LIQUID-LIQUID INTERFACE

-Biochemical Sensor for Bio-relevant Ions

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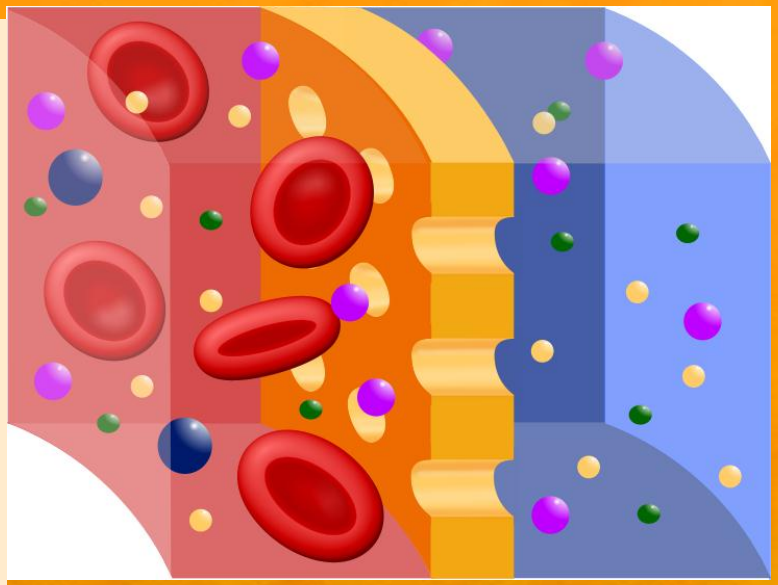
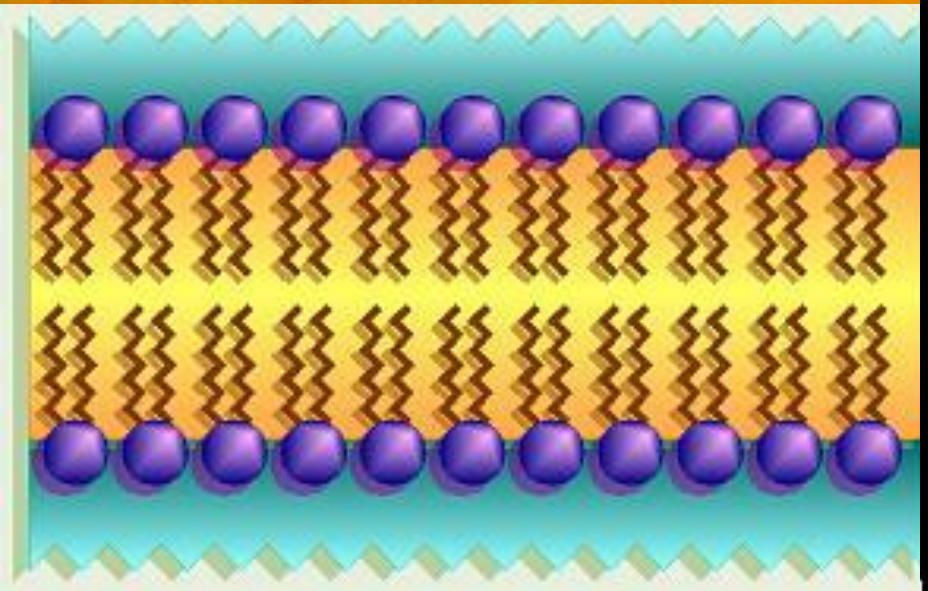
Importance of **INTERFACES** for the Living Systems

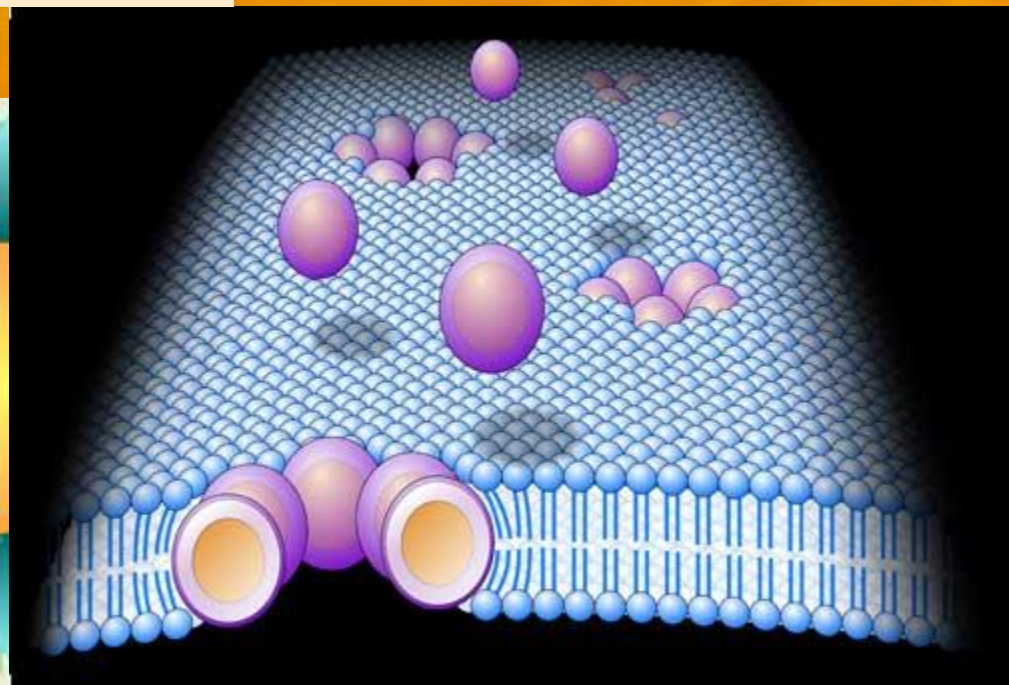
An *INTERFACE* is a *SURFACE* forming a common boundary between two different conjoined phases

The interfaces in living cells (i.e. the membranes) are ubiquitous systems separating two solutions having different features.

MEMBRANES are the most important BARRIERS of our lives!



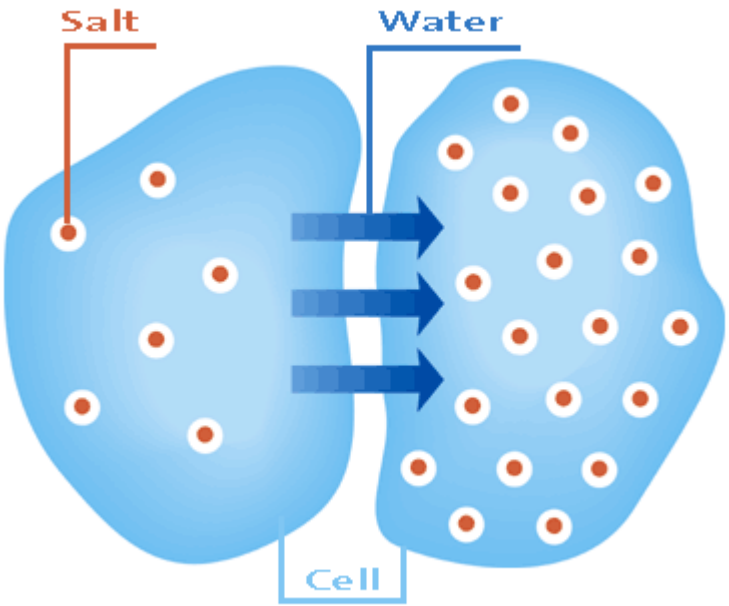


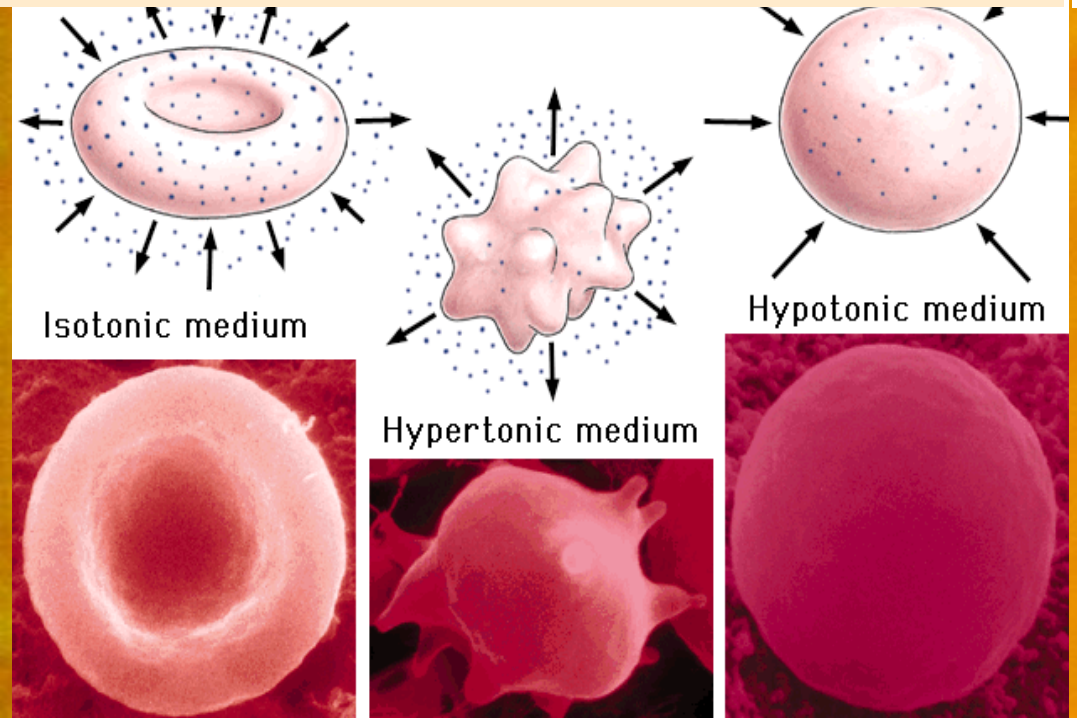


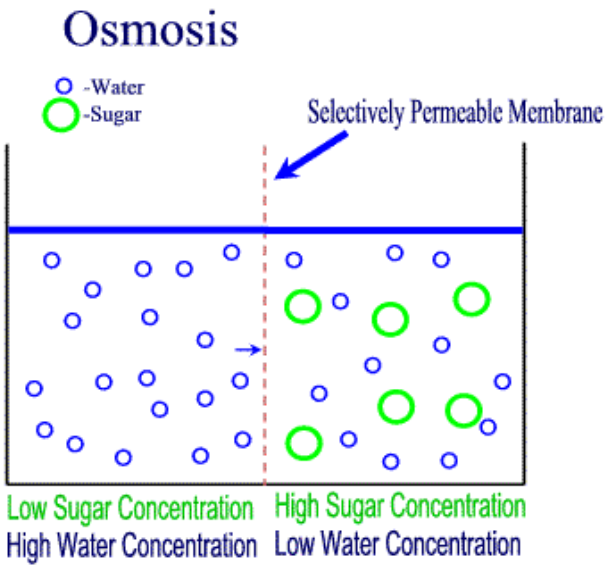
Examples for processes that need Interface

-*Osmosis*-

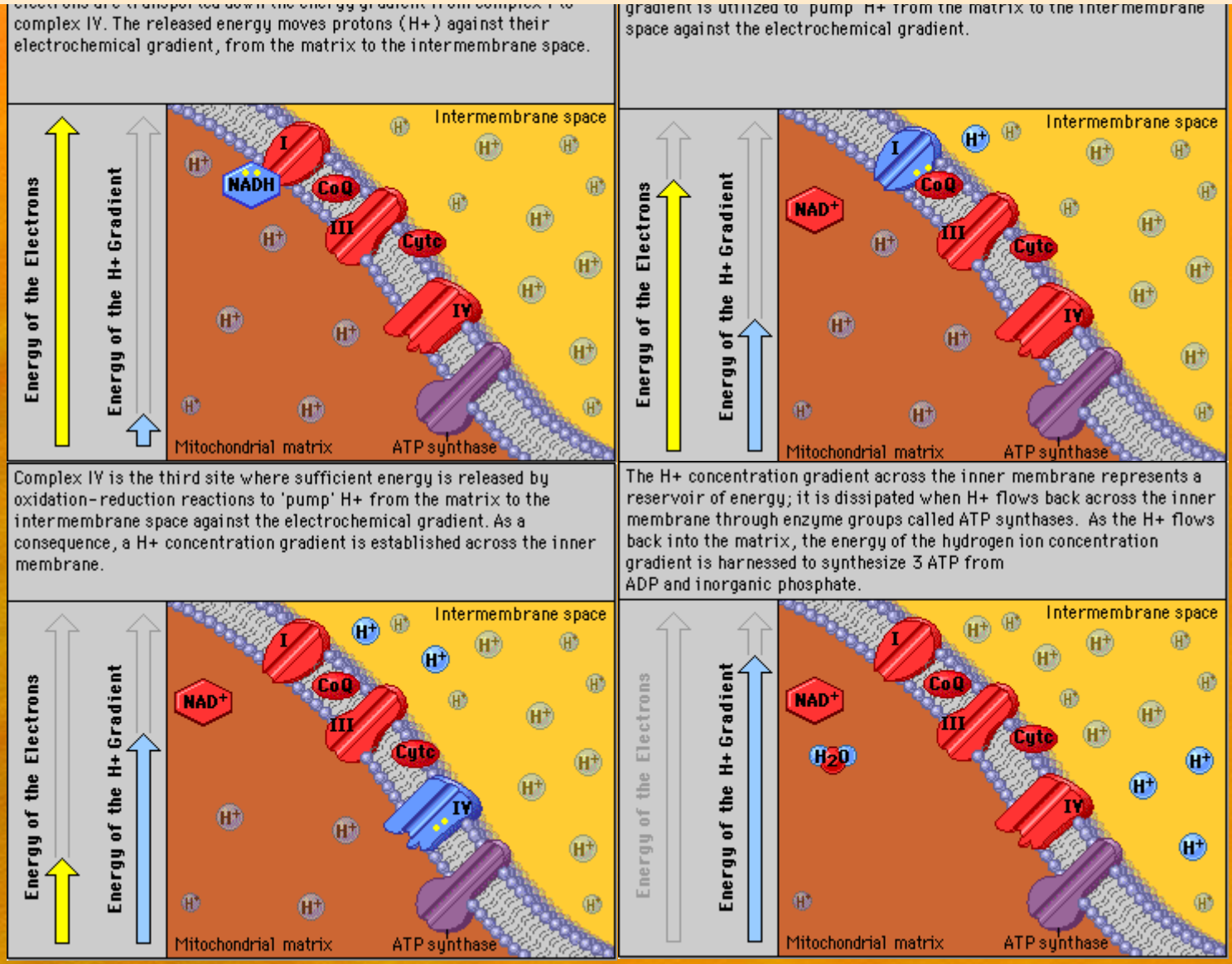
an important physiological process that allows exchange of water between the cells and its environment (occurs across semi-permeable membrane)

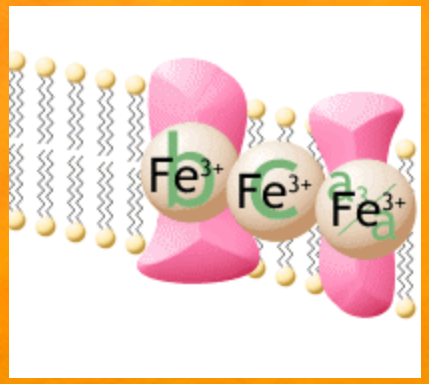


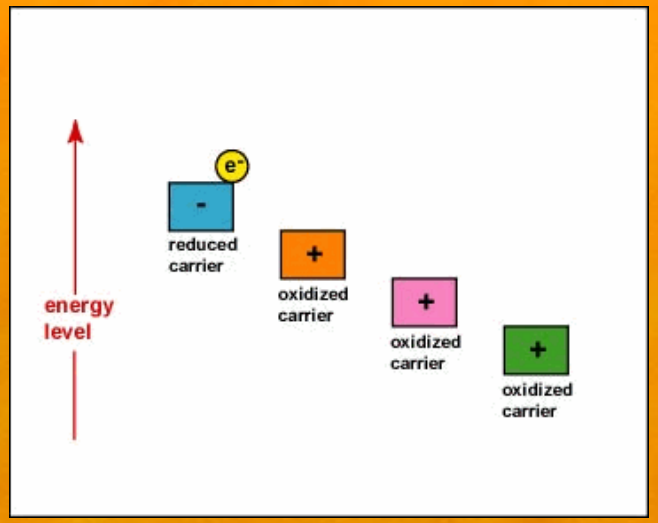


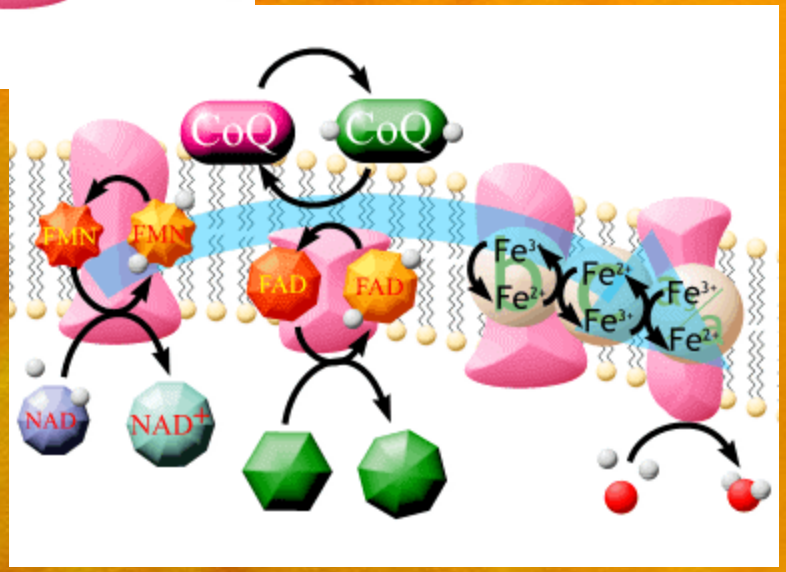


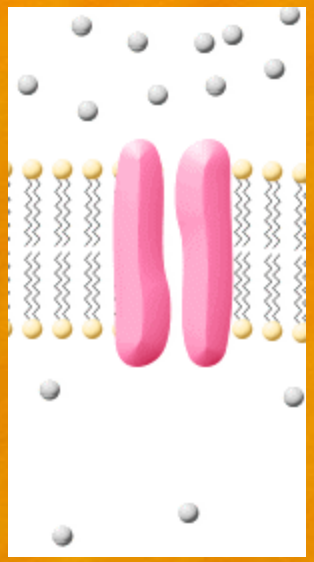
ELECTRON TRANSPORT CHAIN-Processes of Electron/Ion TRANSFER in the Inner Mitochondrial Membrane (major source to ATP production)





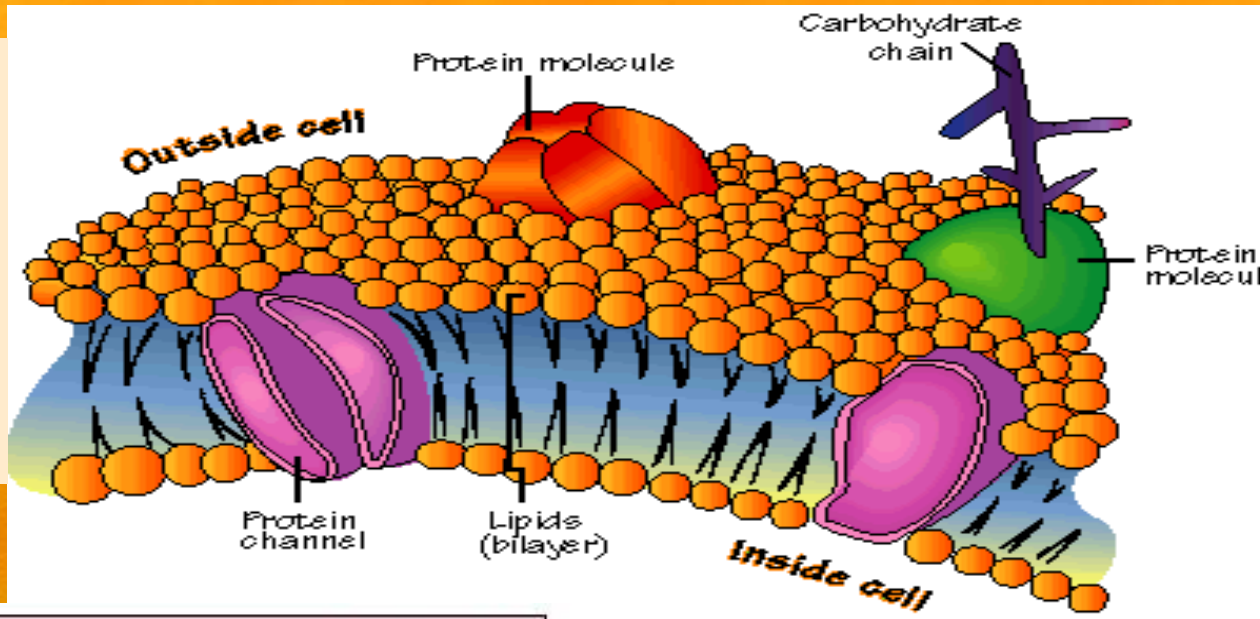


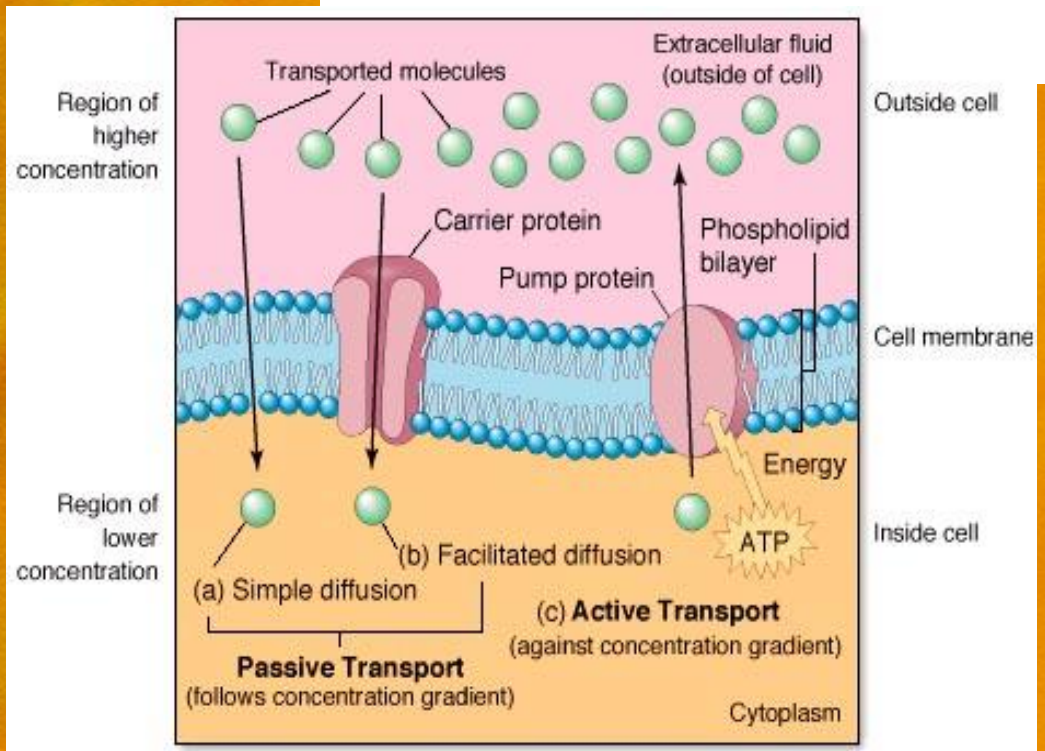




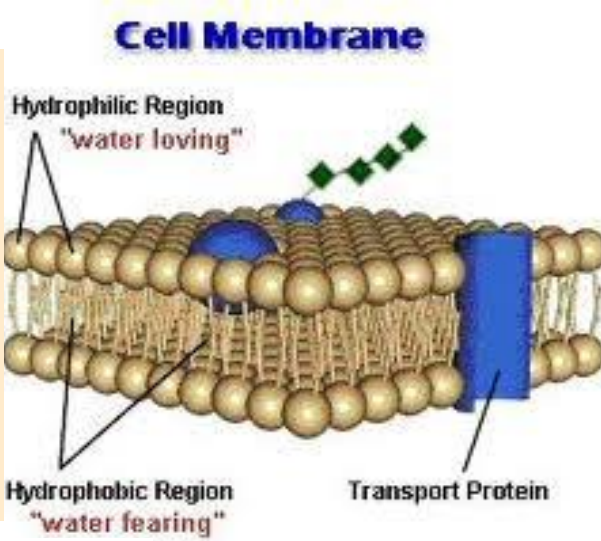
Electron transfer chain-Mitchel
Nobel Prize in1974

Cell Membranes
are natural *Barriers* that regulate the mass transport between the cytosol and the outside of the cells





If we take a look into the structure of the CELL MEMBRANES, we can see that this interface (i.e. the Cell Membrane) has a very complex structure. It consists mainly of ***phospholipid bilayer***, **Proteins**, *carbohydrates*, *cholesterol*….
…mainly, ***LIPOPHILIC SUBSTANCES*** dominate in the structure of the cell membrane



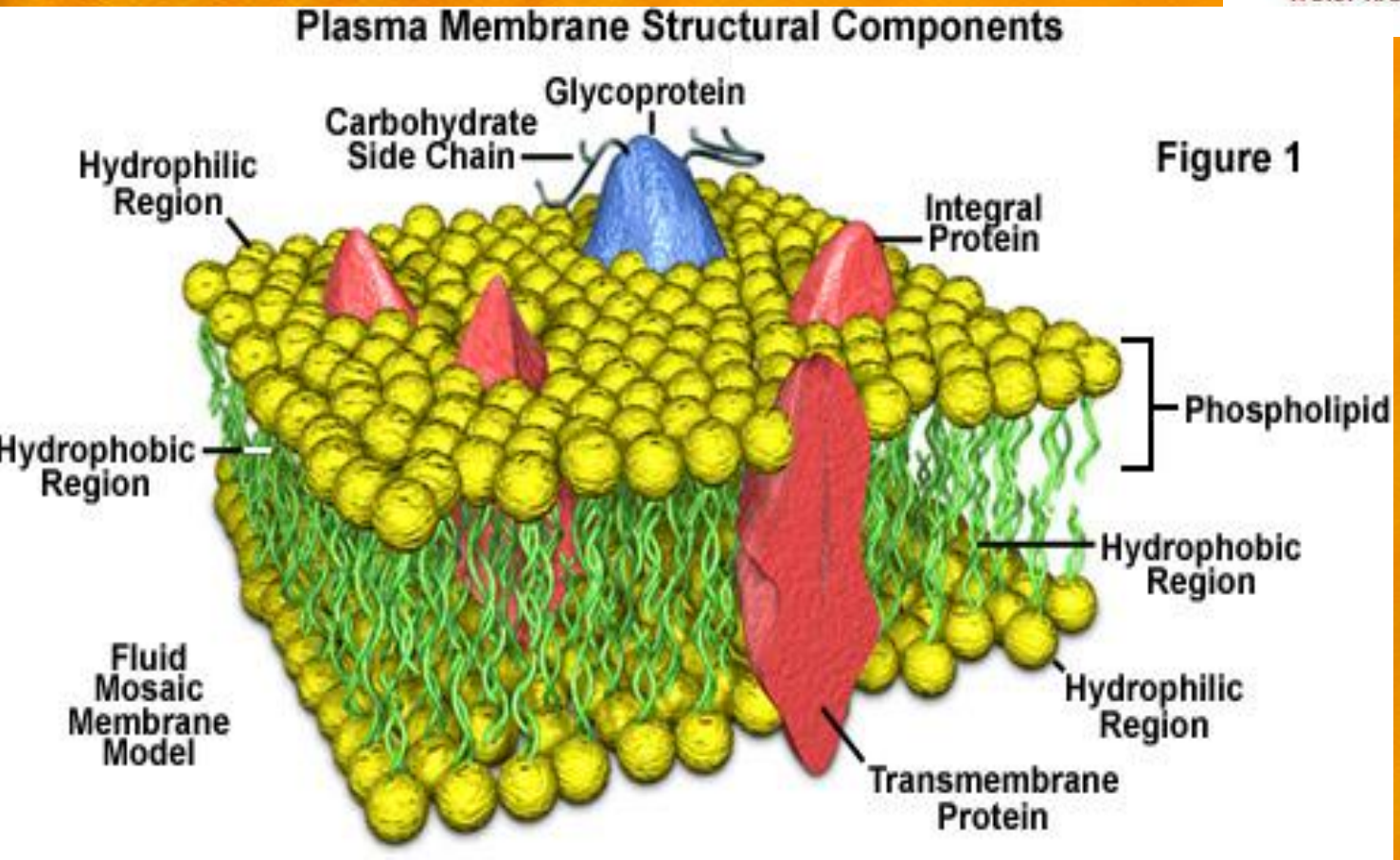


Figure 1

Molecules go through membranes mainly via:

