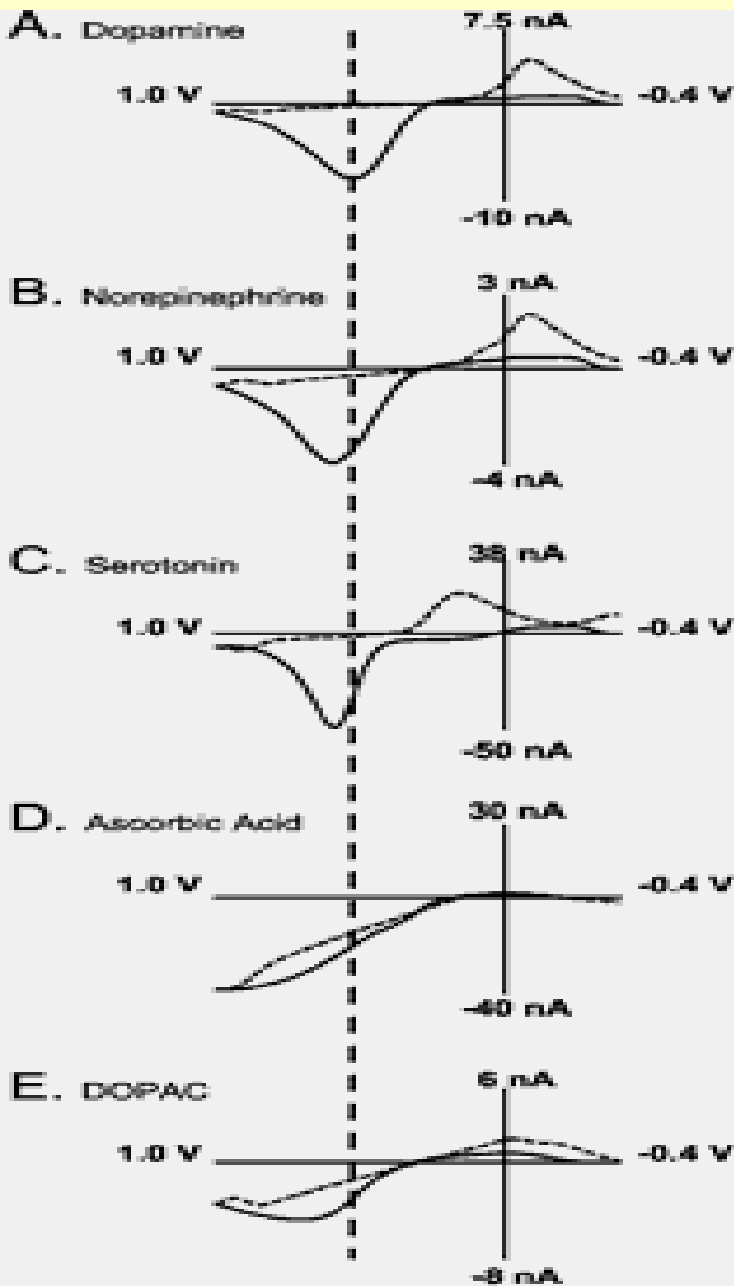
-Powerfull tool for probing the electrochemical activity of single living cells at different spots (**cell topography**)



- Detection of **active sites of Enzymes**
- Detection of **human breast cancer cells**



Cyclic Voltammograms of some NUEORTRANSMITTERS



A), cyclic voltammogram for 2 $\mu\text{mol/L}$ **dopamine**.