- ***Passive transport***

  -Movement across semipermeable membrane

  --no additional energy is required

- ***Active transport***

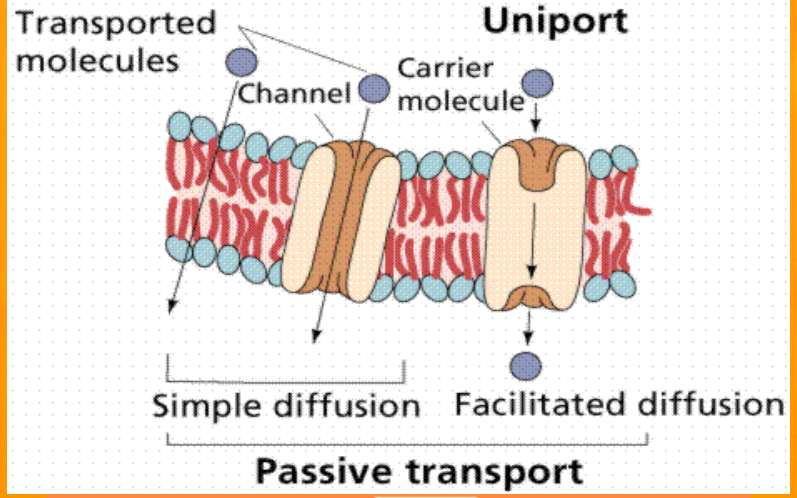
  -Movement across semipermeable membrane in direction OPPOSITE to the concentration gradient

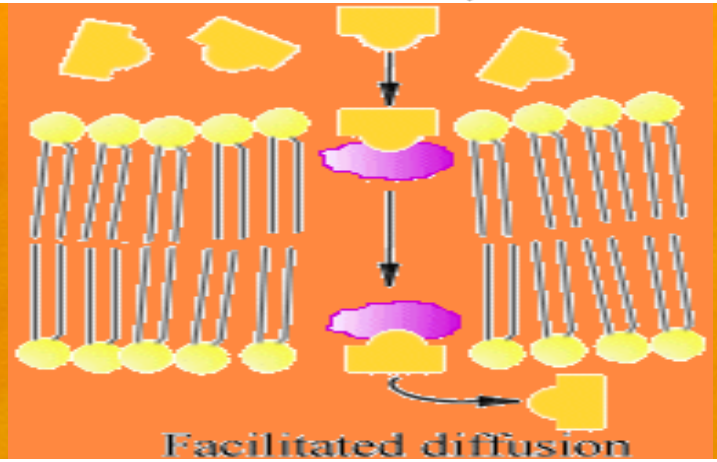
  -Additional energy (mainly coming from ATP) is required

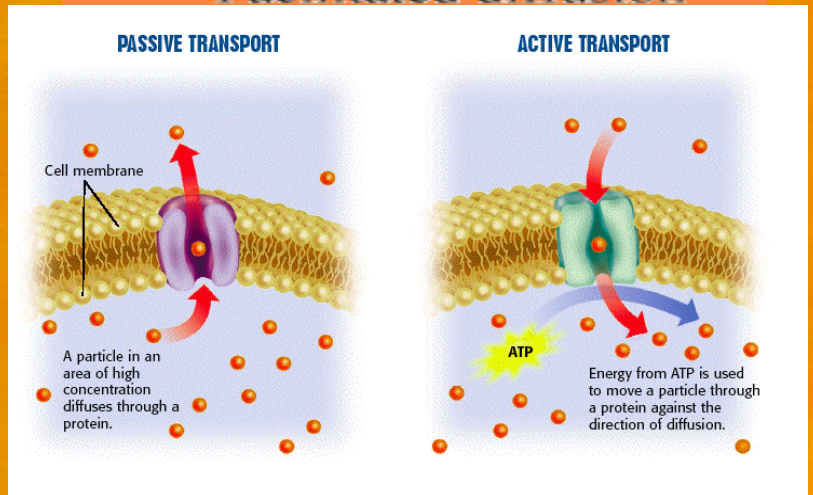
- ***Facilitated transport***

  -The transport of a given molecule is facilitated by a given ligand by which the molecule makes a complex

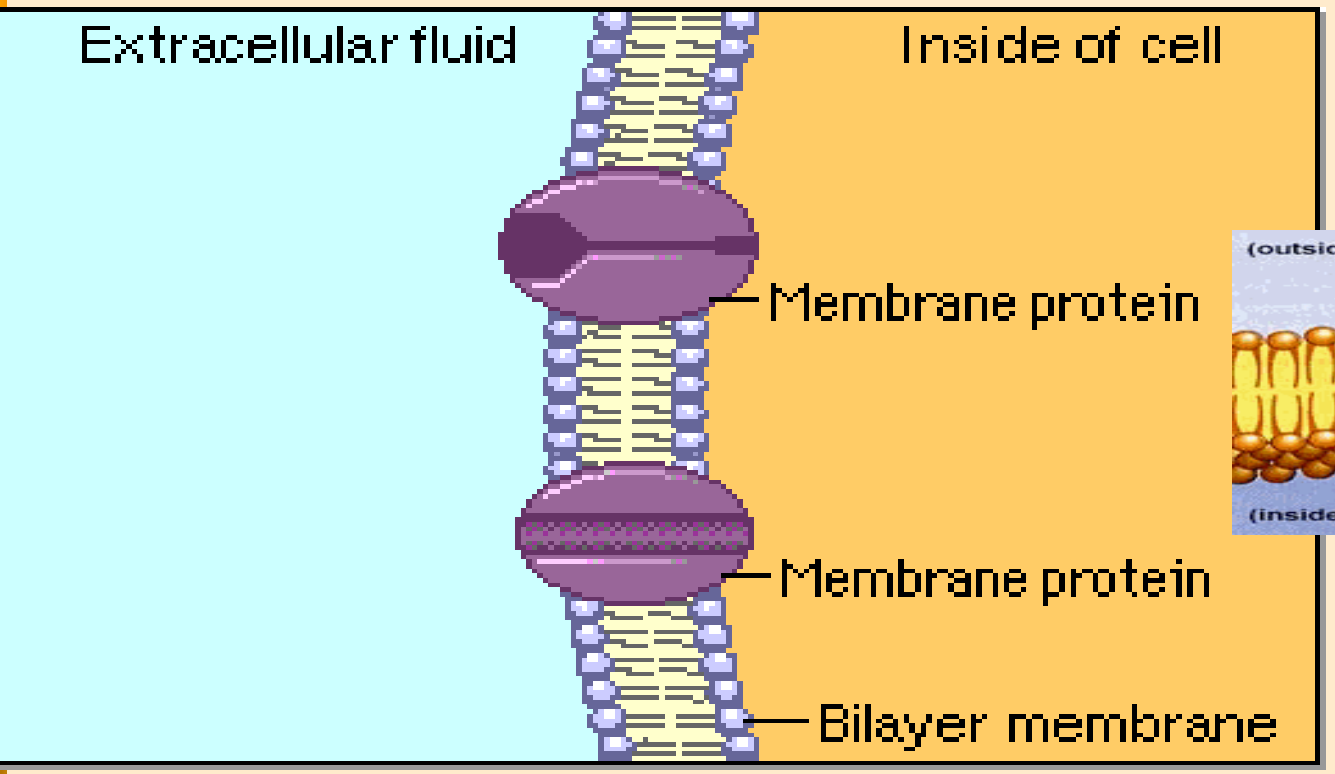
  - no additional energy is required

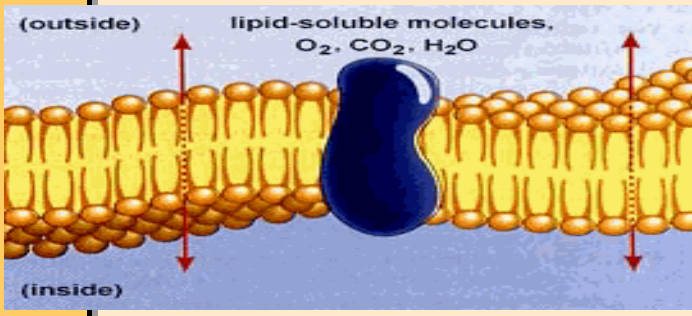






Most of the NEUTRAL Molecules can pass rather easily via the cell membranes
(either by passive diffusion, or in facilitated manner)

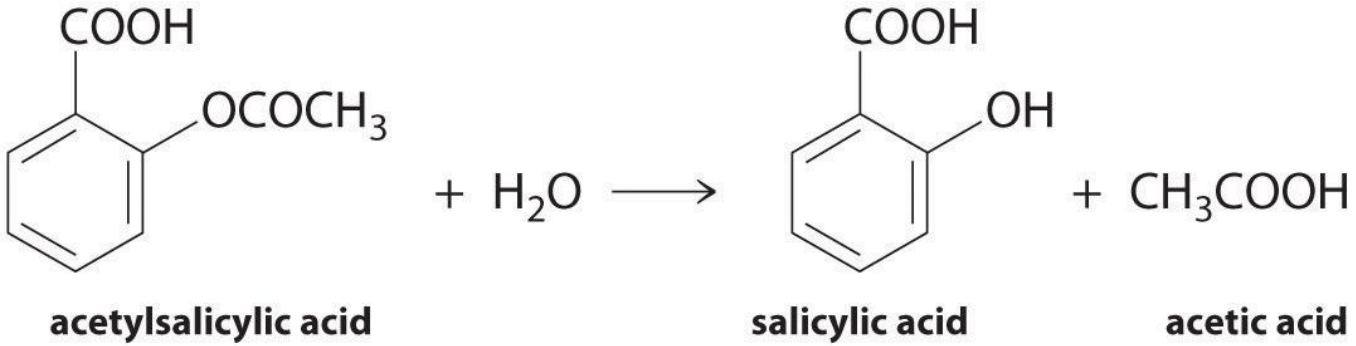




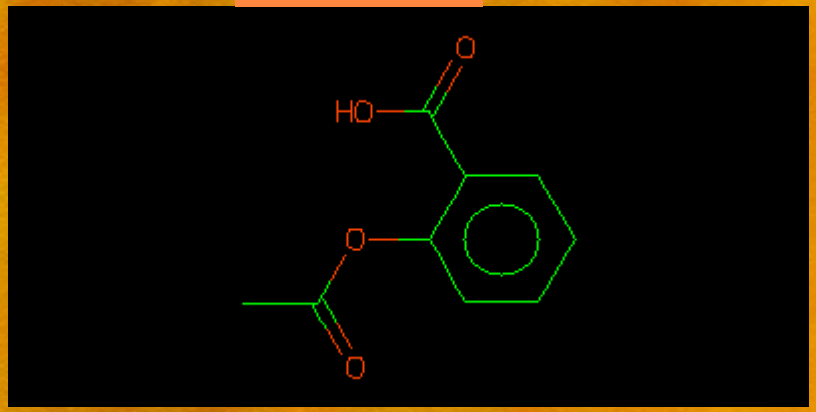
BUT, WHAT HAPPENS WITH THE TRANSPORT OF IONS ACROSS CELL MEMBRANES????

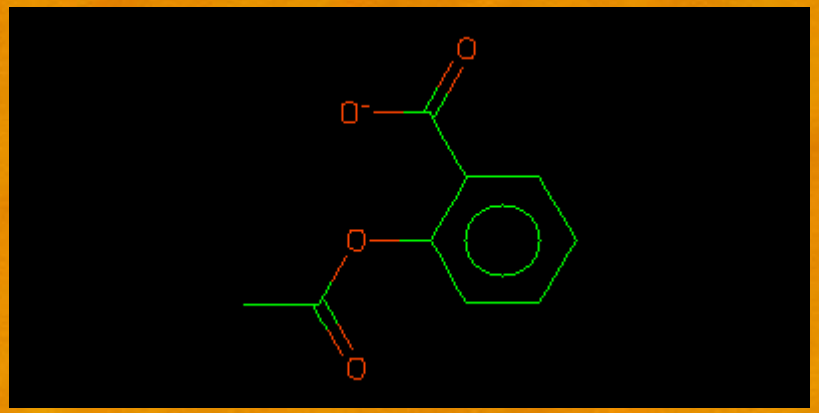
Virtually all drug-like molecules are weak acids or bases and they mainly exist as ions under physiological conditions.

<u>Example</u>: ***Aspirin***

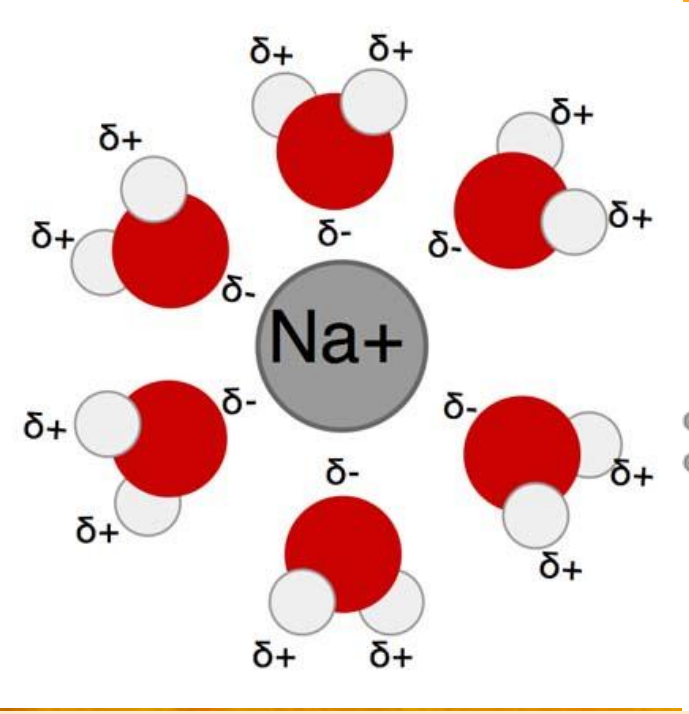


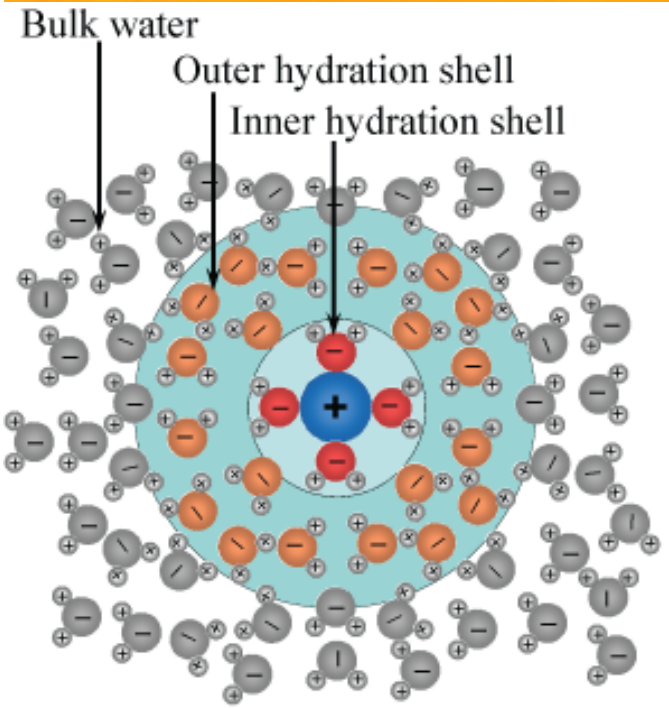
Aspirin
pKa = 3.5

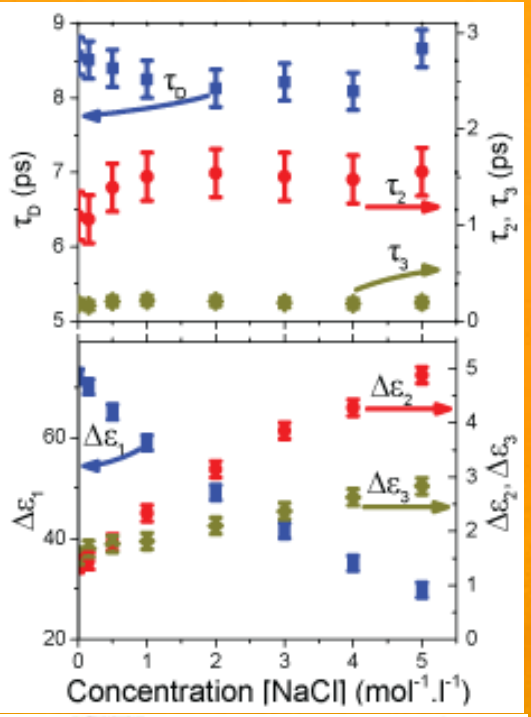




The <u>hydrophilicity</u> of a given <u>ions</u> vs. their neutral parental compounds <u>increases</u> dramatically! That means-every ion has much bigger affinity to dissolve In water compared to its parental neutral predecessor!

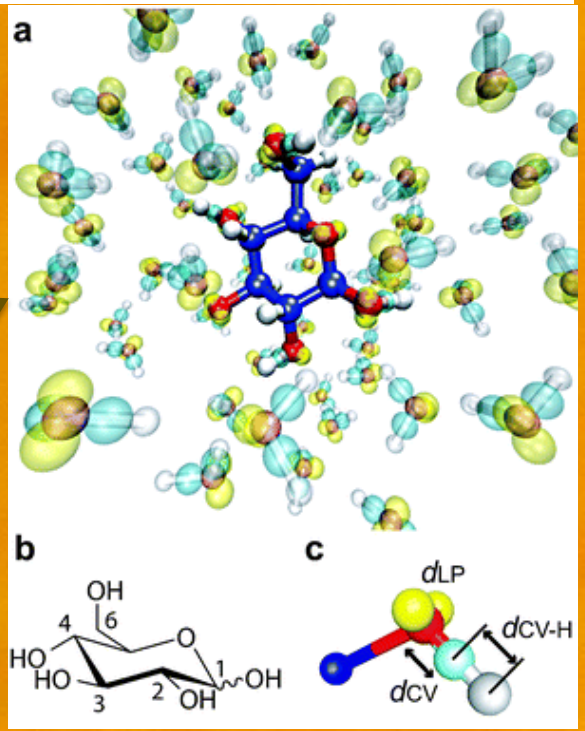






Sodium Na+ ion is strongly hydrated ion in water
At least three water-molecules shells are formed around it!!

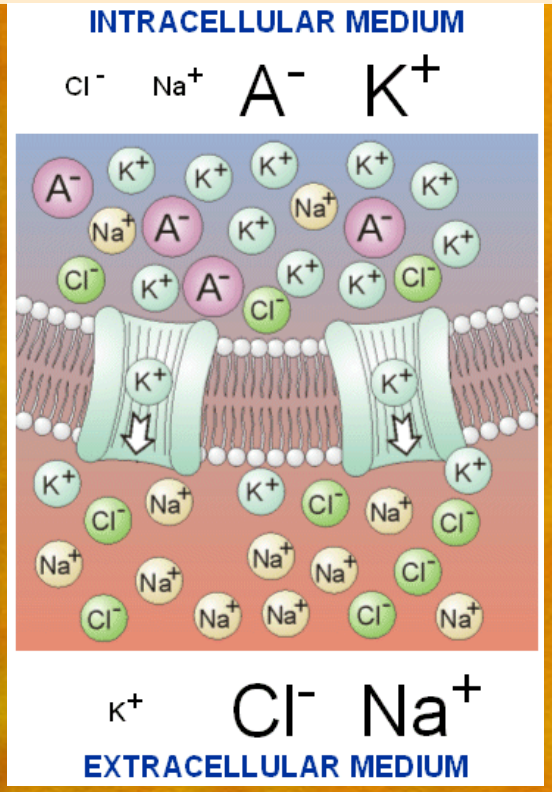
Glucose-is a neutral molecule quite nicely soluble in water, BUT
hydrated with only 2 water-shell molecules

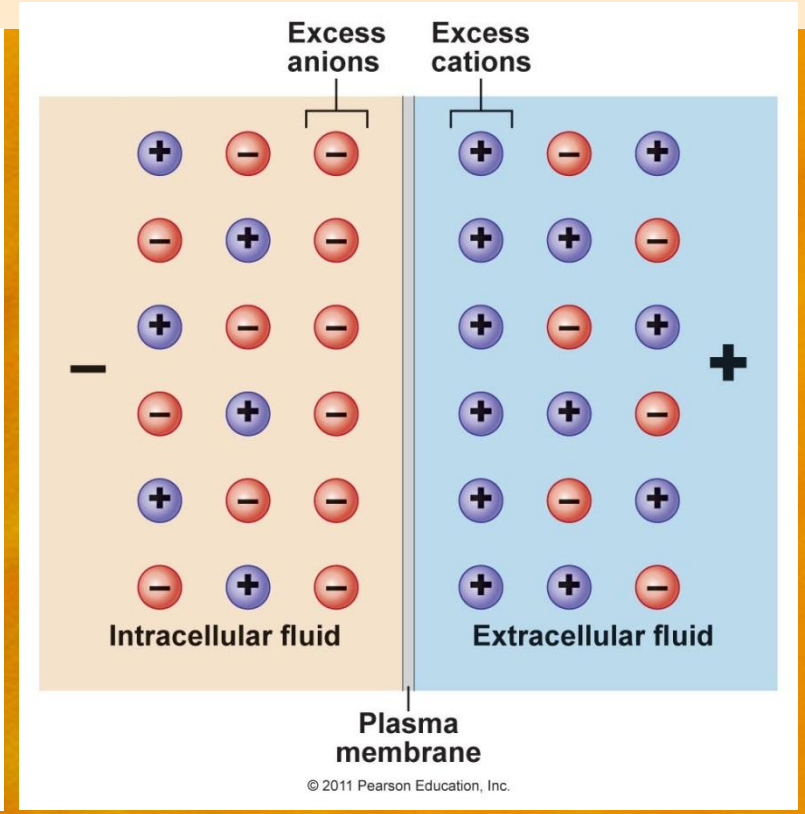


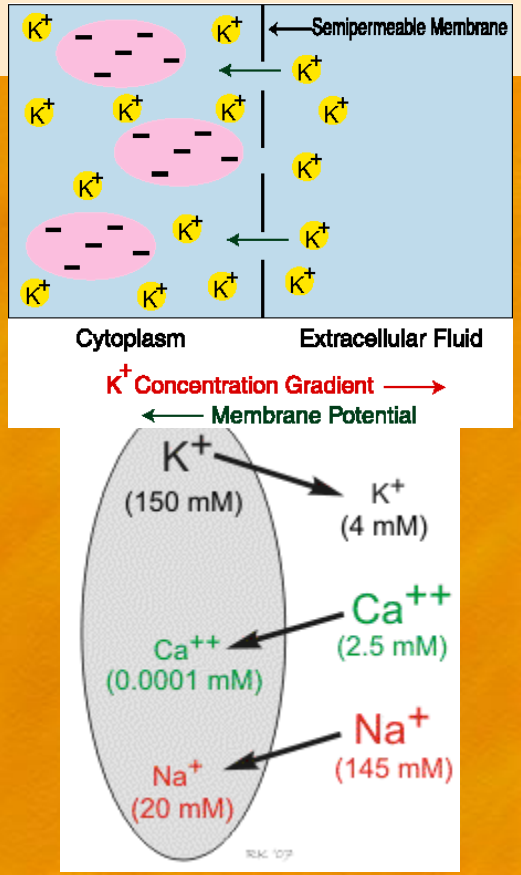
Many drugs and physiologically active compounds are often rejected to crossing the cell membrane, when present in ionized forms!!!

For some ions, there are specific channels that are crossing bridges between Both sides of the cell membranes.

For other ions-membrane potential is a driving force that allows them entering or exiting the cytosol





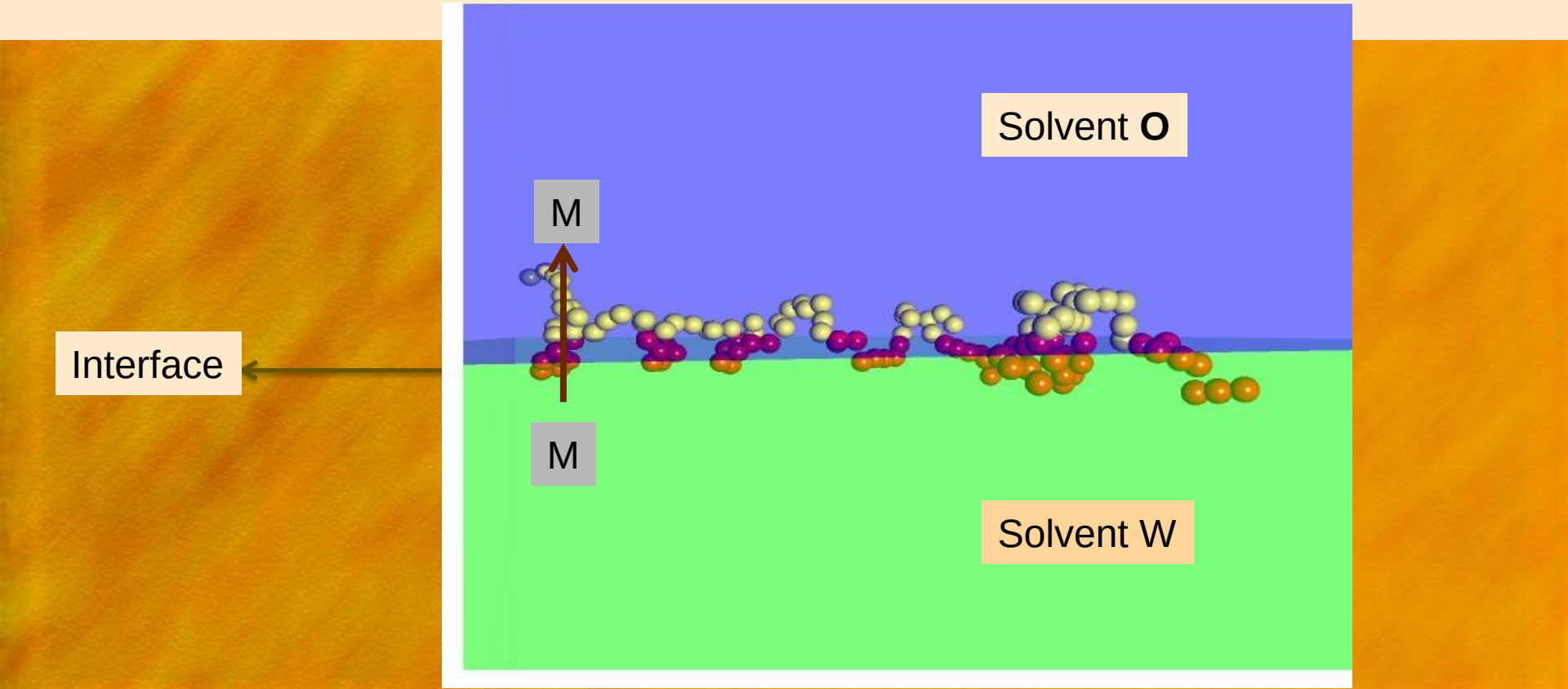


A main parameter that determines whether a given solute can go across an interface separating two solutions is the

STANDARD GIBBS ENERGY OF TRANSFER-$\Delta G^{\ominus}$

For a given solute "**M**", the standard Gibbs energy of transfer of "M" $\Delta G^{\ominus}$ from a given solvent "**W**" to conjoined immiscible solvent "**O**" is defined as a difference between solvation energies of compound M in the two solvents, i.e.

$\Delta G^{\ominus}_{M(W \rightarrow O)}$ = ***E***solvation(of M in "O") – ***E***solvation(of M in "W")



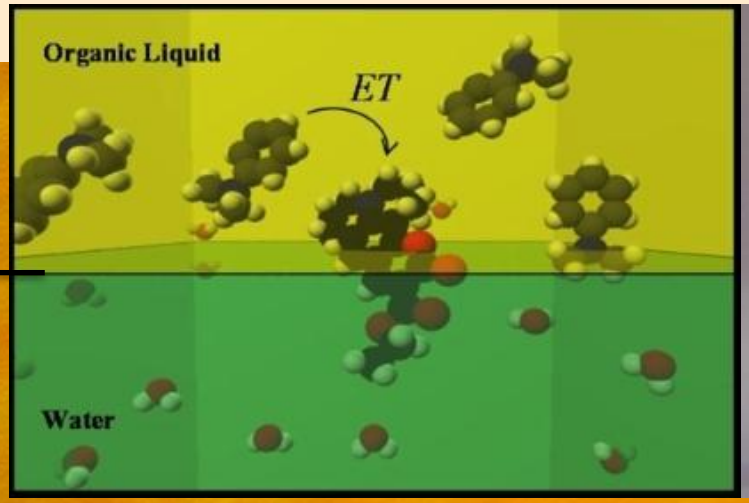
The standard Gibbs energy of transfer of the compound „M“ is linked to its standard partition coefficient P_M via:

$$P_M = \exp\left(-\frac{\Delta G_M^{\theta(w\rightarrow o)}}{RT}\right) \qquad P_M = \frac{a_{M(o)}}{a_{M(w)}}$$

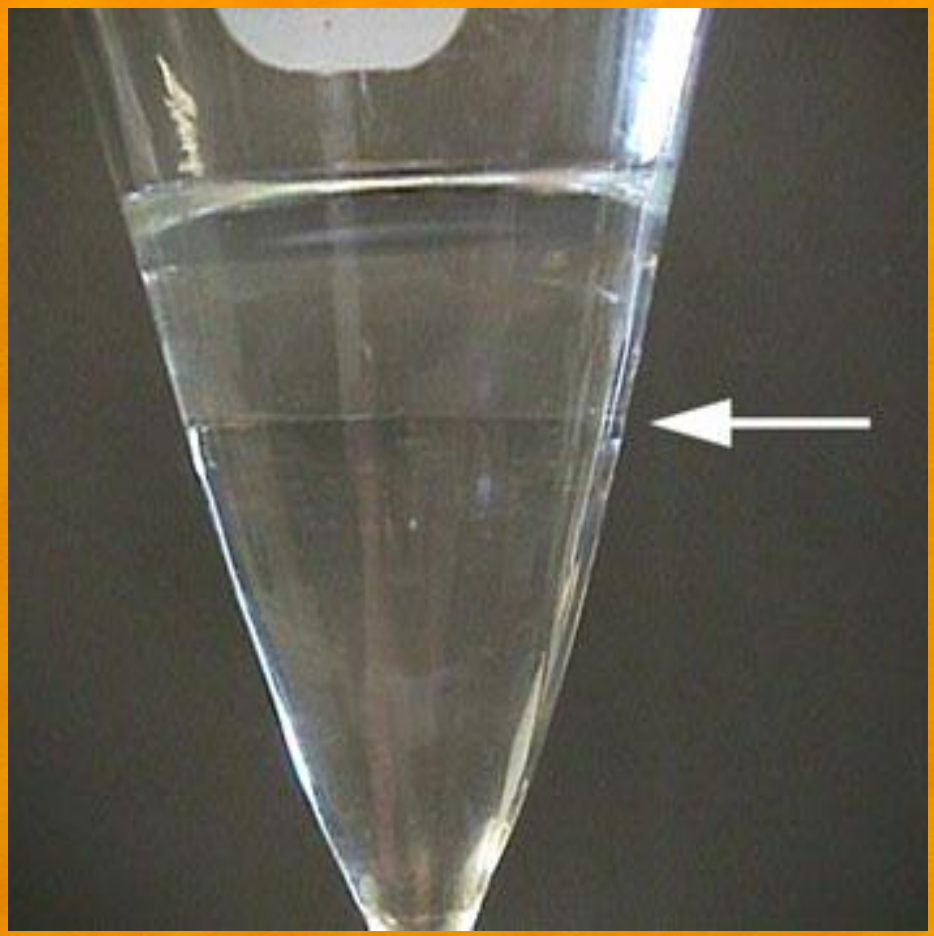
So, if we can determine the partition coefficient P, we can estimate the standard Gibbs energy of transfer of given compound, and we can assess its ability to cross a given interface (membrane)

Because it is quite difficult to perform experiments in real Cell membranes, commonly one uses the Interface between two immiscible liquid solvents as a good approximation mimicking the biological membranes

Liquid-Liquid Interface



For neutral molecules, we can directly get access to the standard partition coefficient P of given compound by various partitioning techniques (chromatography, shake flask, extraction…)



Importance of the partition coefficient

Measure of the **lipophilicity** of the compounds

Prediction of the transport through membranes

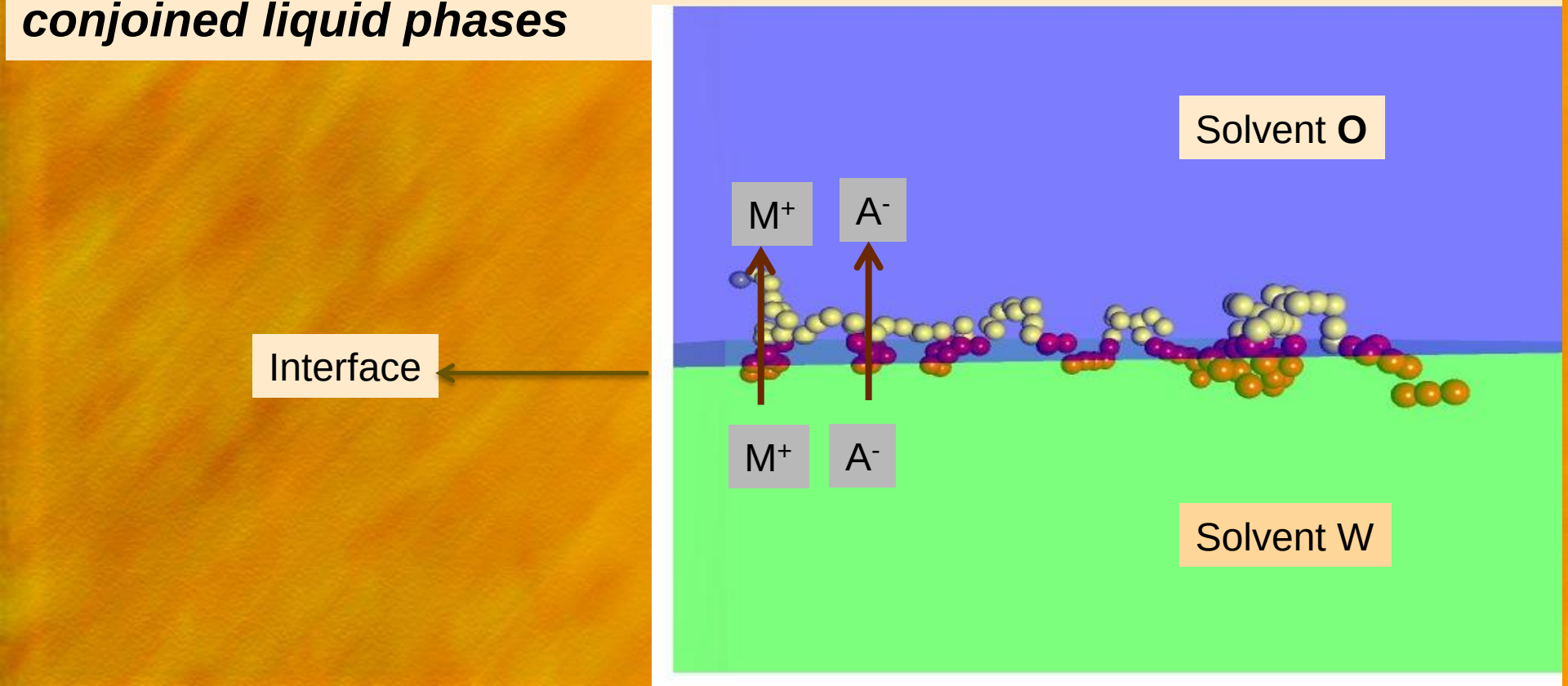
Toxicity

QSA-Relationships and QSP-Relationships

Drug design

For *IONS*, however, the *standard partition coefficient P* of given ION CAN NOT be assessed precisely by using the common partitioning techniques (shake flask, extraction…)

The reason: NO SINGLE ION CAN SOLELY CROSS THE LIQUID-LIQUID INTERFACE. *Its partition from one to other Solvent is always followed by transfer of a counter ion*.
This is DUE TO THE CHARGE BALANCING requirements in both conjoined liquid phases



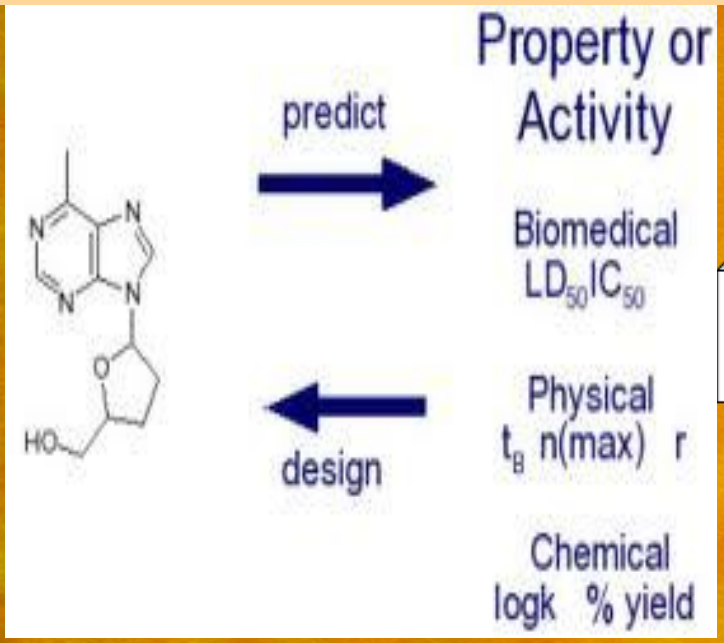
Why do we need the $\Delta G^{\ominus}$ data for IONIC COMPOUNDS?

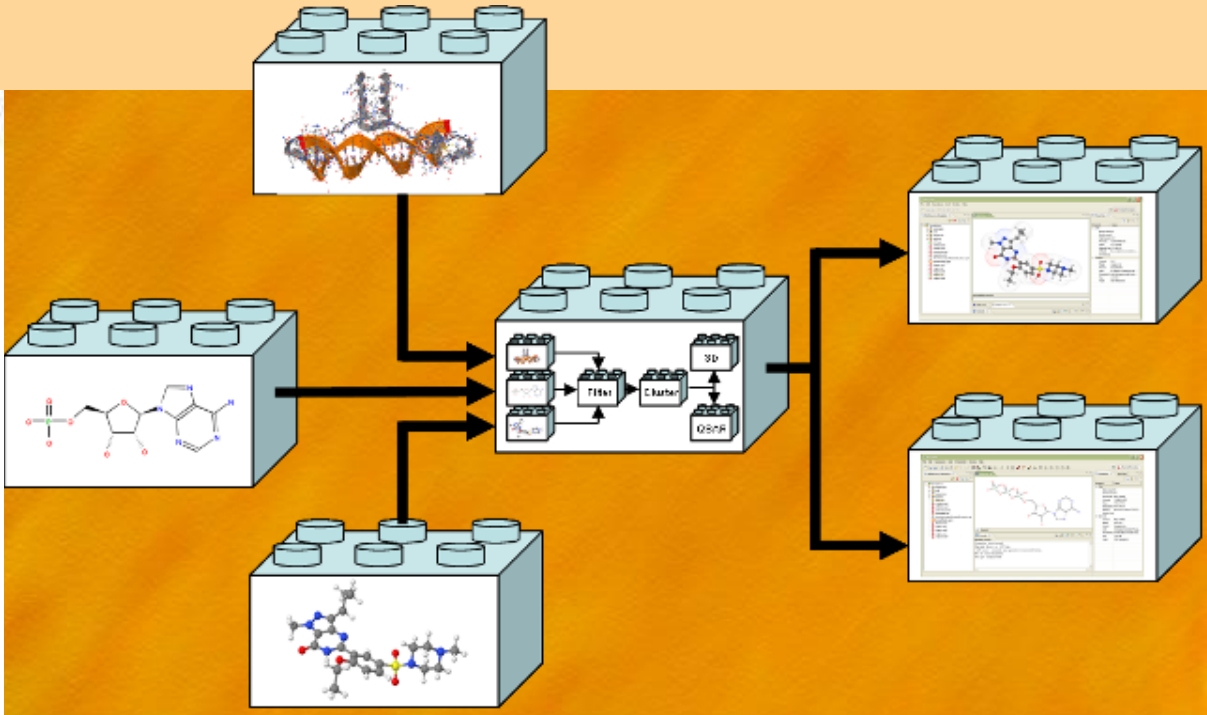
-Almost 90% of the drugs and medicaments are in IONIZED FORM under Physiological conditions!!!

-Data are needed especially in the pharmacy and medicine in order to assess the potential of a given drug …and

-In order to DESIGN an efficient drug in pharmacy (by the QSPR and QSAR Studies)-in such calculations one always needs data for $\Delta G^{\ominus}$

….

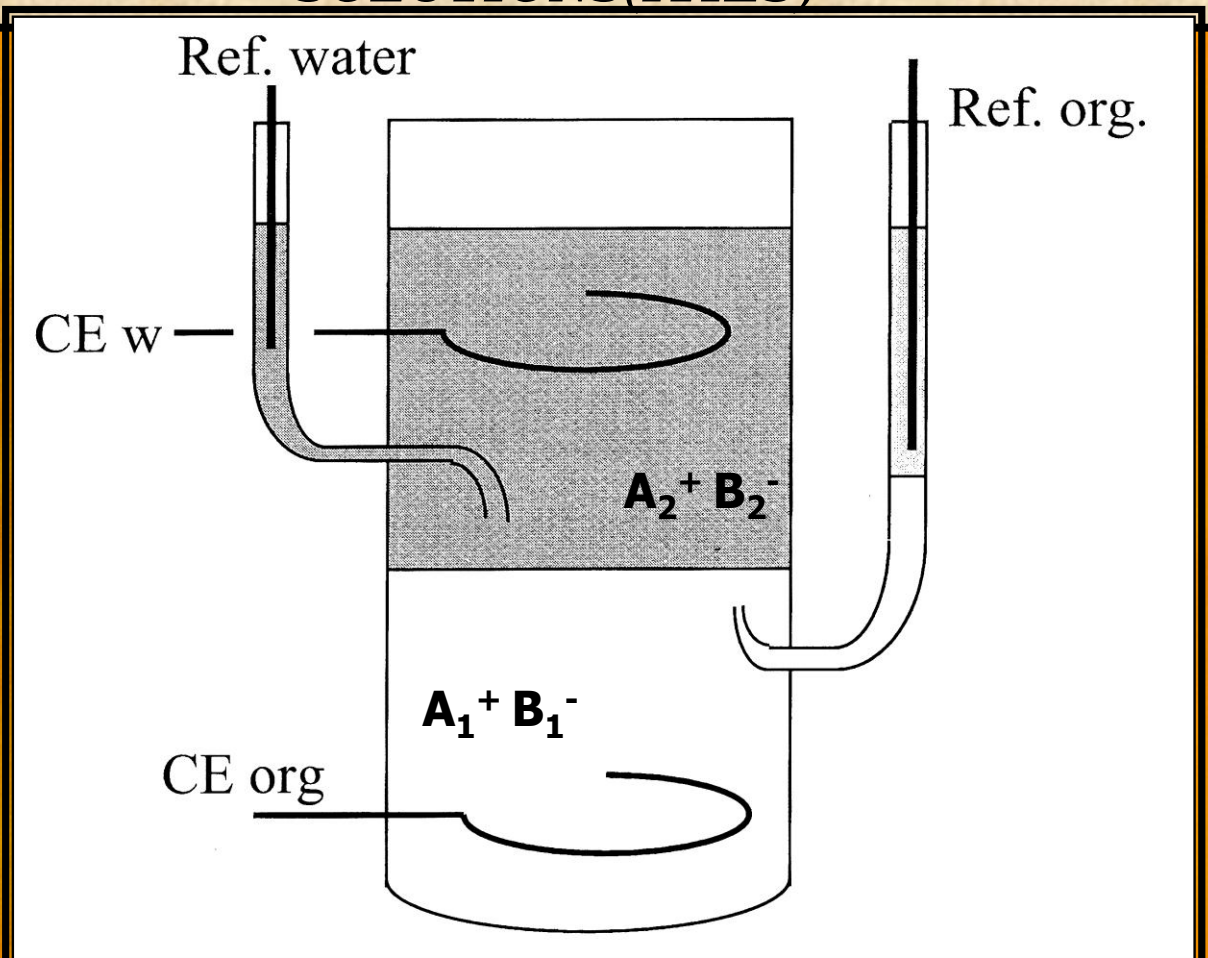




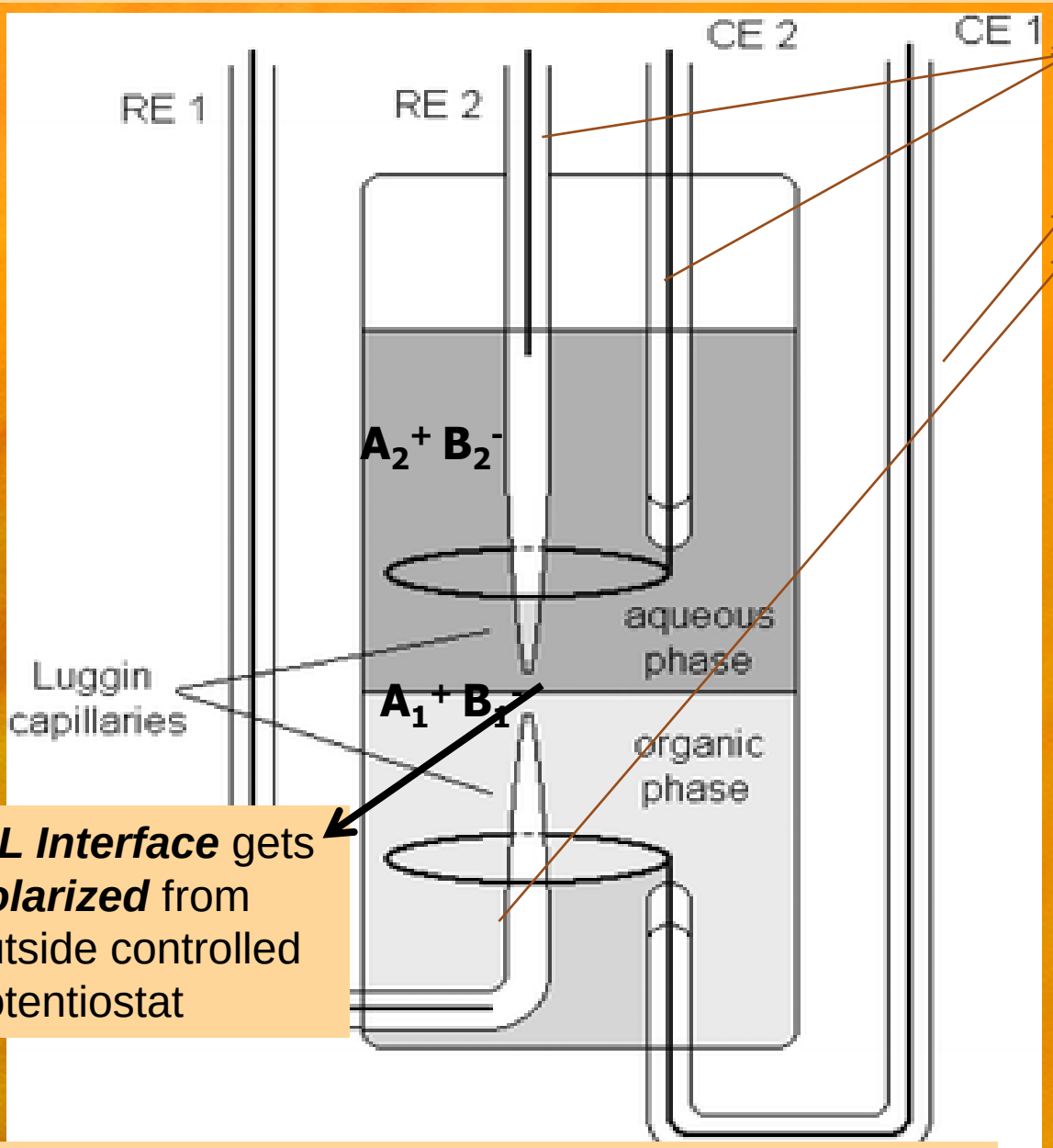
So, for the determination of ΔG^{o} of single ions one requires POTENTIOSTATIC CONTROLLING OF THE INTERFACIAL POTENTIAL ESTABLISHED AT THE LIQUID|LIQUID INTERFACE

The first voltammetric technique to achieve this was the:

FOUR ELECTRODE VOLTAMMETRY *at the* ***INTERFACE BETWEEN TWO IMMISCIBLE ELECTROLYTE SOLUTIONS(ITIES)***



Strategy: Bringing into contact two Immiscible electrolyte solutions



L-L Interface gets ***polarized*** from outside controlled potentiostat

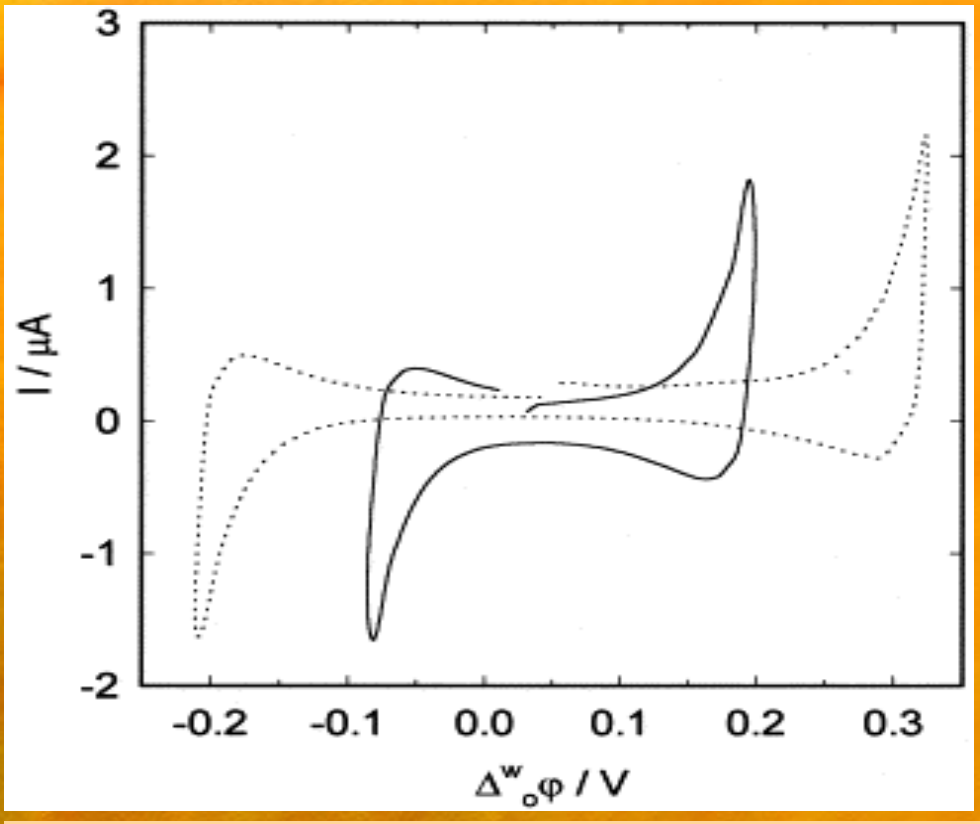
Voltammetric cell used in Voltammetry at ITES

In the aqueous phase: 1 Reference and 1 Counter electrode

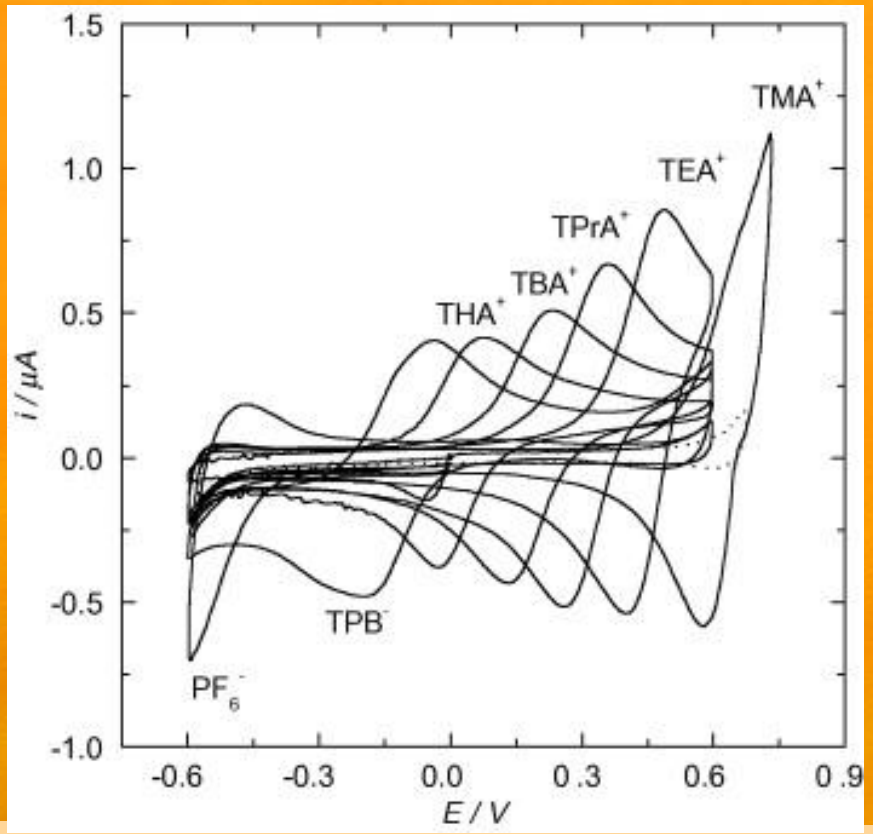
Same Electrodes also in the Organic phase!

In aqueous phase: A highly HYDROPHILIC Electrolyte ($A_2^+ B_2^-$ = LiCl) Is dissolved (0.1 M);

In organic phase: A highly LIPOPHILIC Electrolyte ($A_1^+ B_1^-$ = TBNTPB- Tetrabutylammonium-Tetraphenyl borate) (0.1 M) is dissolved.