(B), cyclic voltammogram for 2 $\mu\text{mol/L}$ **norepinephrine**

(C), cyclic voltammogram for 2 $\mu\text{mol/L}$ **serotonin**

(D), cyclic voltammogram for 200 $\mu\text{mol/L}$ **ascorbic acid**

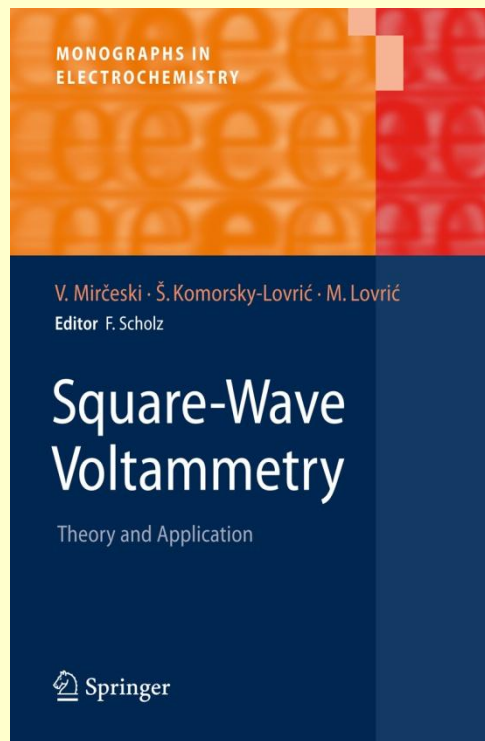
(E), cyclic voltammogram for 20 $\mu\text{mol/L}$ **DOPAC**

ЗАКЛУЧОЦИ

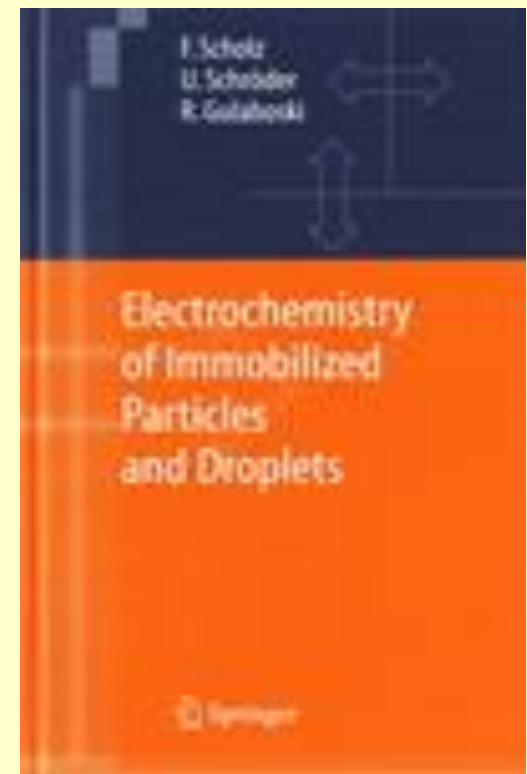
- Волтаметријата е едноставна и моќна техника
За испитување на механизмот на акција на
Невротрансмитерите
- може да даде податоци за брзината на интеракции
На невротрансмитерите со дадени супстанции
- преку тие податоци, може да се утврди кои супстанции
(лекови, метални јони, физиолошки молекули) ...влијаат
Врз својствата на невротрансмитерите и нивното дејство
- начин на следење на трансфер преку мембрани
- техника што е чиста, едноставна и кошта 2500 евра!!!



Rubin Gulaboski, in
ELECTROCHEMICAL DICTIONARY (2008)
 A. J. Bard, G. Inzelt, F. Scholz (editors)



F. Scholz, U. Schroeder, **R. Gulaboski**



R. Gulaboski, C. M. Pereira in
Handbook of Food Analysis Instruments (2008)
 Semih Otles (Ed.)

Acknowledgments

A. v. Humboldt Foundation
Prof. Markus Hoth
Dr Ivan Bogeski



Prof. Fritz Scholz
Greifswald University



Prof. Valentin Mirceski
Macedonia University



Prof. Milivoj and Sebojka Lovric
Croatia



**The speaker's attendance
at this conference was sponsored
by the
Alexander von Humboldt Foundation.**

▶ <http://www.humboldt-foundation.de>