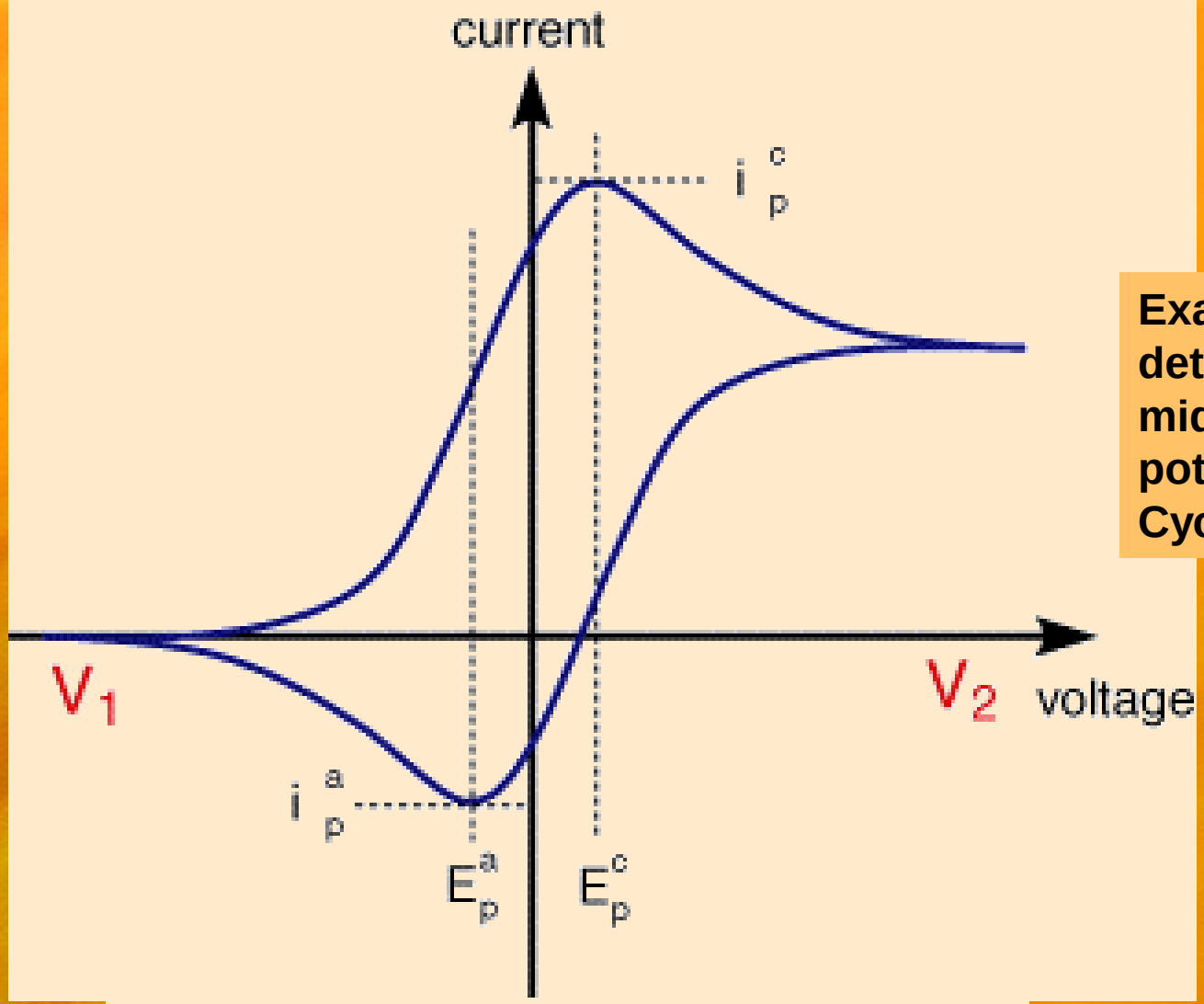


Cyclic voltammograms recorded with 4 electrode voltammetry at ITES when NO transferable ion is present in the system-ideally polarizable Interface



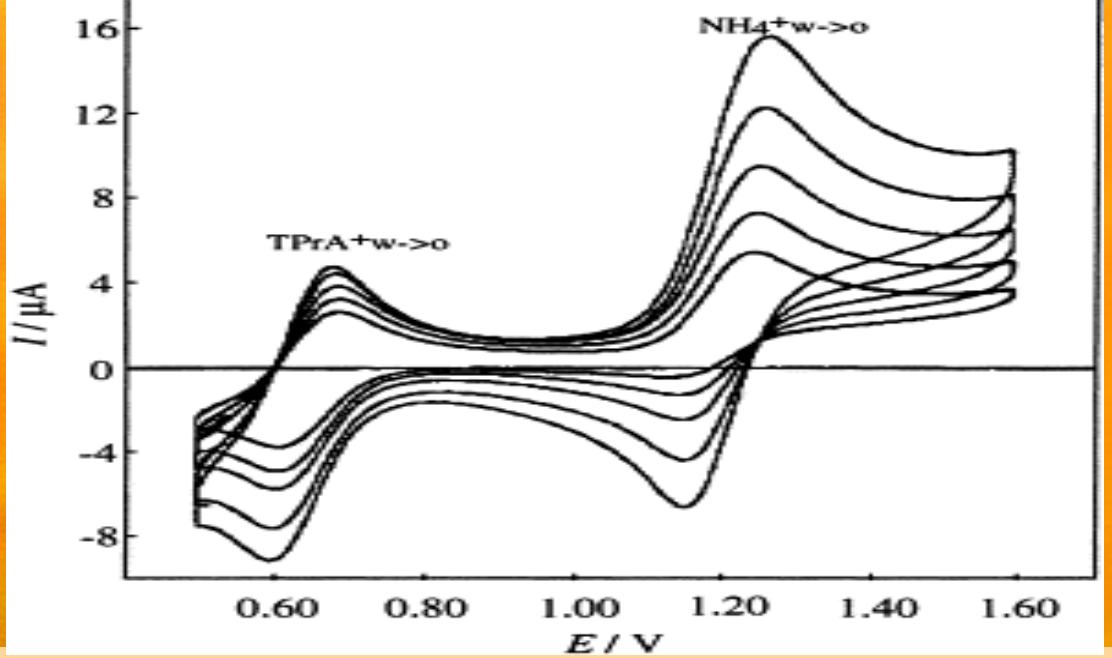
Cyclic voltammograms recorded with 4 electrode voltammetry at ITES when transferable ions are present in the system

By using a *REFERENCE STANDARD ion* (i.e. some ion with known ΔG^{e} value, FROM THE MID-PEAK POTENTIAL OF PARTICULAR CYCLIC VOLTAMMOGRAMS we can determine the ΔG^{e} of a given compound in its ionic form



Example of determining the mid-peak potential from Cyclic voltammogram

Mid-peak potential =
median between cathodic E_p^c and
Anodic E_p^a peak potentials



Actually, from the cyclic voltammograms we can determine the values of the Standard potential of ion transfer of a given ion $\Delta\phi^{\ominus}_{i}$, that is defined as:

$$\Delta_{\mathrm{o}}^{\mathrm{w}}\phi = \phi^{\mathrm{w}} - \phi^{\mathrm{o}} = \Delta_{\mathrm{o}}^{\mathrm{w}}\phi_i^{\ominus} + \frac{RT}{z_i F}\ln\left(\frac{a_i^{\mathrm{o}}}{a_i^{\mathrm{w}}}\right)$$

$\Delta\phi^{\ominus}_{i}$ is linked to the standard Gibbs energy of ion transfer $\Delta G^{\ominus}_{i}$ with the relation:

$$\Delta_{\mathrm{o}}^{\mathrm{w}}\phi_i^{\ominus} = -\frac{\Delta G_{\mathrm{tr},i}^{\ominus,\mathrm{w}\rightarrow\mathrm{o}}}{z_i F}$$

RECENT ACHIEVEMENTS WITH THIS TECHNIQUE:

-determination of ΔG^{e-}values of amino acids in cationic and anionic forms;

-determination of ΔG^{e-}values of some pollutants (nitro phenols)

-determination of ΔG^{e-}values of antioxidants (polyphenols)

-determination of ΔG^{e} values of many medicaments and drugs

-determination of ΔG^{e-}values of neurotransmitters (acetylcholine)

-determination of ΔG^{e-}values of psychotropic drugs!

-Constructing Bio-SENSORS for THESE SUBSTANCES

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Evaluation of the lipophilic properties of opioids, amphetamine-like drugs, and metabolites through electrochemical studies at the interface between two immiscible solutions

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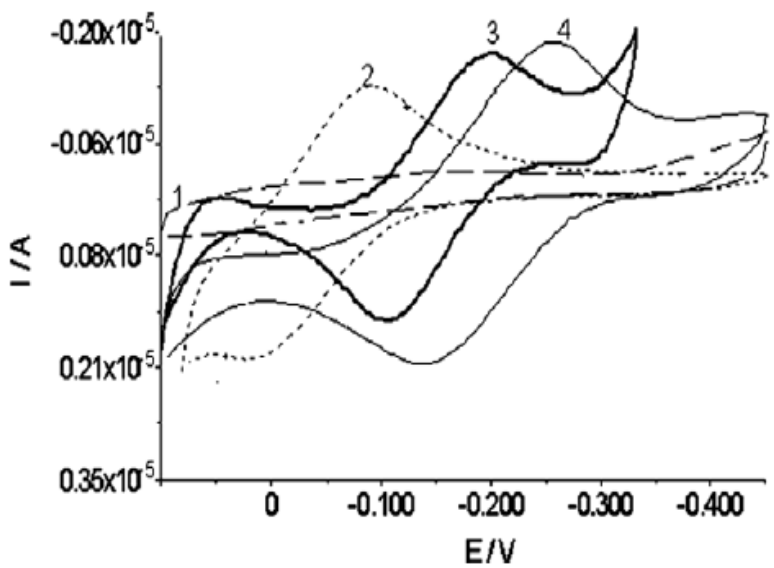
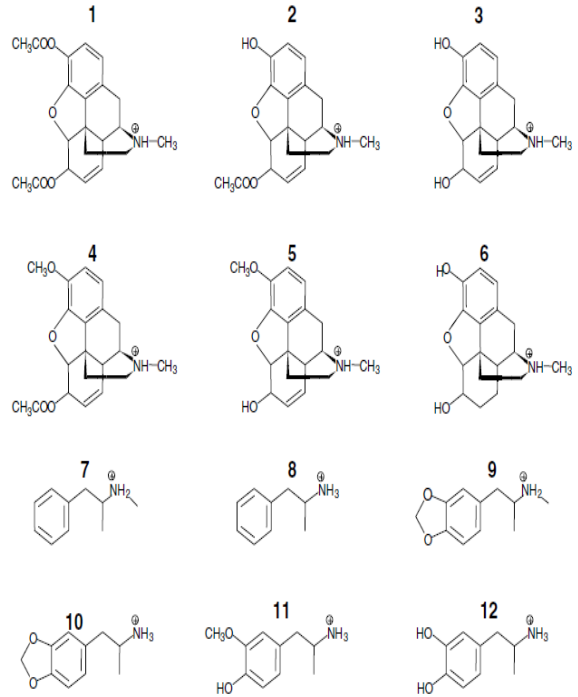
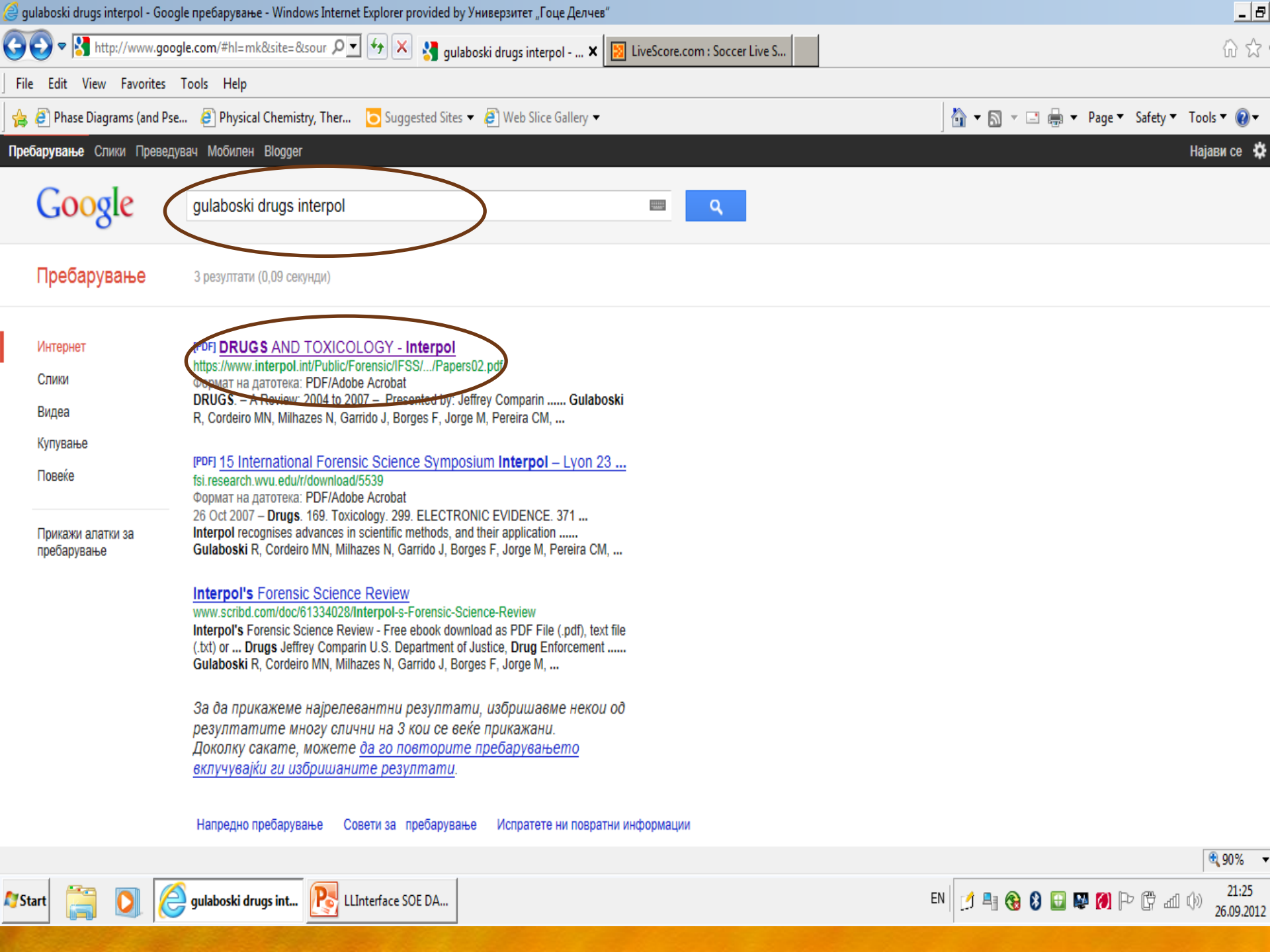


Fig. 3. Representative cyclic voltammograms of the compounds: blank (curve 1), heroin (curve 2), codeine (curve 3), and morphine (curve 4). The scan rate was 25 mV/s, and the concentration of the compounds was 0.25 mmol/L.



g. 1. Chemical structures of the studied compounds: heroin (1), 6-MAM (2), morphine (3), acetylcodeine (4), codeine (5), dihydrocodeine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File Edit View Favorites Tools Help
Phase Diagrams (and Pse... Physical Chemistry, Ther... Suggested Sites Web Slice Gallery
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Пребарување Слики Преведувач Мобилен Blogger
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Пребарување
3 резултати (0,09 секунди)
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Слики
Видеа
Купување
Повеќе
Прикажи алатки за пребарување
[PDF] DRUGS AND TOXICOLOGY - Interpol
https://www.interpol.int/Public/Forensic/IFSS/.../Papers02.pdf
Формат на датотека: PDF/Adobe Acrobat
DRUGS. – A Review: 2004 to 2007 – Presented by: Jeffrey Comparin ..... Gulaboski R, Cordeiro MN, Milhazes N, Garrido J, Borges F, Jorge M, Pereira CM, ...
[PDF] 15 International Forensic Science Symposium Interpol – Lyon 23 ...
fsi.research.wvu.edu/r/download/5539
Формат на датотека: PDF/Adobe Acrobat
26 Oct 2007 – Drugs. 169. Toxicology. 299. ELECTRONIC EVIDENCE. 371 ... Interpol recognises advances in scientific methods, and their application ..... Gulaboski R, Cordeiro MN, Milhazes N, Garrido J, Borges F, Jorge M, Pereira CM, ...
Interpol's Forensic Science Review
www.scribd.com/doc/61334028/Interpol-s-Forensic-Science-Review
Interpol's Forensic Science Review - Free ebook download as PDF File (.pdf), text file (.txt) or ... Drugs Jeffrey Comparin U.S. Department of Justice, Drug Enforcement ..... Gulaboski R, Cordeiro MN, Milhazes N, Garrido J, Borges F, Jorge M, ...
За да прикажеме најрелевантни резултати, избришавме некои од резултатите многу слични на 3 кои се веќе прикажани.
Доколку сакате, можете да го повторите пребарувањето вклучувајќи ги избришаните резултати.
Напредно пребарување Совети за пребарување Испратете ни повратни информации
90%
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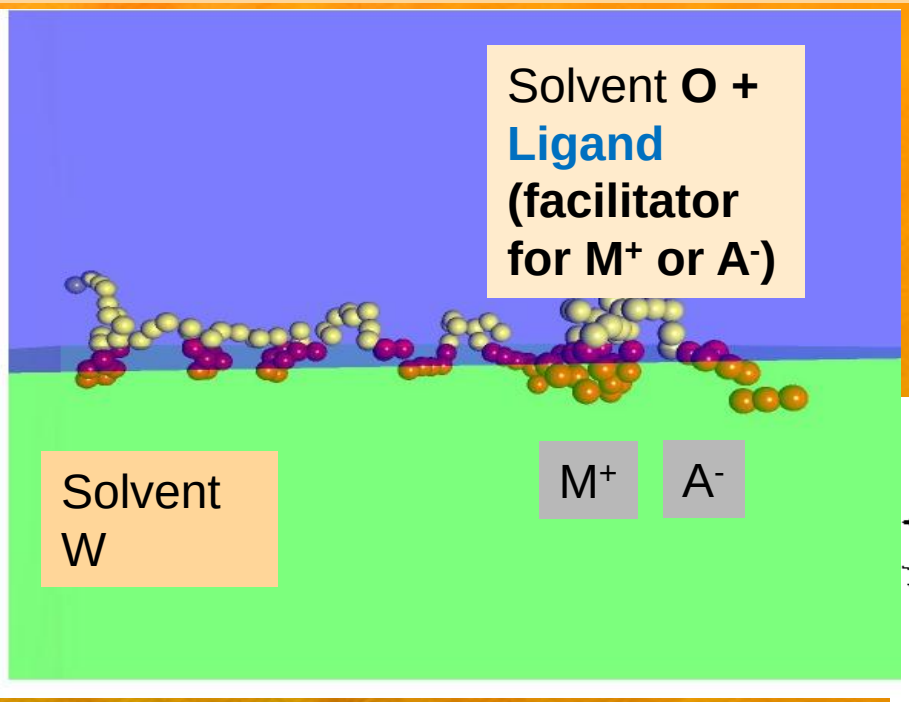
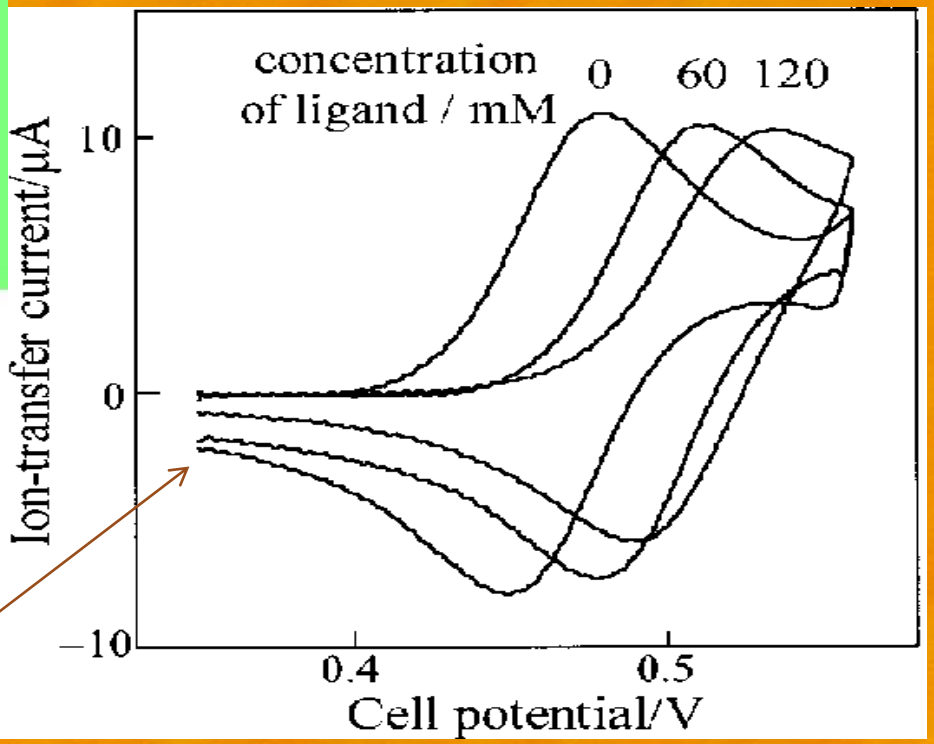
26.09.2012

There are plenty of ionic drugs that are too hydrophilic and their transfer from water to organic solvent can not be achieved

Strategy: USE LIGAND (chelator) in organic phase to "assist (facilitate) the ion transfer" across Liquid-Liquid Interface





Voltammograms the assisted ion transfer of Lithium ions

Construction of PARTITION DIAGRAMS with help of 4-Electrodes Voltammetry at ITES

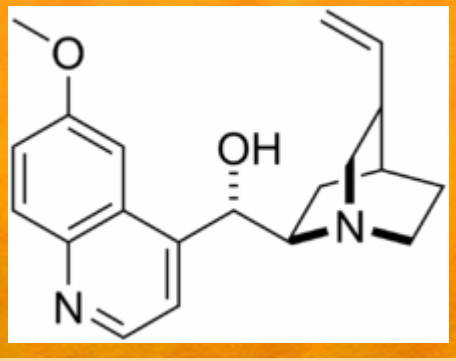
One of the greatest achievements of 4-electrodes voltammetry at ITES is the Construction of so-called PARTITION IONIC DIAGRAMS for the compounds studied.

The ***methodology*** of the ionic partition diagrams ***consists in determining equiconcentration boundaries as a function of the interfacial potential difference and the aqueous pH*** by taking account of the thermodynamic equilibria governing the distribution of the various acid:base forms of the molecule involved in the ionic transfer.

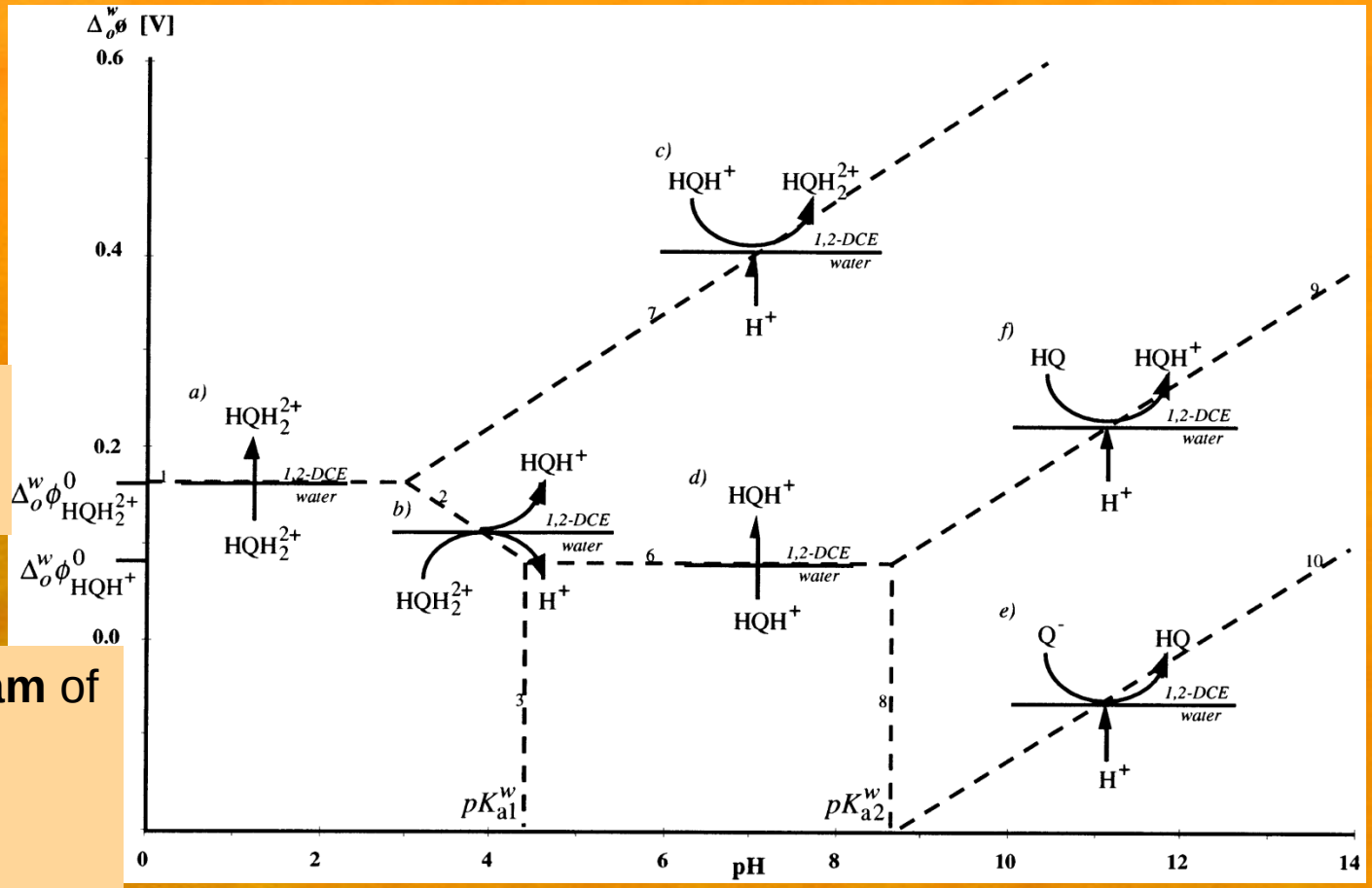
The ionic partition diagram defines the domains of predominance of each species either in the aqueous or in the organic phase, and it offers a global and direct visualization of all the transfer mechanisms.

$$\Delta_o^w \phi_{LH^+}^{1/2} = \Delta_o^w \phi_{H^+}^0 + \frac{RT}{2F} \ln\left(\frac{D_L}{D_{LH^+}}\right) - \frac{2.303RT}{F} pK_a^{DCE} + \frac{2.303RT}{F} pH^w$$

Equation for estimating the relevant parameters of ion transfer by the So-called “assisted (facilitated) ion transfer” across Liquid-Liquid Interface



Structure of Quinidine-antiarrhythmic agent



Ionic partition diagram of ***Quinidine*** at Water-Dichlorethan interface

What information can we get from the partition diagrams?

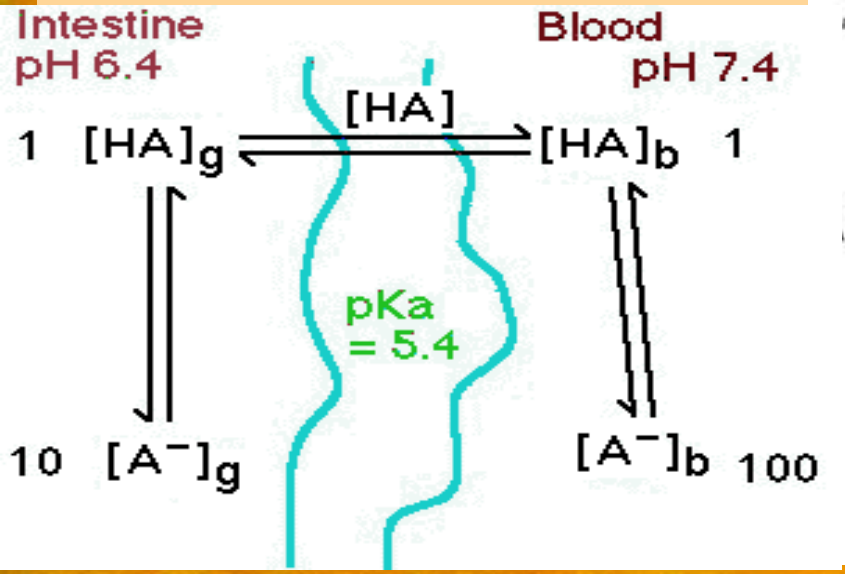
-we can assess the Gibbs energy of transfer of a given ionic compound in different pH's

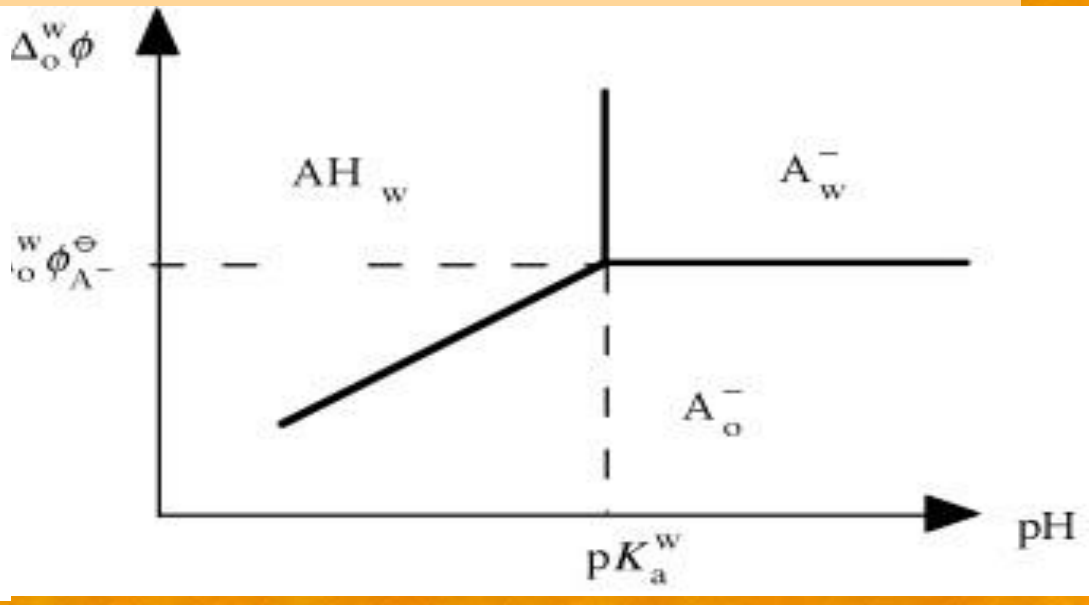
-we can determine the ionization constant in organic phase

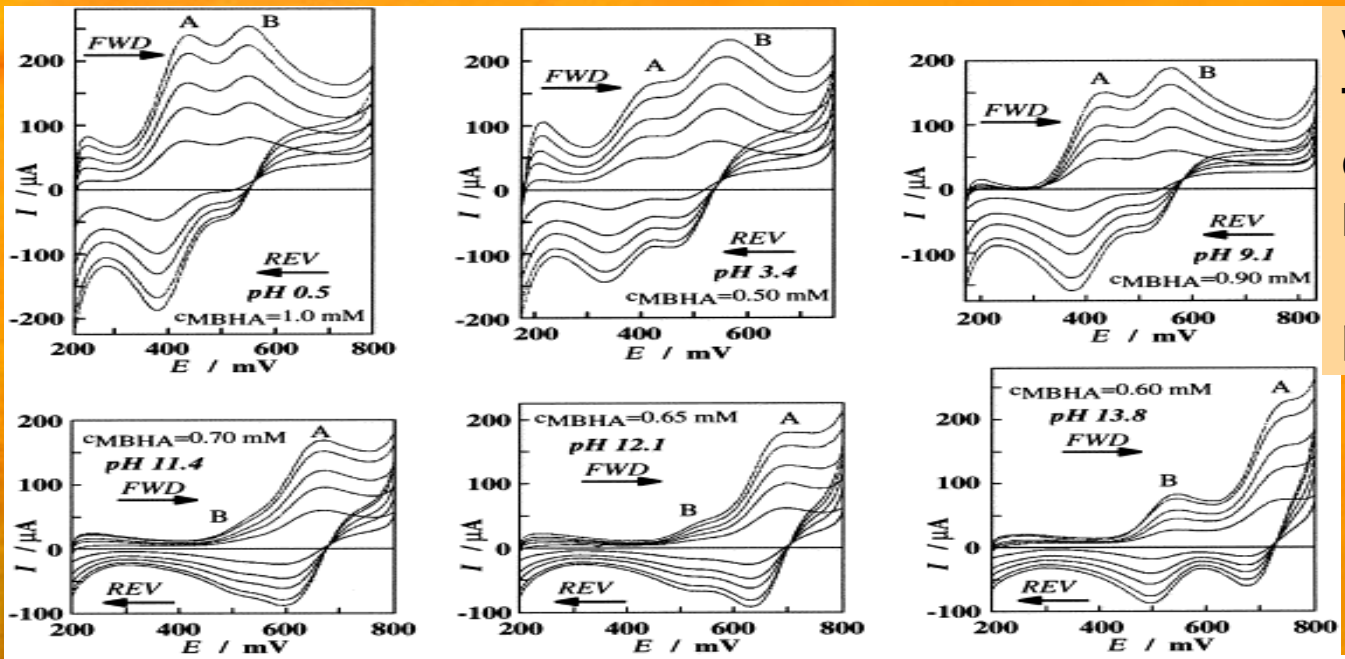
-we can use these data for QSPR and QSAR studies

-we can assess the potential efficiency of a given medicament

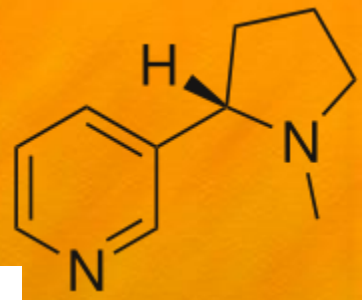
…



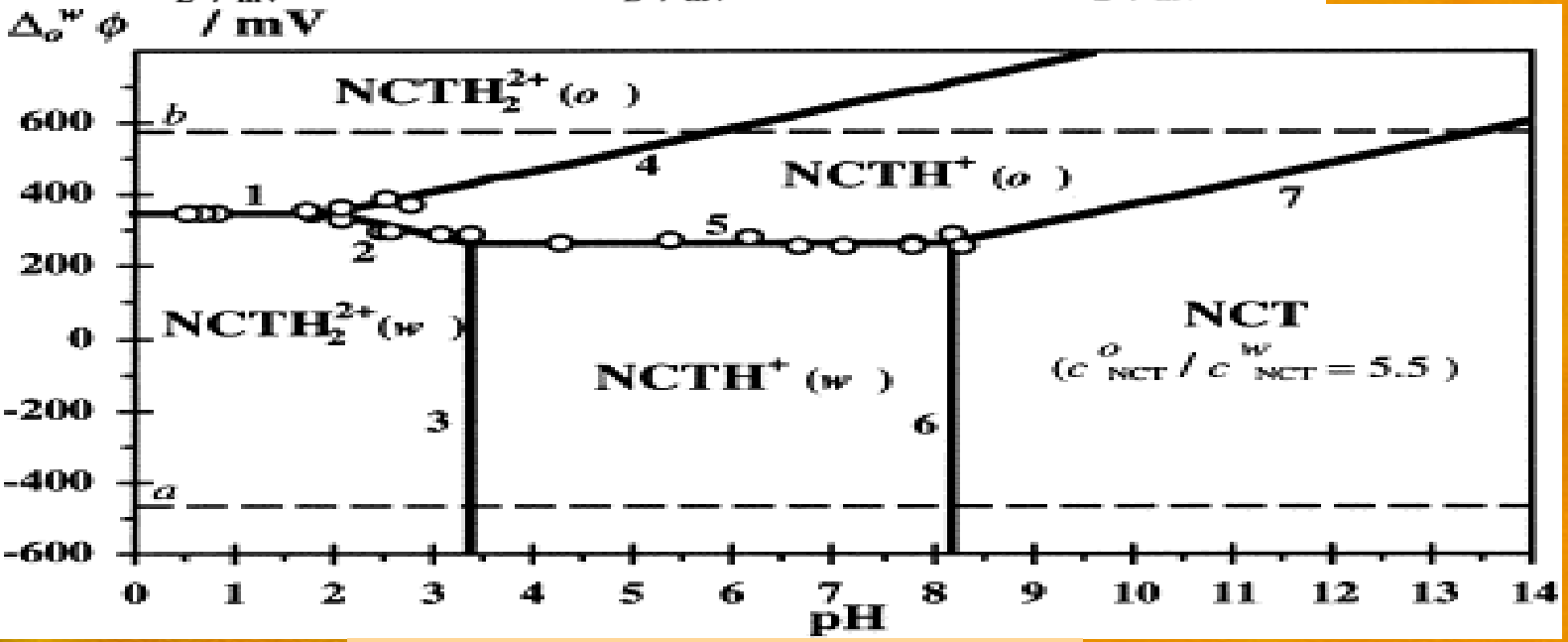




Voltammograms showing Transfer of NICOTINE in cationic form across the Interface of water and dichlorethan- pH dependence



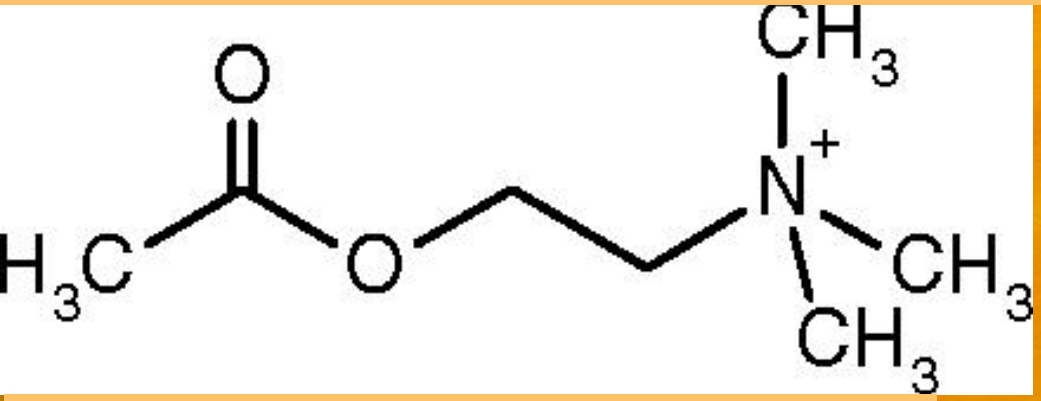
Structure of Nicotine



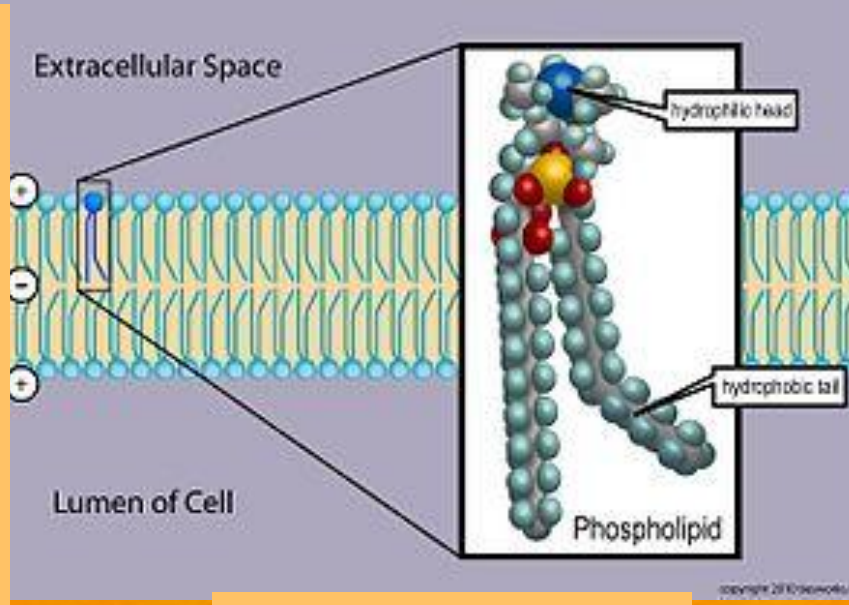
Partition diagram of NICOTINE

Another achievement of this technique is the possibility to study interactions between Important biomolecules and the Cell-membrane constituents!

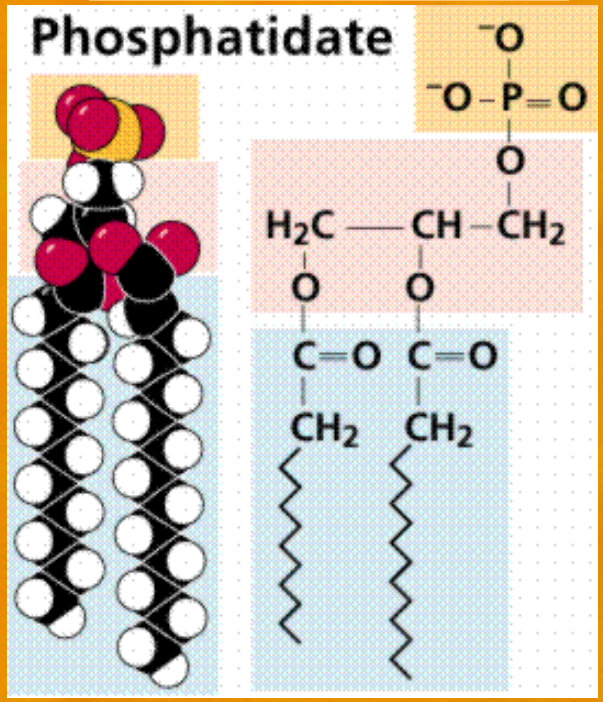
Example: how acetylcholine's transfer Is affected by phospholipids



Acetylcholine (Important neurotransmitter)



phospholipids



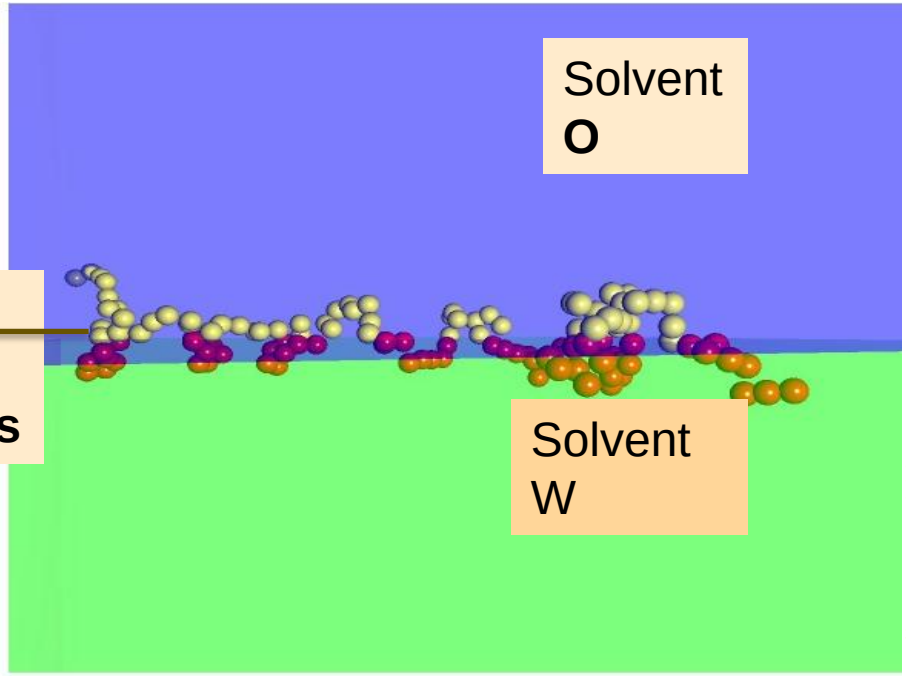
Electrochemical Study of Ion Transfer of Acetylcholine Across the Interface of Water and a Lipid-Modified 1,2-Dichloroethane

Rubin Gulaboski, Carlos M. Pereira,* M. Natália D. S. Cordeiro,‡ Ivan Bogeski,† Elisabete Ferreira, David Ribeiro, Mariana Chirea, and A. Fernando Silva

Departamento de Química, Faculdade de Ciências, Universidade do Porto, 4169-007 Porto, Portugal

Received: February 22, 2005; In Final Form: April 7, 2005

The ion transfer of acetylcholine (AcH^+) ions across the unmodified and phospholipid-modified water|1,2-dichloroethane (DCE) interface has been studied by means of square-wave and cyclic voltammetry, as well as by electrochemical impedance spectroscopy. After being transferred in the organic phase, the AcH^+ ions undergo chemical reactions with the phospholipids. The overall behavior of the experimental system studied in the presence of phospholipids has been compared with the theoretical results of an ECrev reaction. The kinetic parameters of the chemical interactions between AcH^+ and the phospholipids have been determined from the voltammetric and impedance measurements. Additional characterization of those interactions has been made by using the surface tension measurements.



Interface modified with **phospholipids**

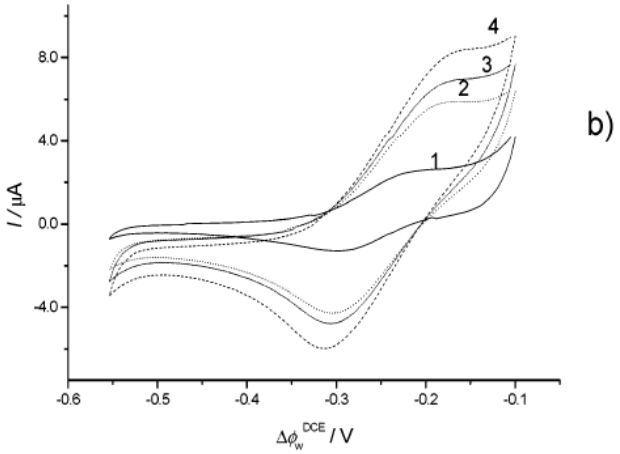


Figure 1. Square-wave (a) and cyclic (b) voltammograms showing the transfer of AcH^+ across the water|DCE interface. The experimental conditions were as follows: SW frequency $f = 8$ Hz, potential increment $dE = 1$ mV, SW amplitude $E_{sw} = 50$ mV, starting potential $E_s = -0.150$ V (for a) and scan rate v/mV $s^{-1} = 10$ (1), 25 (2), 50 (3), and 75 (4), and starting potential $E_s = -0.100$ V (for b). $c(AcH^+)_w = 0.2$ mM. Here and in all other figures where they appear, the subscripts "net", "f", and "b" stand for the net, forward, and backward components of the current, respectively.

With this technique we can reveal the mechanism of transfer of acetylcholine Across Biological membranes

Figure. Effect of increasing concentration of phospholipid at LL Interface to the recorded Voltammograms of acetylcholine

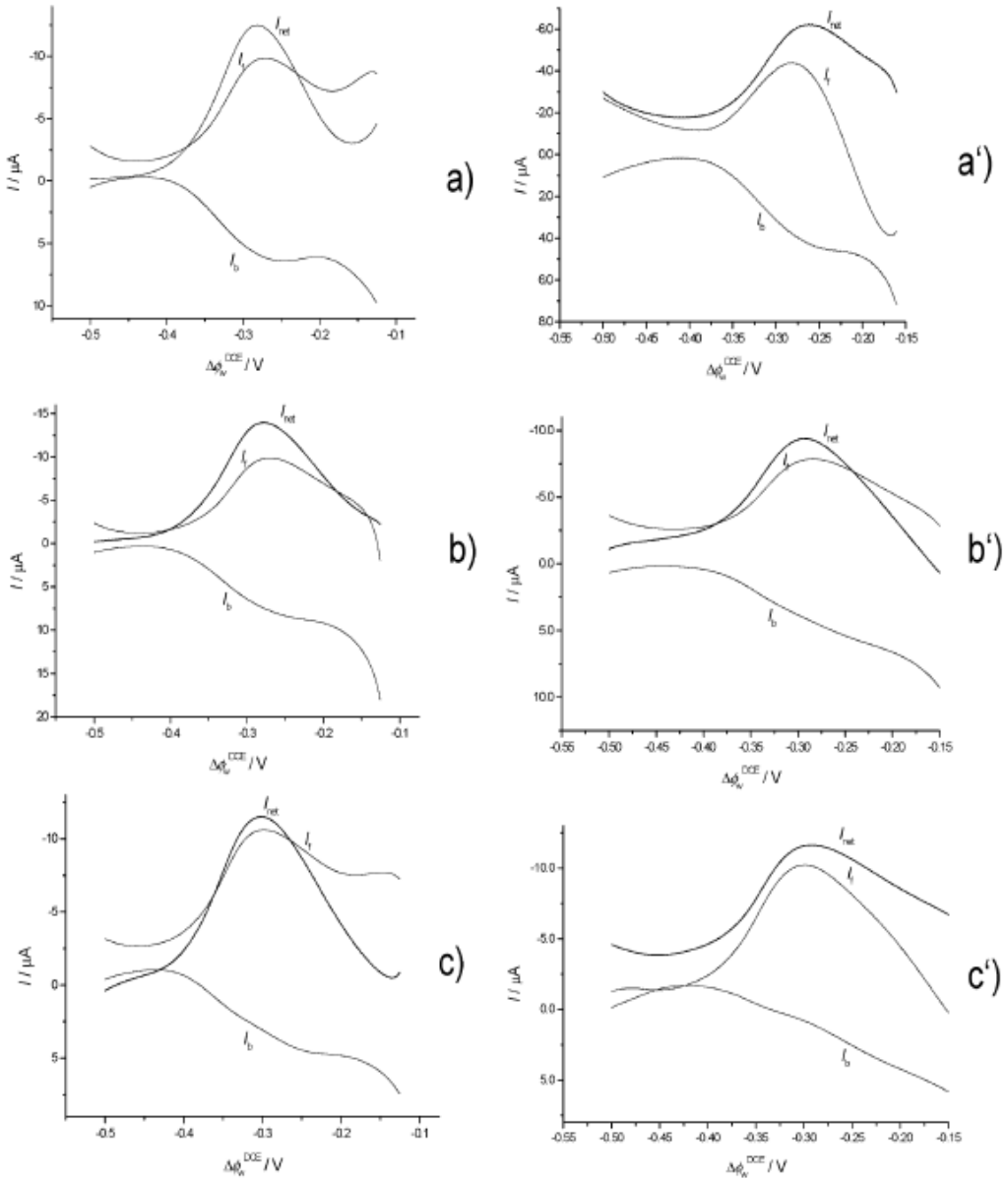


Figure 3. Square-wave voltammograms showing the effect of the DOPC to the shape of the SW current components. The concentration of DOPC was 0 μM (a), 10 μM (b), and 50 μM (c), while $c(AcH^+)_w = 0.5$ mM. Voltammograms (a′)−(c′) are showing the effect of the concentration of AcH^+ to the SW current components, in the presence of 30 μM DOPC in the organic phase. $c(AcH^+)_w$/mM = 0.2 (a′), 0.5 (b′), and 0.75 (c′). The other conditions are the same as those in Figure 1a.

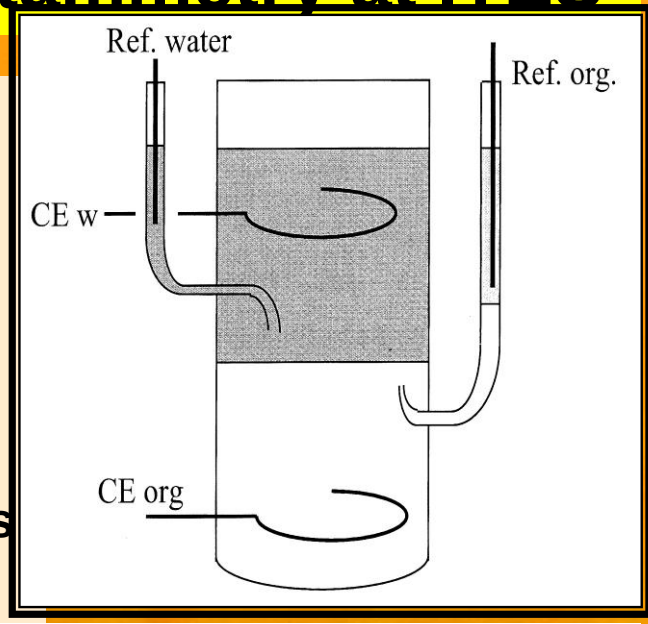
We found that phospholipids facilitate the transfer of acetylcholine across biological membranes, and we could determine the Kinetic and thermodynamic parameters of those interactions between Acetylcholine and the phospholipids

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/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

Gulaboski et al. J. Phys. Chem. B 109, 12549-12559

Limitations of the 4-Electrodes Voltammetry at ITES



-narrow potential window

-many ionizable compounds can not be studied with this technique

-no all organic solvents can be polarized

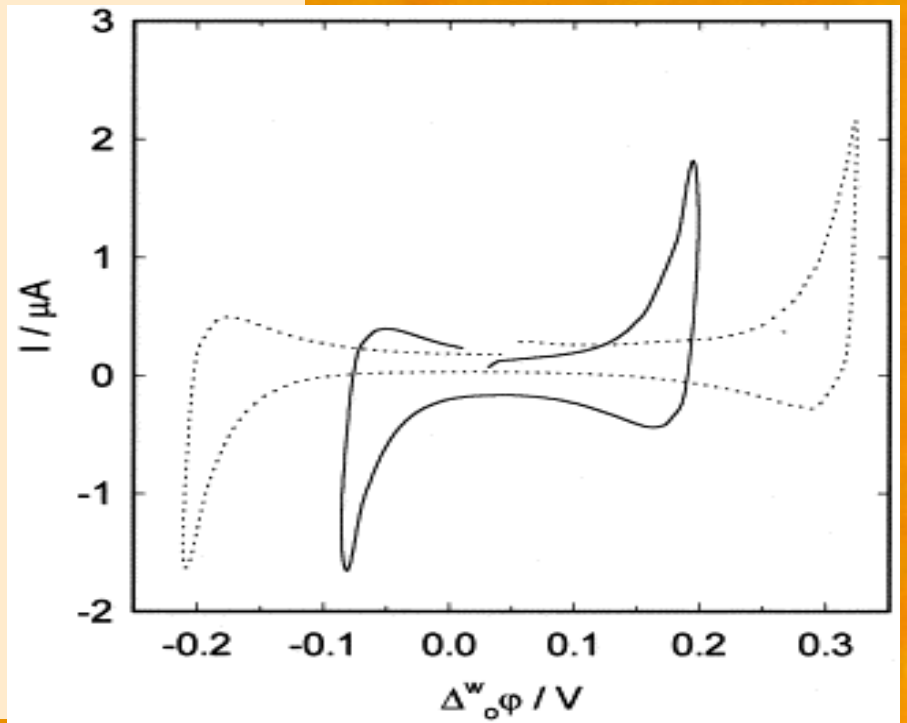
-limited access to some alkyl-chain containing solvents
LL interface water-octanol CAN NOT be Polarized!!!
(*n-octanol is used as reference solvent for partitioning experiments*!)

-it is quite difficult to tackle with the cell in ITES voltammetry measurements

-slow experiments

…solution to overcome these problems?

NEW TECHNIQUE HAS EMERGED called
THREE-PHASE ELECTRODE



Three-phase electrode approach

Scholz et all, *Electrochem. Commun*. *2*, **2000**, 112.
(**Awarded for „The Best Cited Paper“ in 2003**)

reference electrode

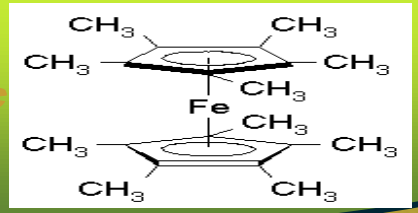
counter electrode

working electrode

three-phase junction

three-phase junction

$dmfc \rightleftharpoons dmfc^{+} + 1e^{-}$

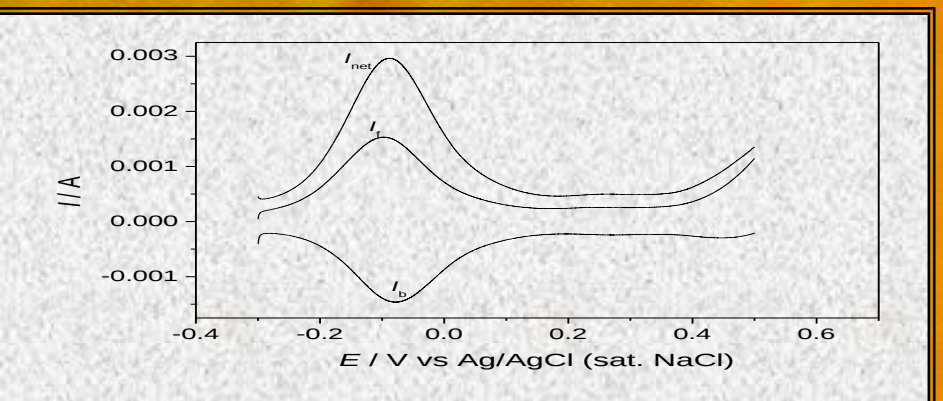


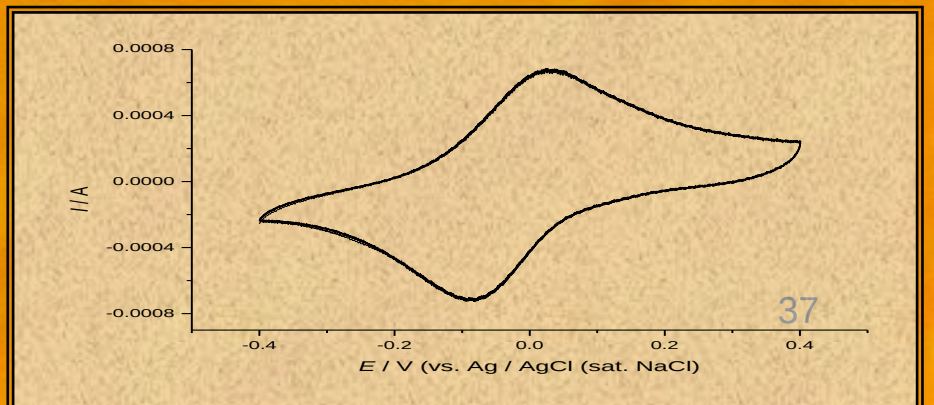
Organic

$X^{-}_{(o)}$

$X^{-}_{(aq)}$

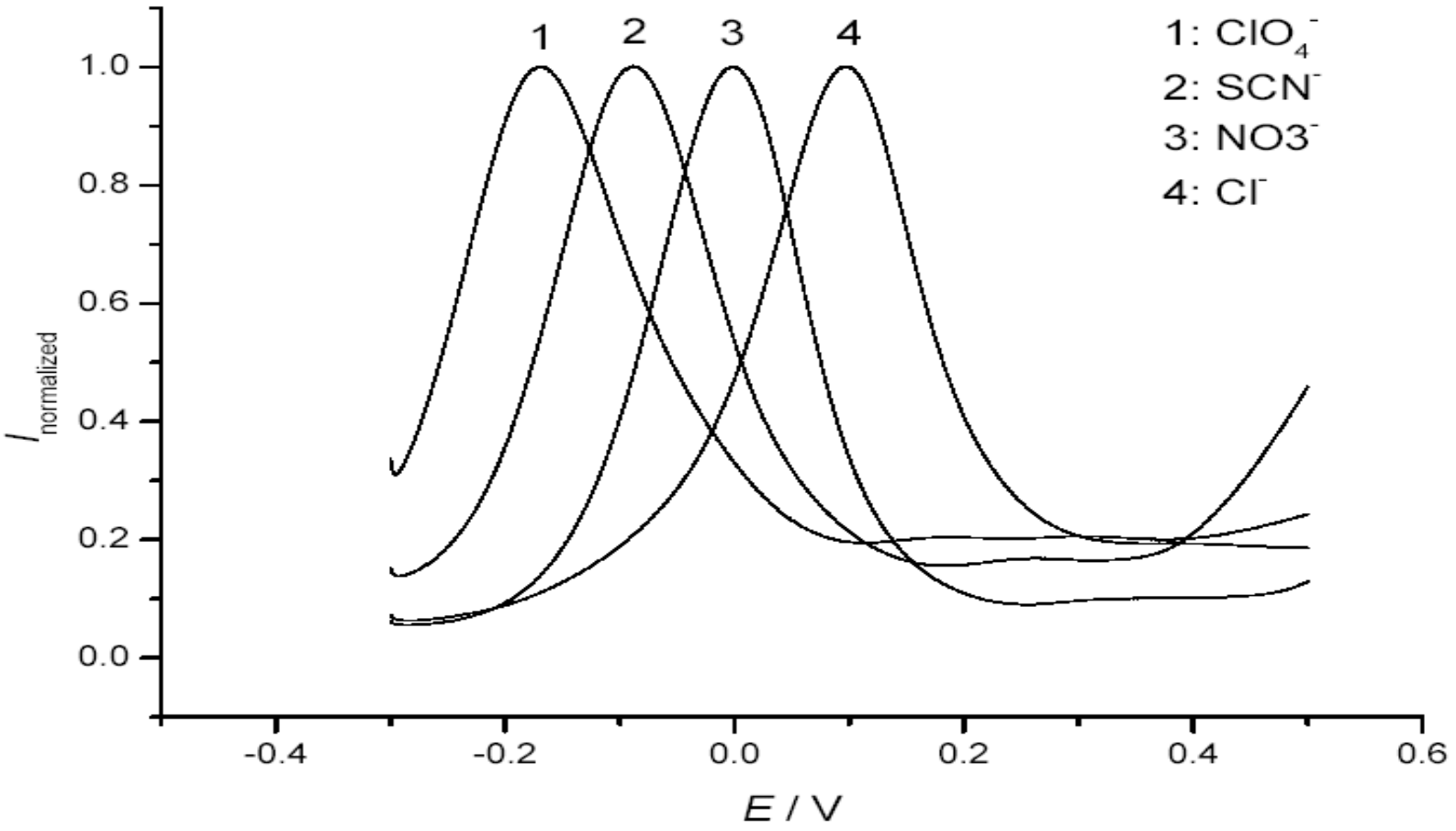
aqueous electrolyte **(Cat^{+}, X^{-})**



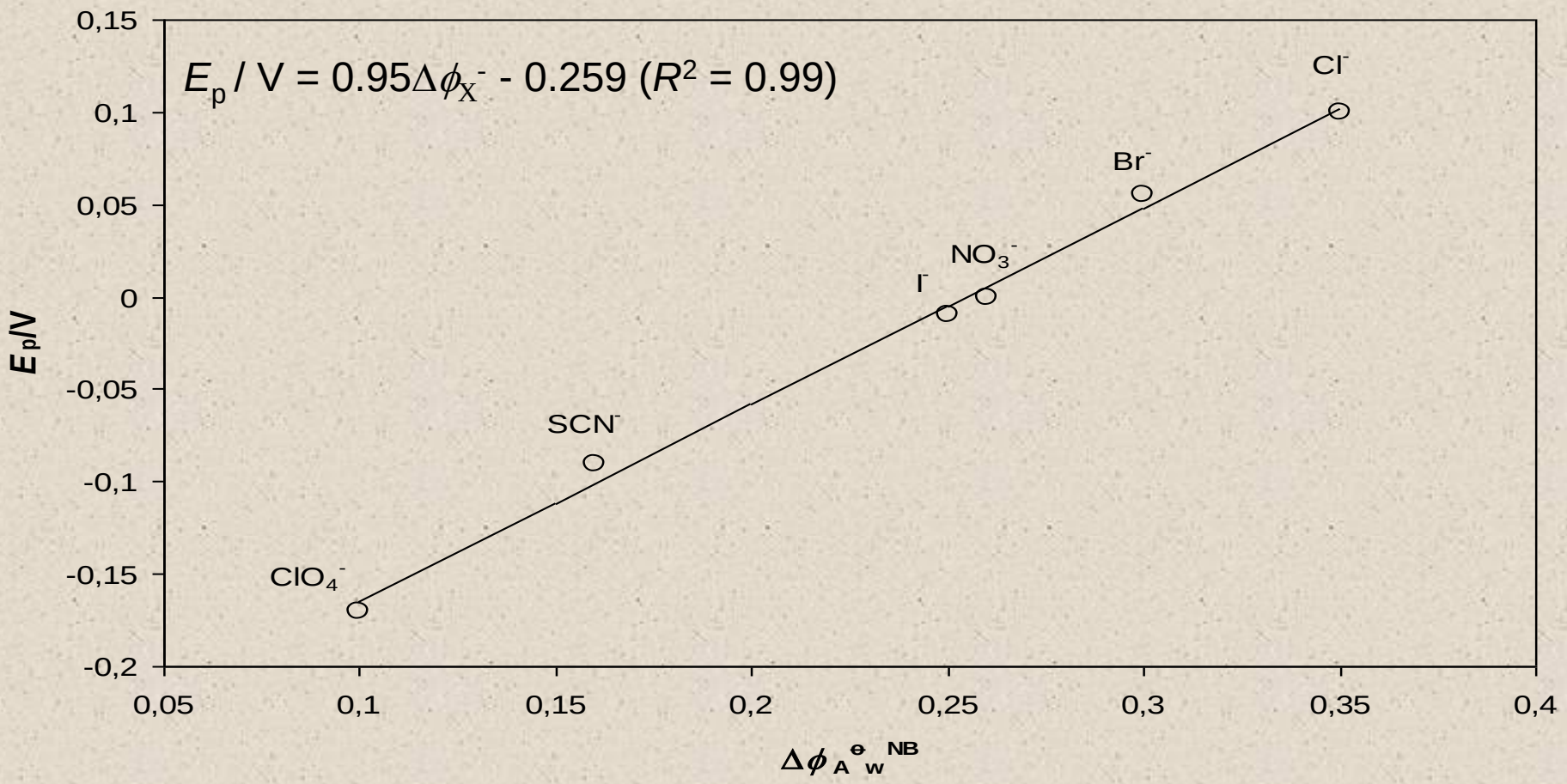


$$dmfc(o) + A^-(w) \Leftrightarrow dmfc^+(o) + A^-(o) + 1e^-$$

$$E_f = E^{\theta}_{dmfc^+/dmfc(o)} - \frac{RT}{F}\ln(c_{(A^-)w}) + \Delta^{o}_{w}\varphi^{\theta}_{A^-} + \frac{RT}{F}\ln(\frac{c_{0(dmfc)o}}{2})$$



Square-wave voltammograms representing the redox reaction of dmfc at WE|NB|w three-phase electrode followed by transfer of common inogranic anions across the w|nitrobenzene interface



Peak potentials of the net SW voltammetric responses of dmfc in NB as a function of **the standard potentials of transfer of anions across water | nitrobenzene interface**

$$E_f = E^{\theta}_{dmfc^+/dmfc(o)} - \frac{RT}{F}\ln(a_{(A^-)w}) + \Delta^o_w\varphi^{\theta}_{A^-} + \frac{RT}{F}\ln(\frac{a_{0(dmfc)o}}{2})$$

Applications of the Three-phase electrode for measuring THERMODYNAMICS of ion transfer at various water|oil phase interfaces

A. water|Nitrobenzene

B. water|*n*-octanol

C. water|Nitrophenyl octyl ether

D. water|D- and L-2-octanol

E. water|D- and L-Menthol

A. Transfer of Ions across the *water*|*nitrobenzene* Interface

- I. ***Inorganic anions***
- **II. *Organic anions-Monoanionic forms of*:**
  - **A. *Phenols***
  - **B. *Cyclo-, Mono, Di-*, and *halogen substituted carboxylic acids***
  - **C. *Amino acids***
  - **D. *Peptides***
  - ***E. Medicaments***

Š. Komorsky-Lovric, K. Riedl, **R. Gulaboski**, V. Mirceski and F. Scholz, *Langmuir* 18 (2002) 8000-8005,

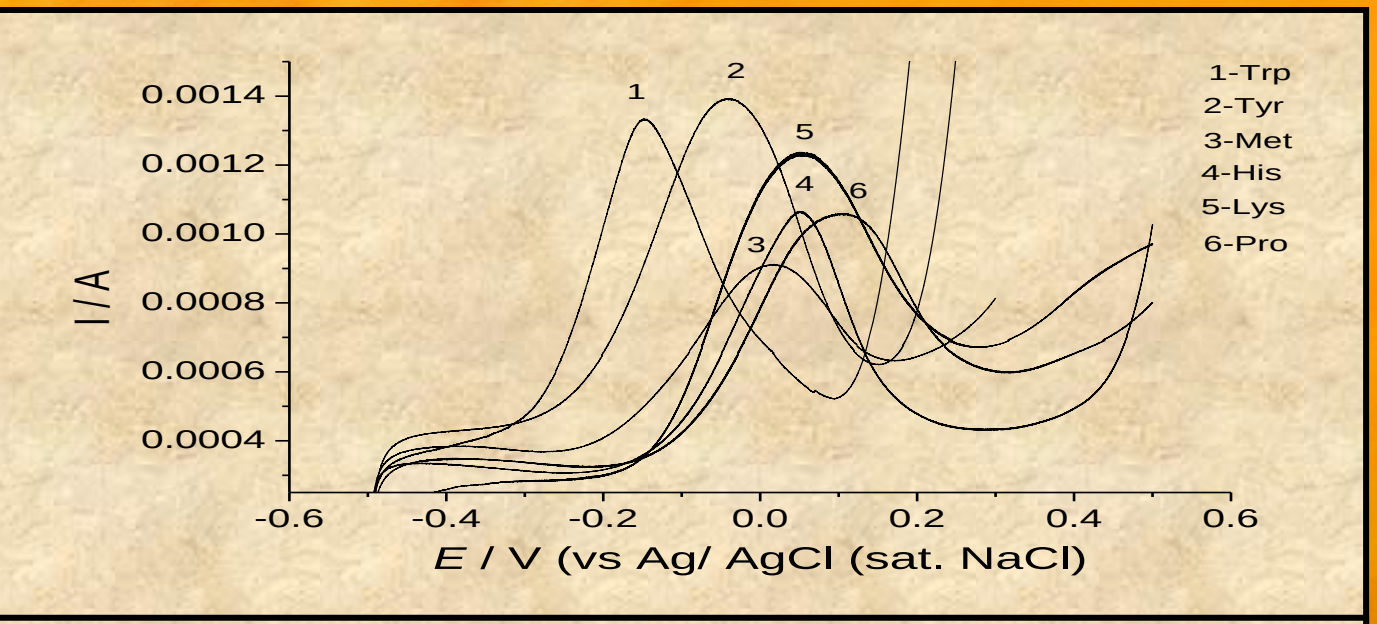
R. Gulaboski, K. Riedl, F. Scholz,*Phys. Chem. Chem. Phys*. 5 (2003) 1284-1289

R. Gulaboski, K. Caban, Z. Stojek, F. Scholz;*Electrochem. Commun*. 6 (2004) 215

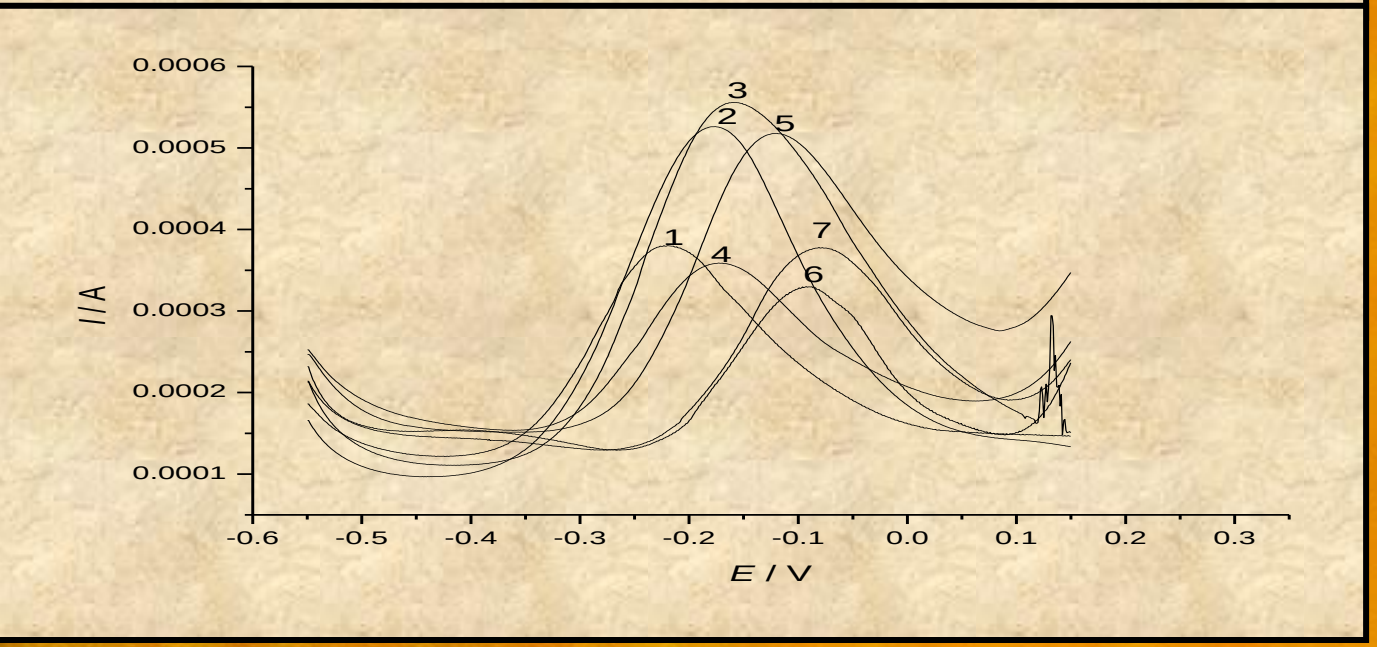
V. Mirceski, **R. Gulaboski**, F. Scholz;*Electrochem. Commun*. 4 (2002) 813-818

V. Mirceski, **R. Gulaboski**, F. Scholz,J. *Electroanal. Chem*. 566 (2004) 351

II. B-C. Standard Gibbs energies of transfer of monoanions of various amino acids and peptides

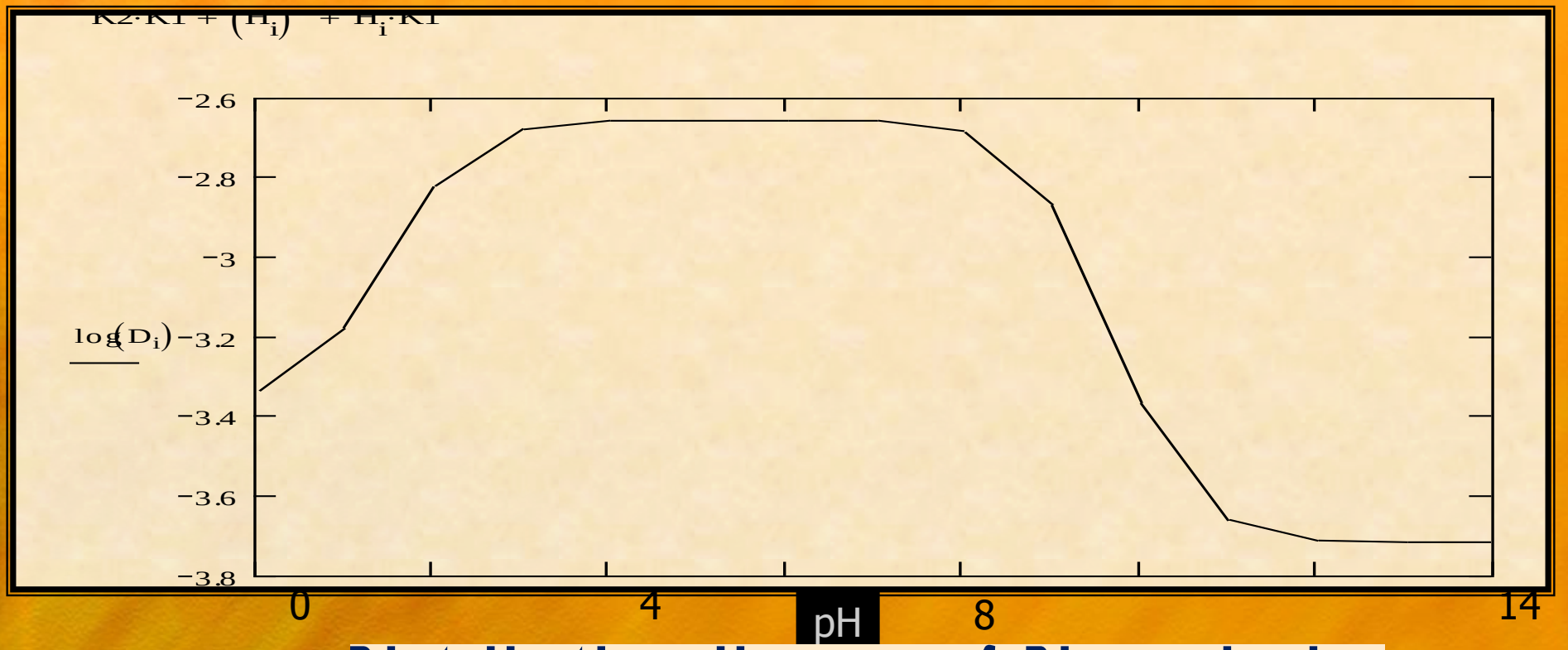


Transfer of monoanions of aminoacids



Transfer of monoanions of some Trp-X peptides

Data obtained by this methodology can be used for constructing Distribution Diagrams of many compounds



Distribution diagram of Phenyalanine

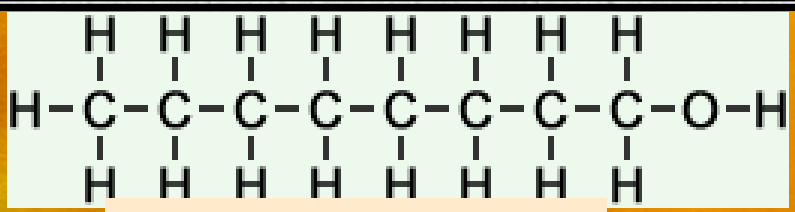
R. Gulaboski, V. Mirceski, F. Scholz;*Amino Acids* 24 (2003) 149–154

R. Gulaboski, F. Scholz, *J. Phys, Chem. B* 107 (2003) 5650-5657

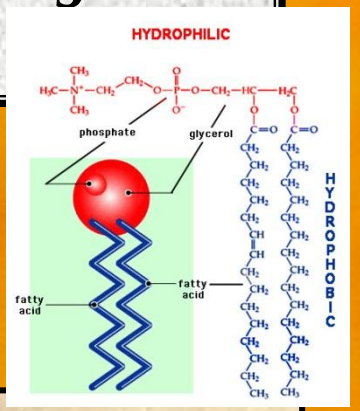
TRANSFER OF ANIONS ACROSS THE WATER|n-OCTANOL INTERFACE

- among the organic solvents used for studying the lipophilicity of solutes,
n-OCTANOL is certainly the most important one

- It is an ideal mimic for the biological membranes
(amphipathic nature similar to those of the lipides in biological membranes, long alkyl side chain and OH group)



Structure of n-octanol

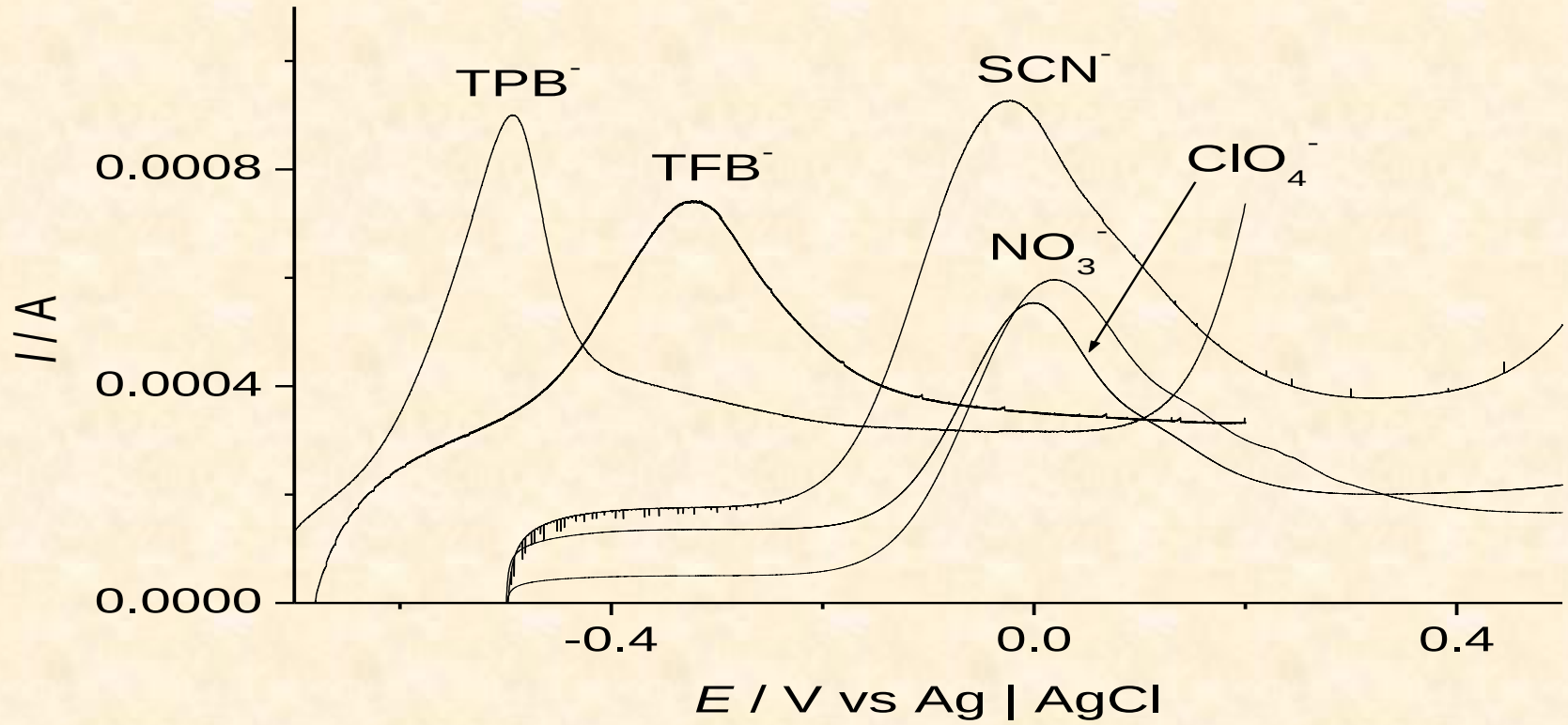


Structure of phospholipids

- **No data** in the literature about the standard ***ion potentials*** of transfer across the interface **water|*n*-octanol**:
Reason: ***non-polarizability*** of the interface water|n-Octanol

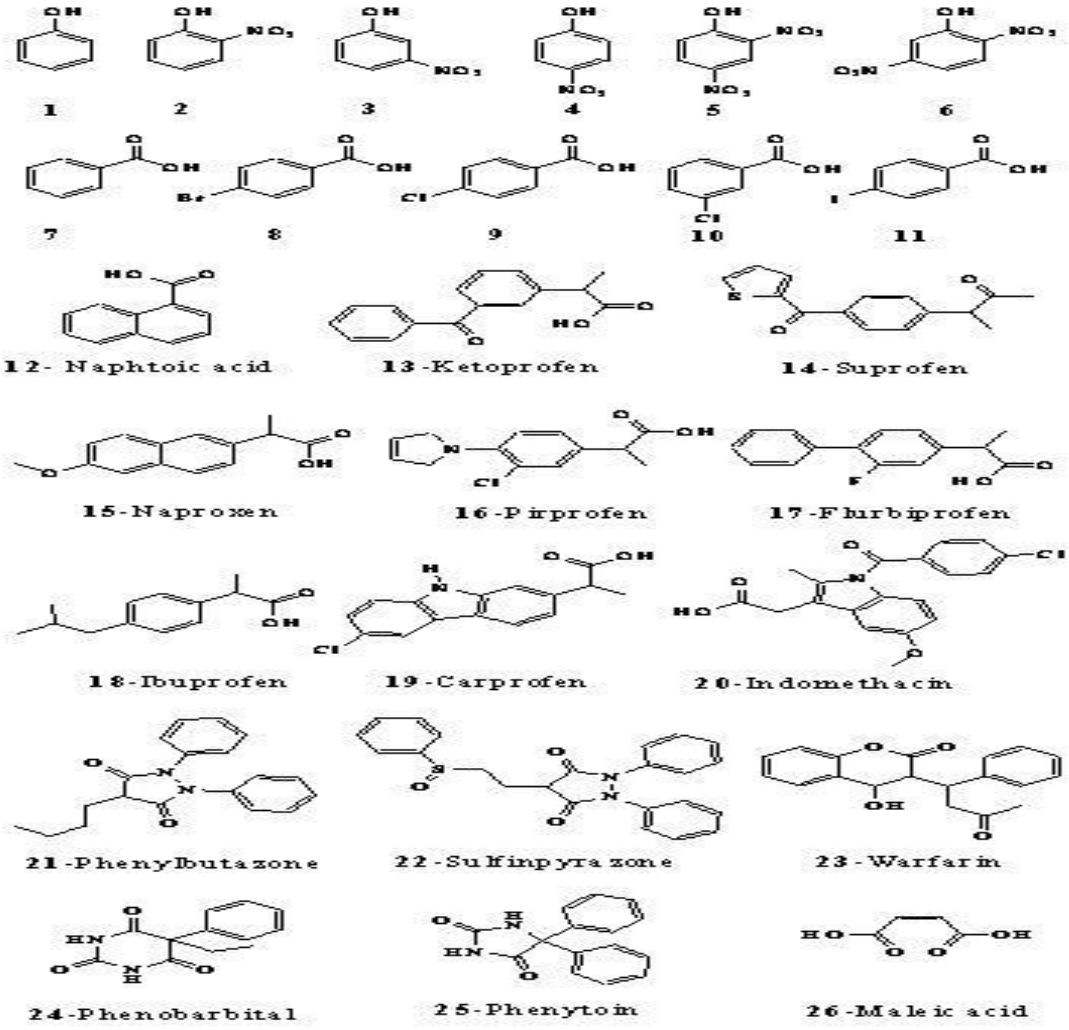
R. Gulaboski, V. Mirceski, F. Scholz;*Electrochem. Commun.* 4 (2002) 277-283
G. Bouchard, A. Galland, P.-A. Carrupt, **R. Gulaboski**, V. Mirceski,
F. Scholz, H. H. Girault, *Phys. Chem. Chem. Phys*. 5 (2003) 3748-3751

$$dmfc(n-oct) + A^-(w) \Leftrightarrow dmfc^+(n-oct) + A^-(n-oct) + 1e^-$$



Transfer of some common anions across water|***n*-octanol** interface

Transfer of anions of medicaments and model compounds across w|n-octanol interface

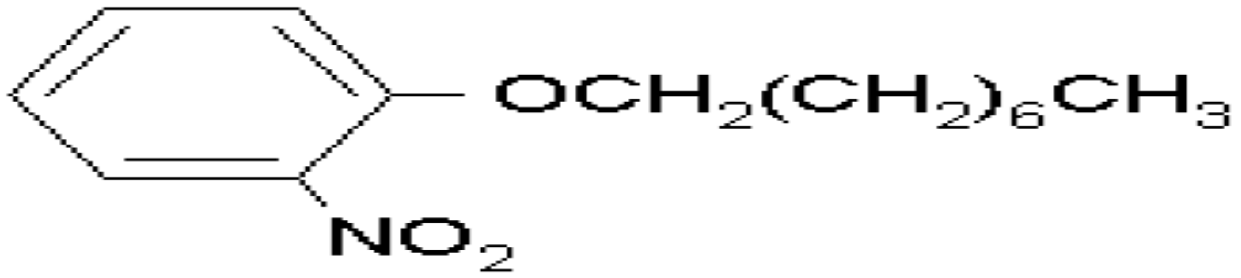


G. Bouchard, A. Galland, P.-A. Carrupt, B. Testa, R. Gulaboski, V. Mirčeski, F. Scholz, H. H. Girault

Comparison of solvation properties of Nitrophenyl octyl ether, Nitrobenzene, and n-Octanol

2-Nitrophenyl octyl ether-used as an alternative solvent for *n*-octanol

It *shares* the structures of
Nitrobenzene and *n*-octanol
Quite polar solvent, but hardly miscible with water!!!
Nice replacement for n-octanol



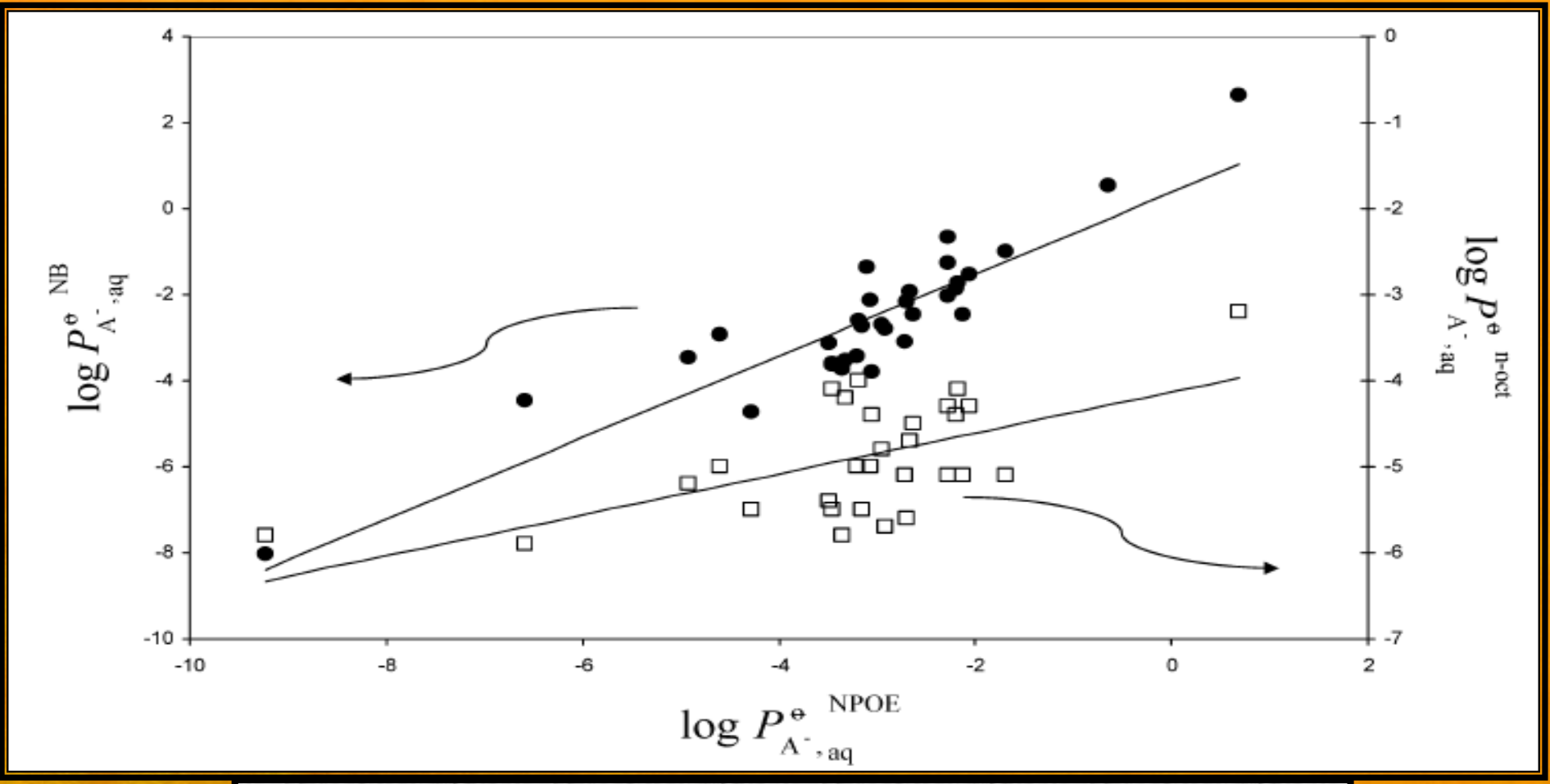
2-Nitrophenyl octyl ether

11. **R. Gulaboski**, A. Galland, G. Bouchard, K. Caban, A. Kretschmer, P.-A. Carrupt, Z. Stojek, H. H. Girault, F. Scholz,*J. Phys. Chem. B*, 108 (2004) 4565

Table 2 Standard Gibbs energies of transfer and partition coefficients of the studied anions.

n°	Compound	$\Delta G_{tr,A}^{0,w\rightarrow NB}$ a)	$\Delta G_{tr,A}^{0,w\rightarrow NPOE}$ a)	$\Delta G_{tr,A}^{0,w\rightarrow OCT}$ a)b)	log $P_{NB}^{0,A}$	log $P_{NPOE}^{0,A}$	log $P_{OCT}^{0,A}$ b)	r (Å)c)
1	Phenol	20.45	19.50	23.13	-3.62	-3.46	-4.10	2.78
2	2-Nitrophenol	14.60	18.00	22.56	-2.59	-3.19	-4.00	2.98
3	3-Nitrophenol	20.00	18.75	23.70	-3.54	-3.32	-4.20	2.98
4	4-Nitrophenol	21.48	17.20	24.82	-3.81	-3.05	-4.40	2.98
5	2,4-Dinitrophenol	8.70	11.62	24.25	-1.54	-2.06	-4.30	3.15
6	2,5-Dinitrophenol	14.00	14.85	25.40	-2.48	-2.63	-4.50	3.15
7	Benzoic acid	21.00	18.95	32.72	-3.72	-3.36	-5.80	2.97
8	4-Bromobenzoic acid	12.00	17.32	28.20	-2.13	-3.07	-5.00	3.15
9	4-Chlorobenzoic acid	12.25	15.23	31.59	-2.17	-2.70	-5.60	3.09
10	3-Chlorobenzoic acid	15.25	16.65	27.08	-2.70	-2.95	-4.80	3.09
11	4-Iodobenzoic acid	14.00	12.00	28.77	-2.48	-2.13	-5.10	3.21
12	Naphtoic acid	15.50	17.80	31.05	-2.74	-3.15	-5.50	3.77
13	Ketoprofen	19.33	18.05	28.20	-3.42	-3.20	-5.00	3.84
14	Suprofen	15.80	16.47	32.15	-2.80	-2.92	-5.70	3.79
15	Naproxen	11.50	12.86	28.77	-2.04	-2.28	-5.10	3.70
16	Pirprofen	5.65	9.55	28.75	-1.00	-1.69	-5.10	3.76
17	Flurbiprofen	10.50	12.35	24.80	-1.86	-2.19	-4.40	3.75
18	Ibuprofen	17.40	15.34	28.77	-3.08	-2.72	-5.10	3.59
19	Carprofen	-14.80	-3.85	18.05	2.62	0.68	-3.20	3.82
20	Indomethacin	11.00	15.05	26.50	-1.95	-2.67	-4.70	4.06
21	Phenylbutazone	3.70	12.85	24.25	-0.65	-2.28	-4.30	4.13
22	Sulfinpyrazone	7.10	12.85	24.25	-1.26	-2.28	-4.30	4.40
23	Warfarine	9.80	12.30	23.13	-1.74	-2.18	-4.10	4.05
24	Phenobarbital	26.75	24.10	31.02	-4.74	-4.27	-5.50	3.64
25	Phenytoine	17.70	19.65	30.45	-3.14	-3.48	-5.40	3.78
26	Maleic acid	20.30	19.50	31.02	-3.60	-3.46	-5.50	2.75
27	Picric acid	-3.00	3.65	n.m.d)	0.53	-0.65	n.m.b)	3.28

a) in kJ.mol^{-1} b) taken from reference [35] c) van der Waals radius of the ion, d) non measured



Comparison between partition coefficients in w|NB and w|NPOE, and w|*n*-oct and w|NPOE

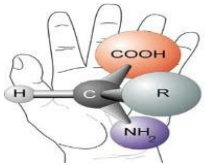
F. Scholz, **R. Gulaboski**, *ChemPhysChem* 2005, 6, 16–28 (**Review**)

3. Quantification of the enantiomeric anion transfer energies across water|chiral liquid interface

graphite electrode

e^-

chiral solvent

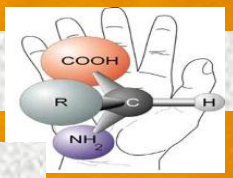


$dmfc^+$

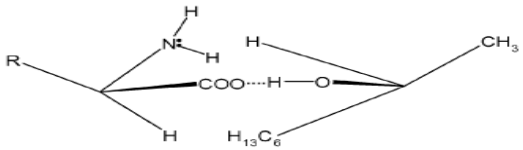
$chiral^-_{(org)}$

aqueous electrolyte (Cat+, chiral-)

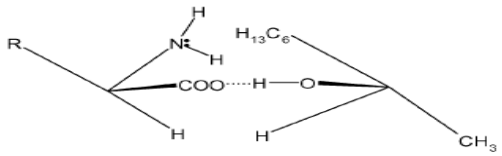
$chiral^-_{(aq)}$



(Racemic mixtures can be separated)



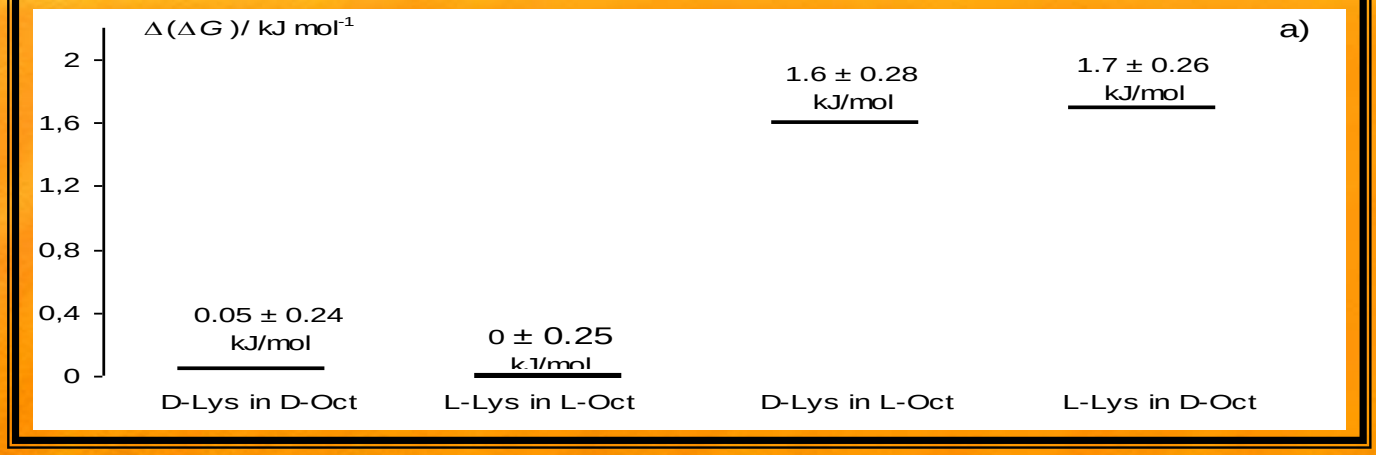
D-ion/D-solvent

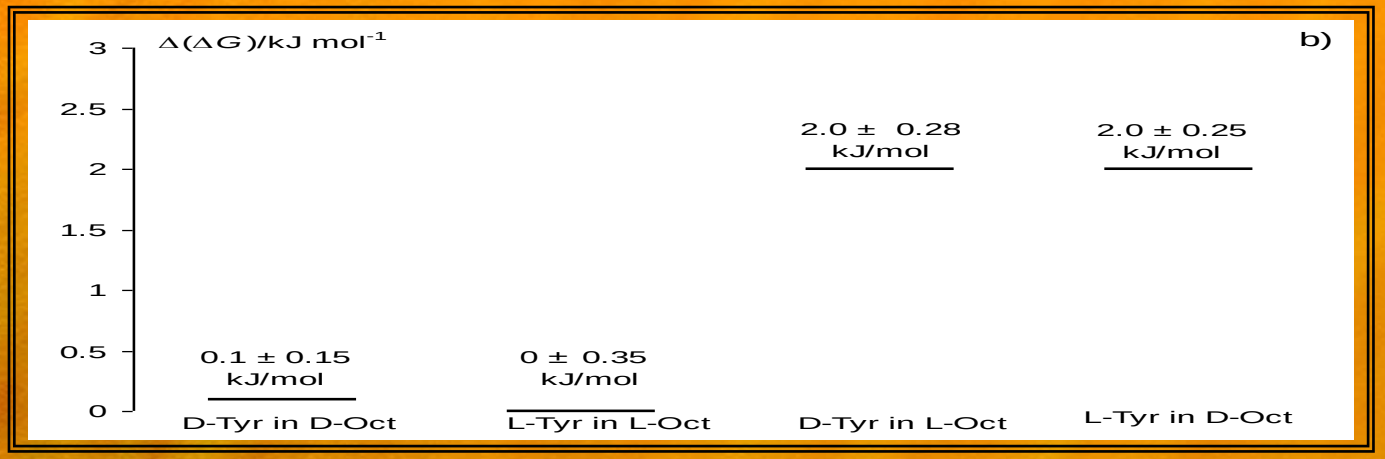


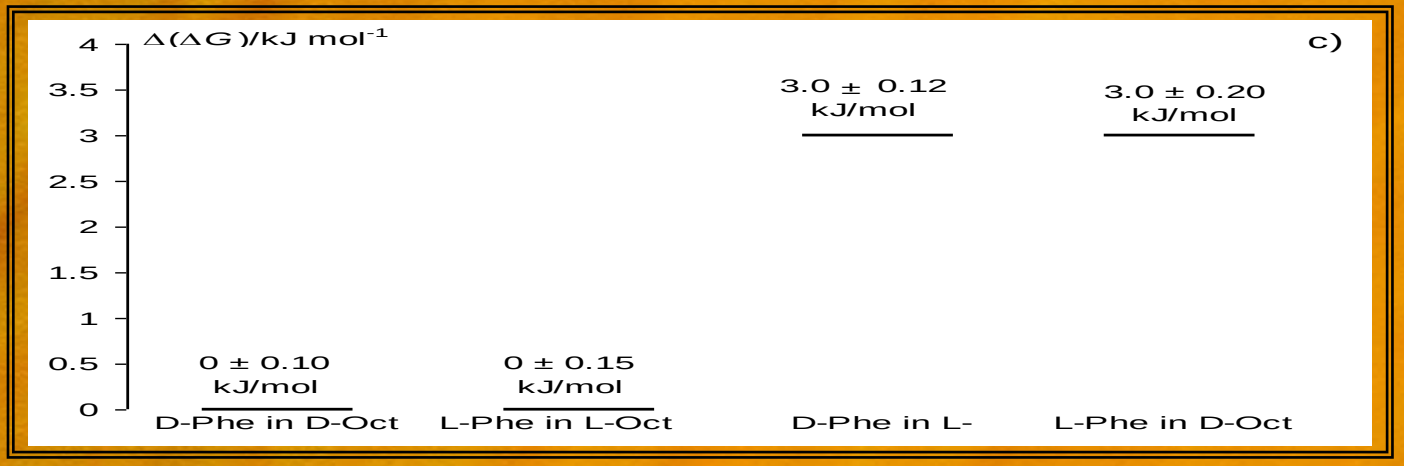
D-ion/L-solvent

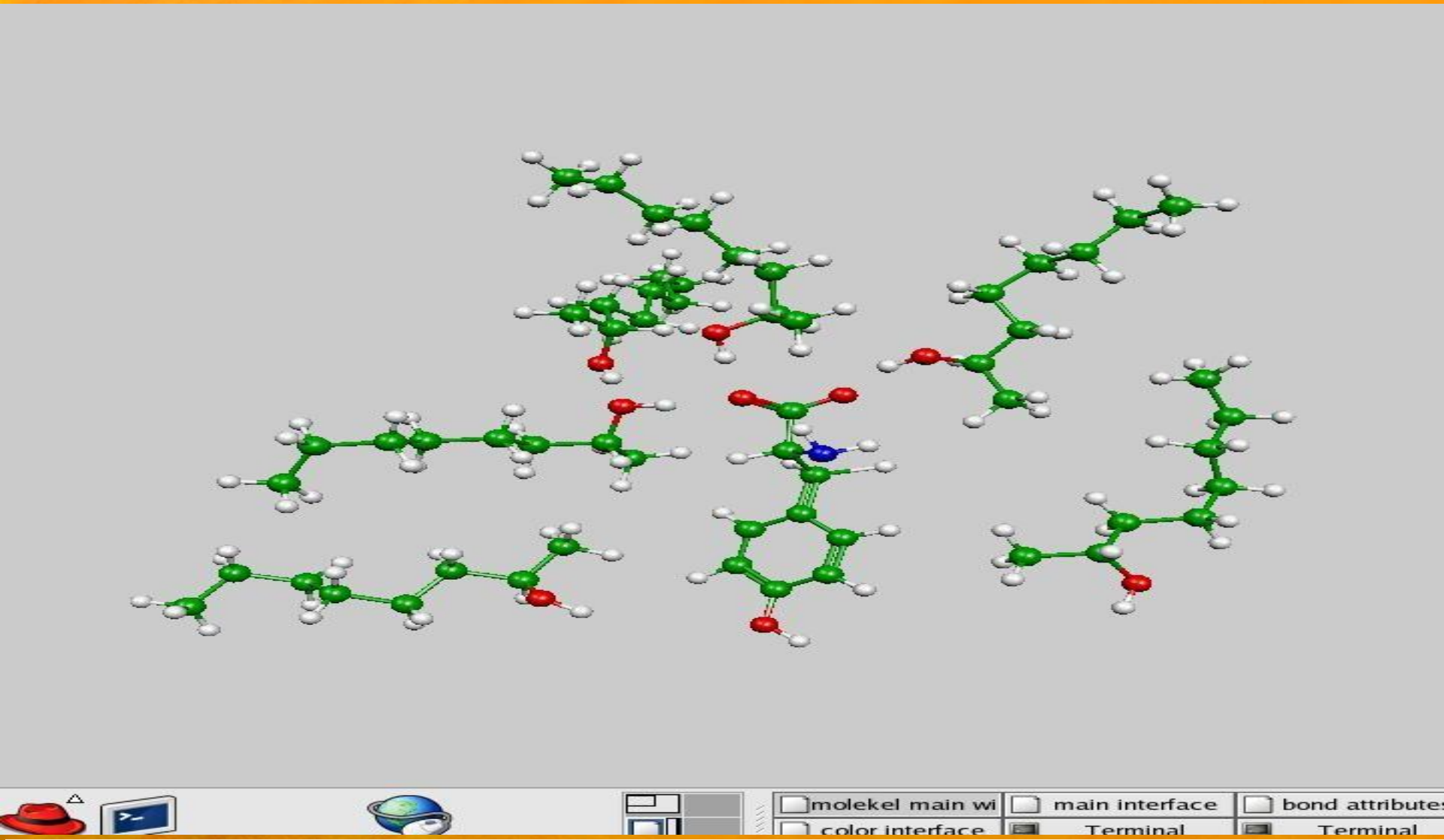
F. Scholz, **R. Gulaboski**, *Faraday Discuss*., 2005, 129, 169–177

F. Scholz, **R. Gulaboski**, V. Mirceski, P. Langer;*Electrochem. Commun*. 4 (2002) 659-662

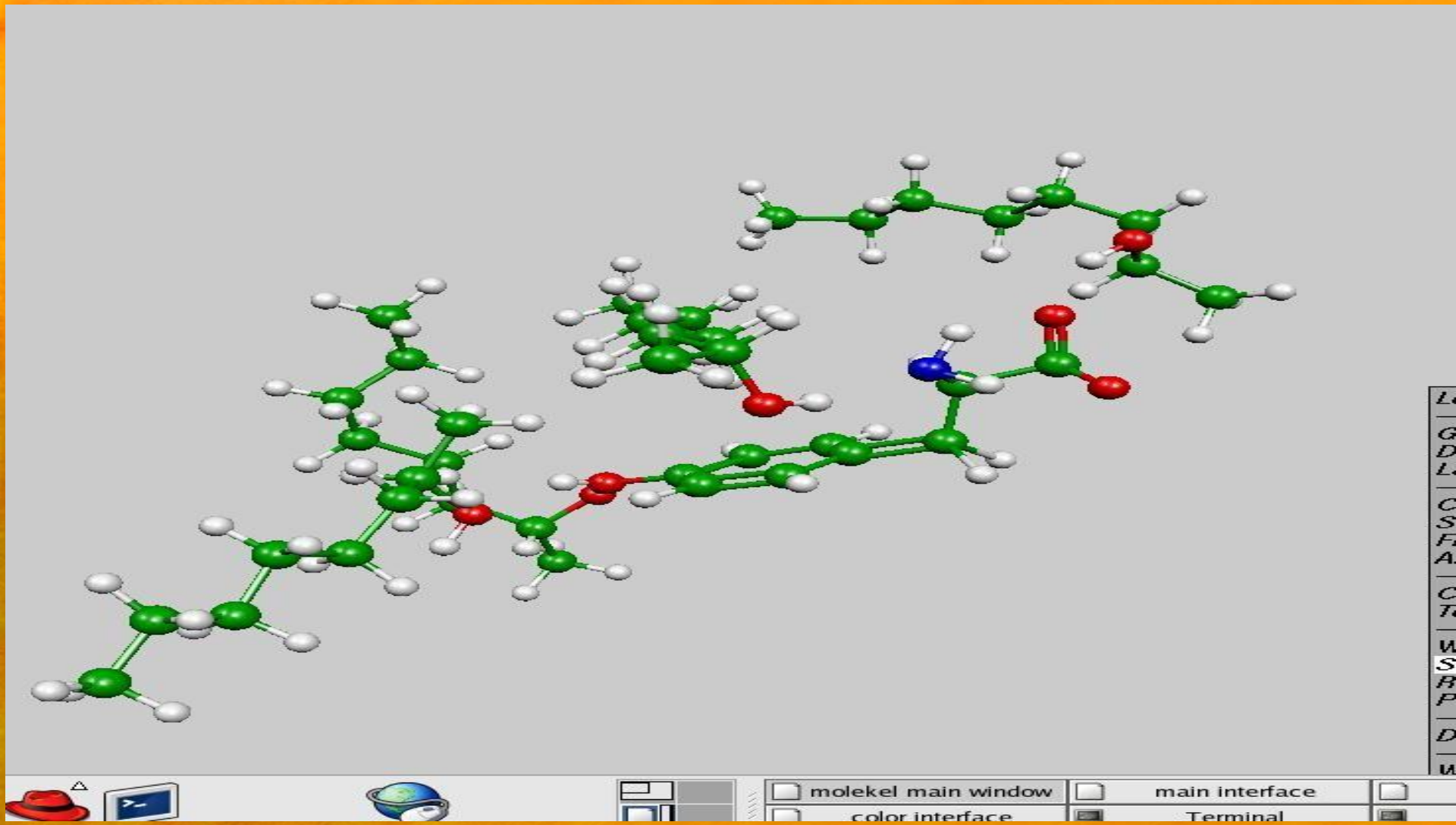

Δ(ΔG)/ kJ mol-1
a)
2
1,6
1,2
0,8
0,4
0
0.05 ± 0.24 kJ/mol
0 ± 0.25 kJ/mol
1.6 ± 0.28 kJ/mol
1.7 ± 0.26 kJ/mol
D-Lys in D-Oct
L-Lys in L-Oct
D-Lys in L-Oct
L-Lys in D-Oct


Δ(ΔG)/kJ mol-1
b)
3
2.5
2
1.5
1
0.5
0
0.1 ± 0.15 kJ/mol
0 ± 0.35 kJ/mol
2.0 ± 0.28 kJ/mol
2.0 ± 0.25 kJ/mol
D-Tyr in D-Oct
L-Tyr in L-Oct
D-Tyr in L-Oct
L-Tyr in D-Oct

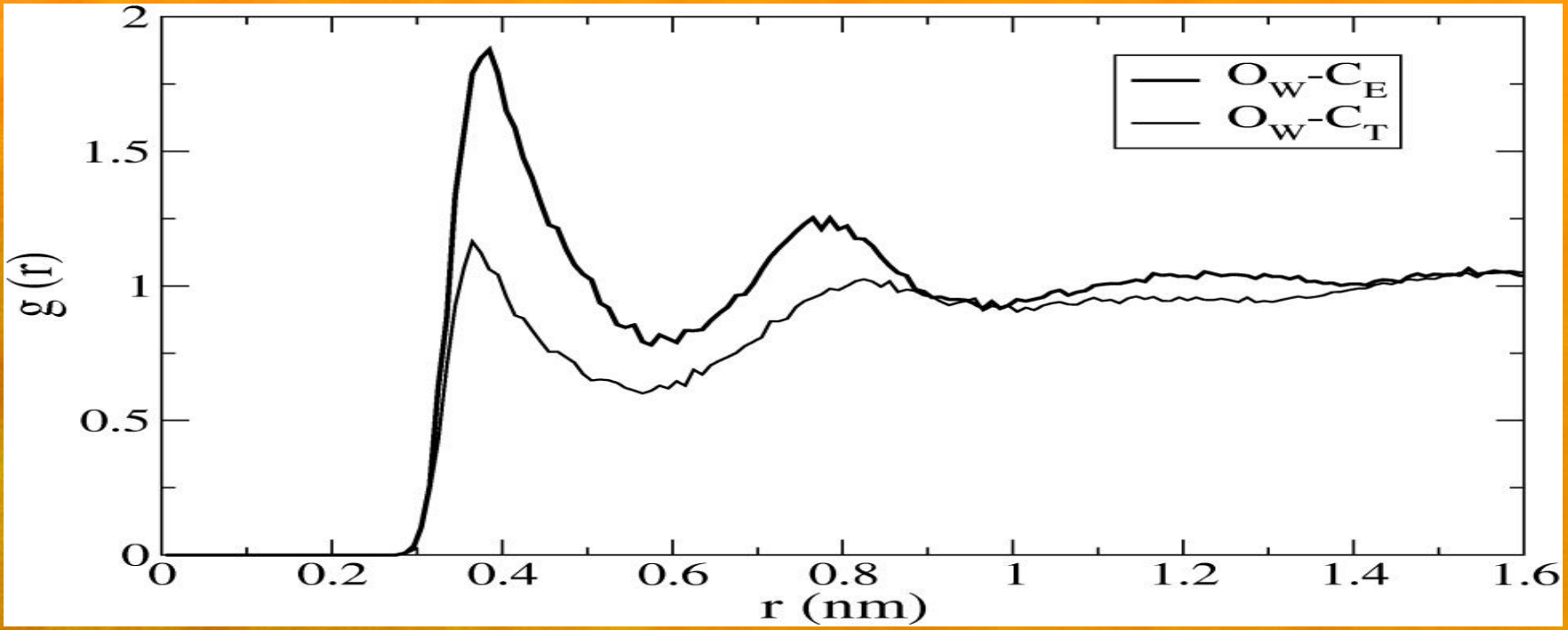

Δ(ΔG)/kJ mol-1
c)
4
3.5
3
2.5
2
1.5
1
0.5
0
0 ± 0.10 kJ/mol
0 ± 0.15 kJ/mol
3.0 ± 0.12 kJ/mol
3.0 ± 0.20 kJ/mol
D-Phe in D-Oct
L-Phe in L-Oct
D-Phe in L-
L-Phe in D-Oct



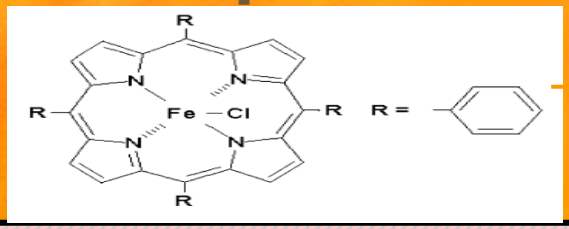
Snapshot from Molecular Dynamic Simulations of L-Tyrosine dissolved in L-octanol



Snapshot from Molecular Dynamic Simulations of L-Tyrosine dissolved in D-octanol


O_W-C_E
O_W-C_T
g(r)
r (nm)
0
0.5
1
1.5
2
0.2
0.4
0.6
0.8
1.2
1.4
1.6

Transfer of cations across the water|Nitrobenzene interface



Fe(III)TPhP

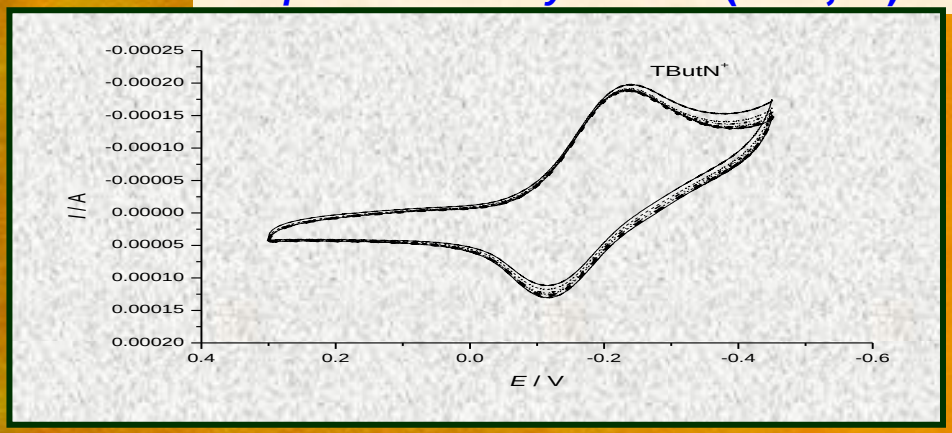
graphite electrode

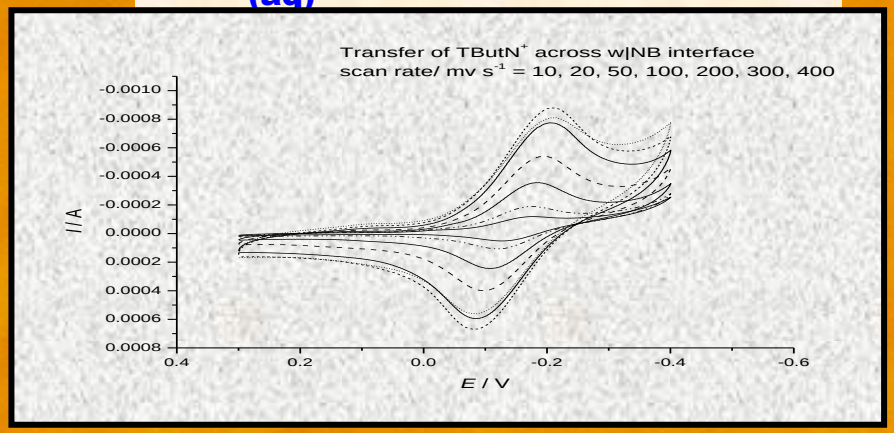
NB **Fe(III)TPhP +e-** ⟷ **Fe(II)TPhP-**

Cat^+

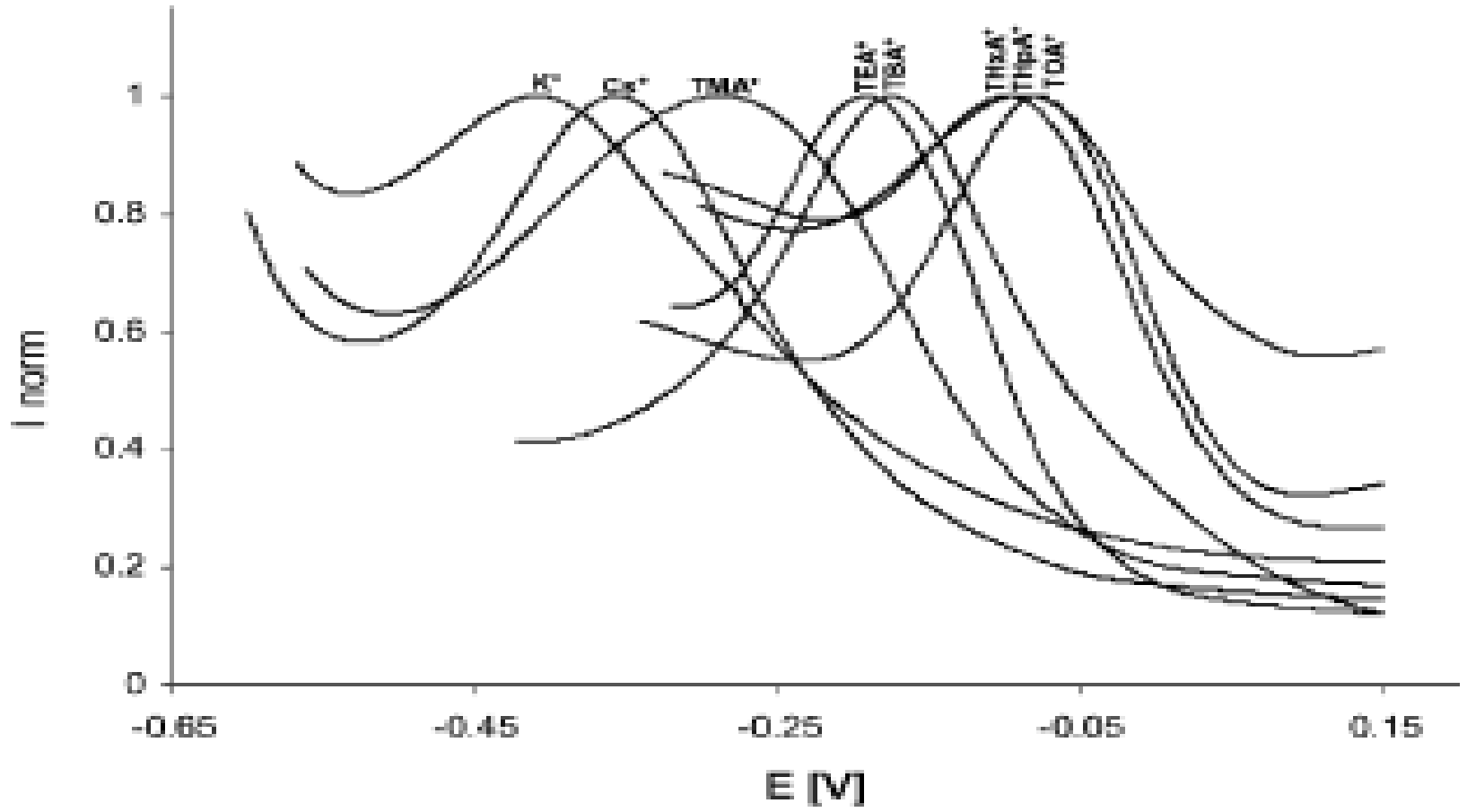
aqueous electrolyte **(Cat^+, A^-)**

$Cat^+_{(aq)}$



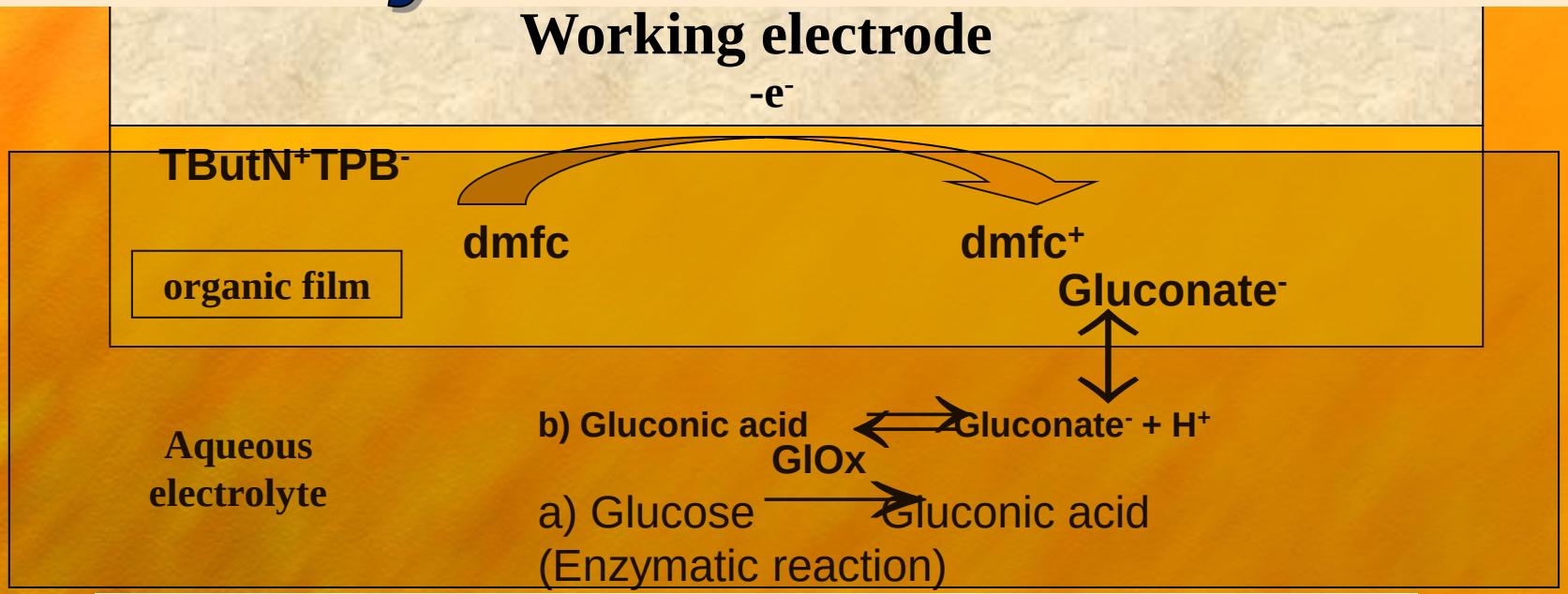


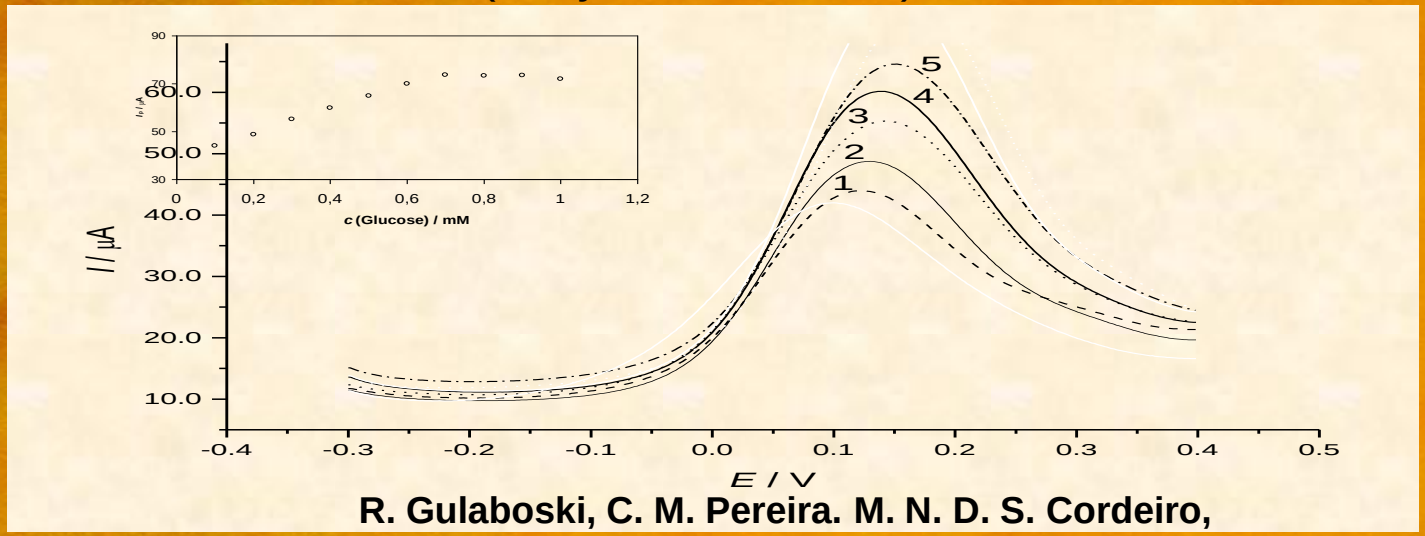
F. Scholz, **R. Gulaboski**, K. Caban,*Electrochem. Commun*. 5 (2003) 929



SW voltammograms showing transfer of some monocations across the w|nitrobenzene interface

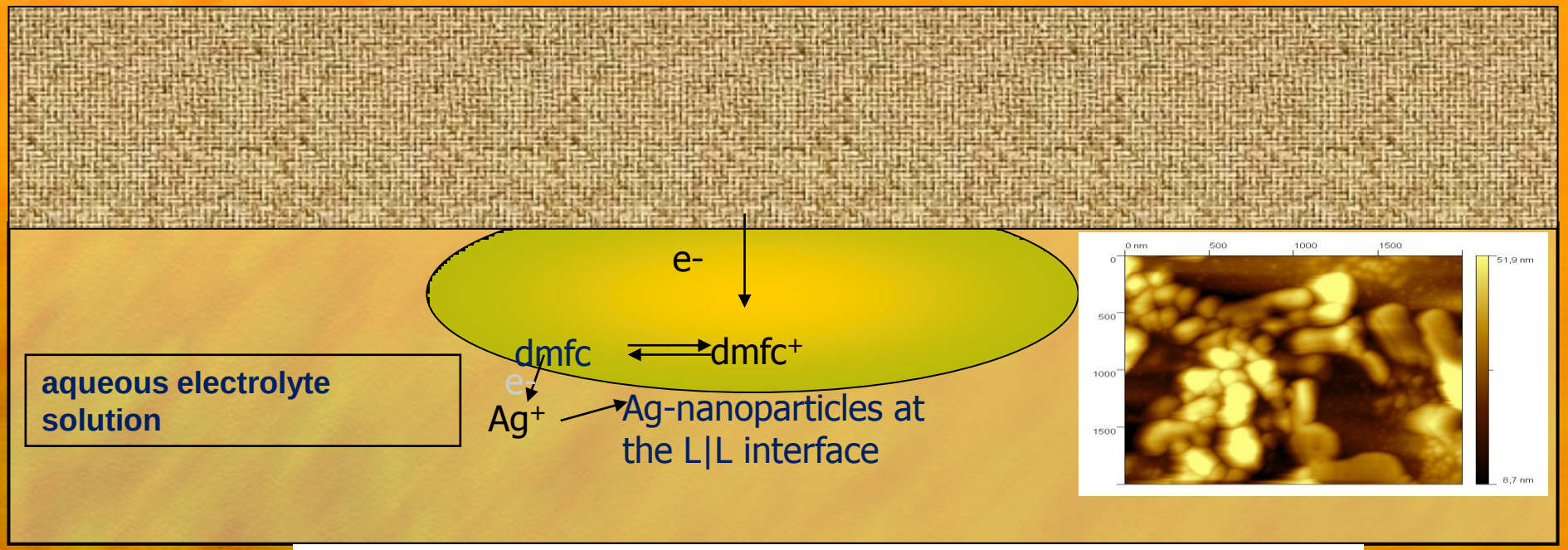
Three-phase electrode-as a tool for making Enzymatic bio-sensors

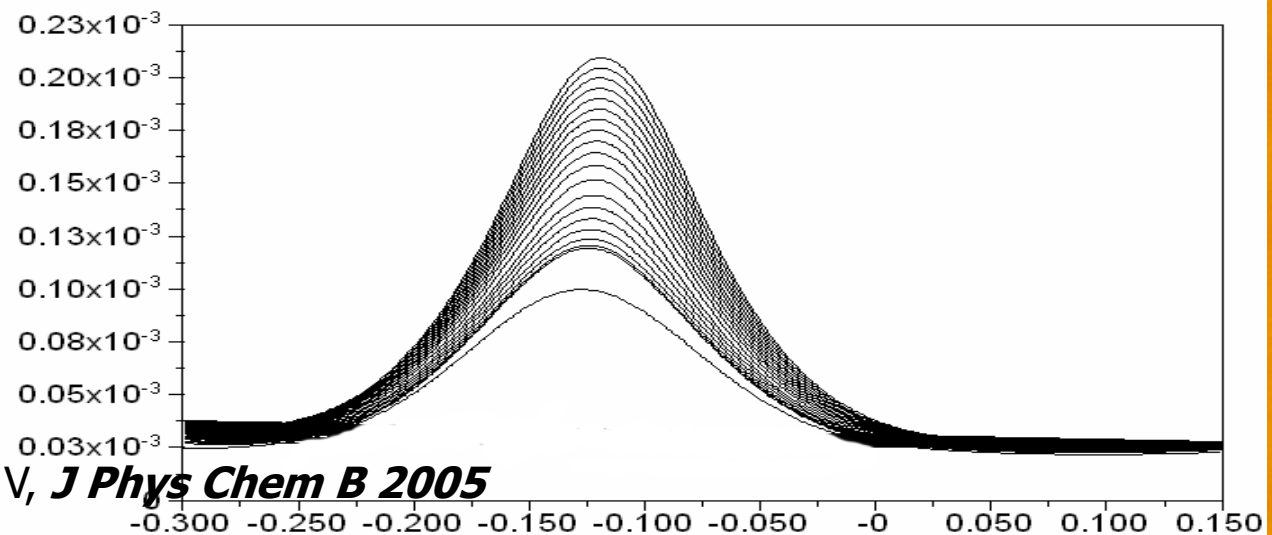




R. Gulaboski, C. M. Pereira. M. N. D. S. Cordeiro, et al. *J. Solid State Electrochem*. 9 (2005) 469-474

Ag-nanoparticles Synthesis at Three-Phase Electrode





Gulaboski R, Mirceski V, ***J Phys Chem B 2005***

…Many other Applications of Three-Phase Electrode Approach (some of them will be mentioned in the talk of Prof. Mirceski)

Conclusions:

Ion transfer processes studied by *three-phase electrodes:*

-common three-electrode setup

-simple, precise and fast determinations of *thermodynamic and kinetic parameters*

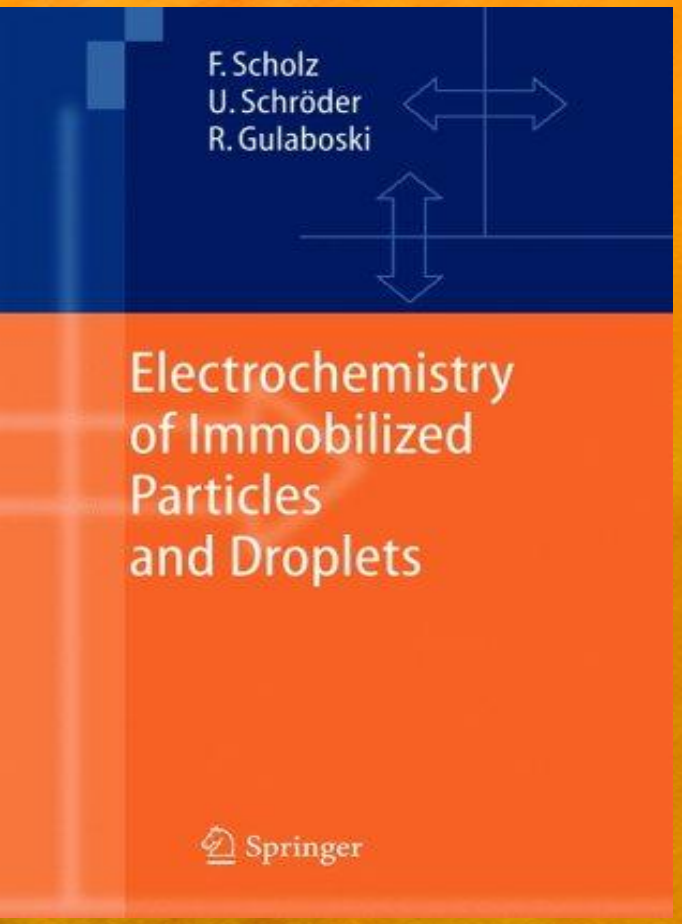
-the approach applicable to different organic solvents (octanol(s), menthol, nitrobenzene, dichlorethan, nitrophenyl-octyl ether, ionic liquids,...)

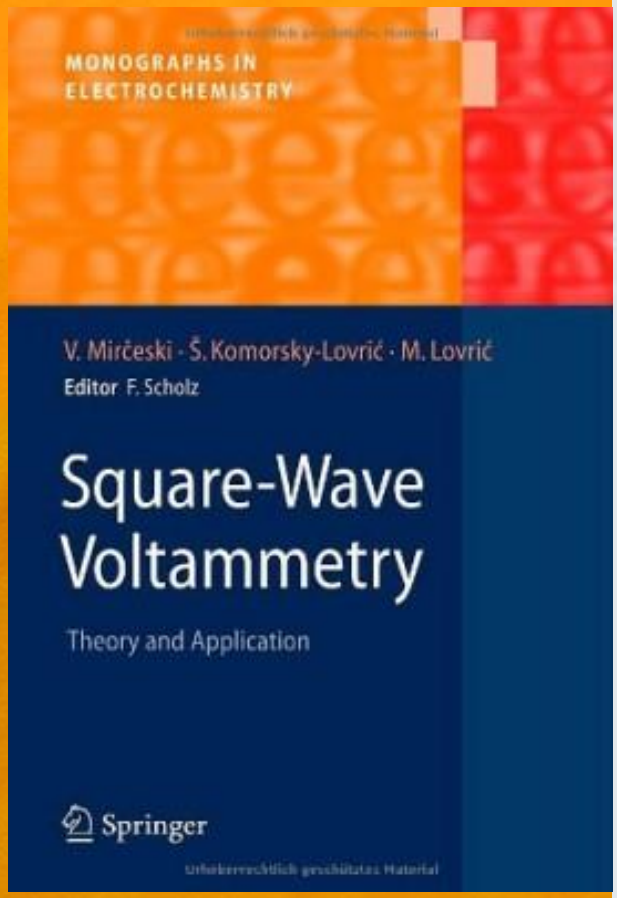
-a huge data base of new determined standard Gibbs energies of transfer of various ions as well as of k_s values

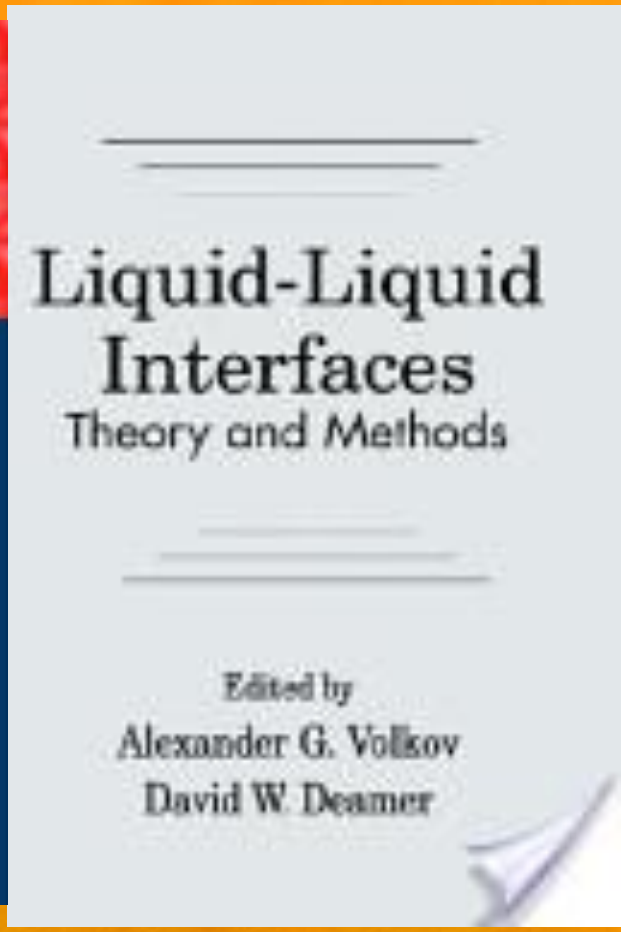
-Potential applications as a sensor and by the ion separation processes

-MD Simulations needed for molecular understanding

Relevant Literature







Which effects affect the lipophilicity of ions?

Energy of solvation=

Energy of making a cavity in the solvent to accomodate the solute

Energy of reorganization of solvent molecules

Short-term interactions
(H-bonds, van der Walls interactions, electrostatic interactions)

First model of ion-solvent interaction:

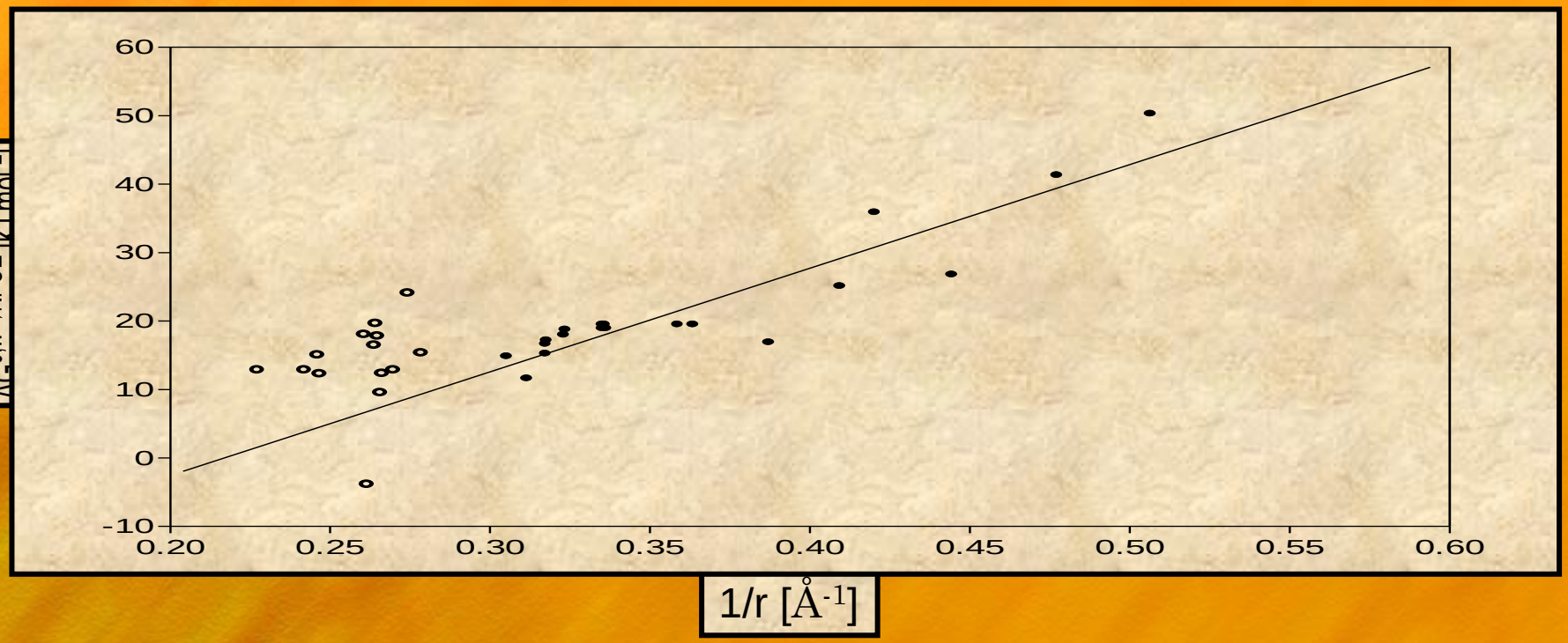
Born electrostatic theory:

$$\Delta_w^{\infty} G^{\theta}_{\text{Born}} = -\frac{N_A z^2 e^2}{8\pi\varepsilon_0 r}\left(\frac{1}{\varepsilon_{(w)}} - \frac{1}{\varepsilon_{(o)}}\right)$$

Major weaknesses:

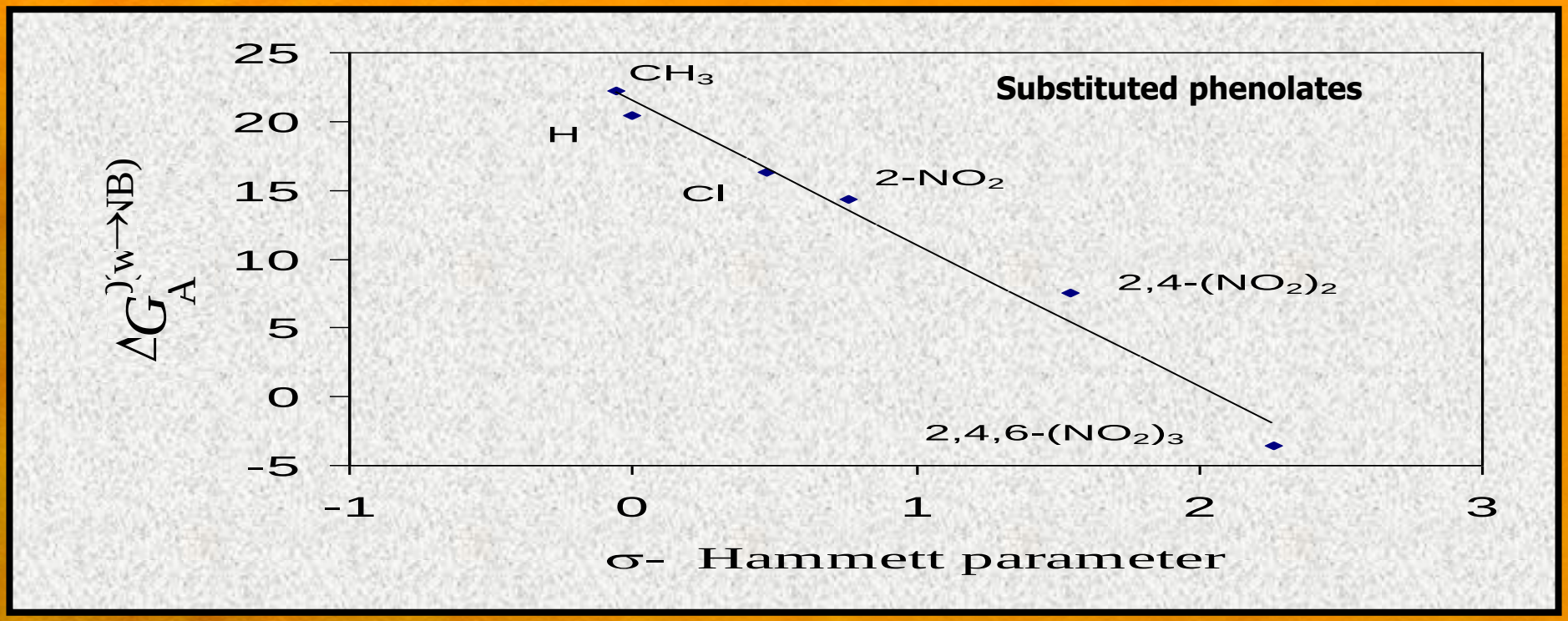
Neglects the charge delocalization effects

Neglects the energy of cavity formation


60
50
40
30
20
10
0
-10
0.20
0.25
0.30
0.35
0.40
0.45
0.50
0.55
0.60
1/r [Å-1]

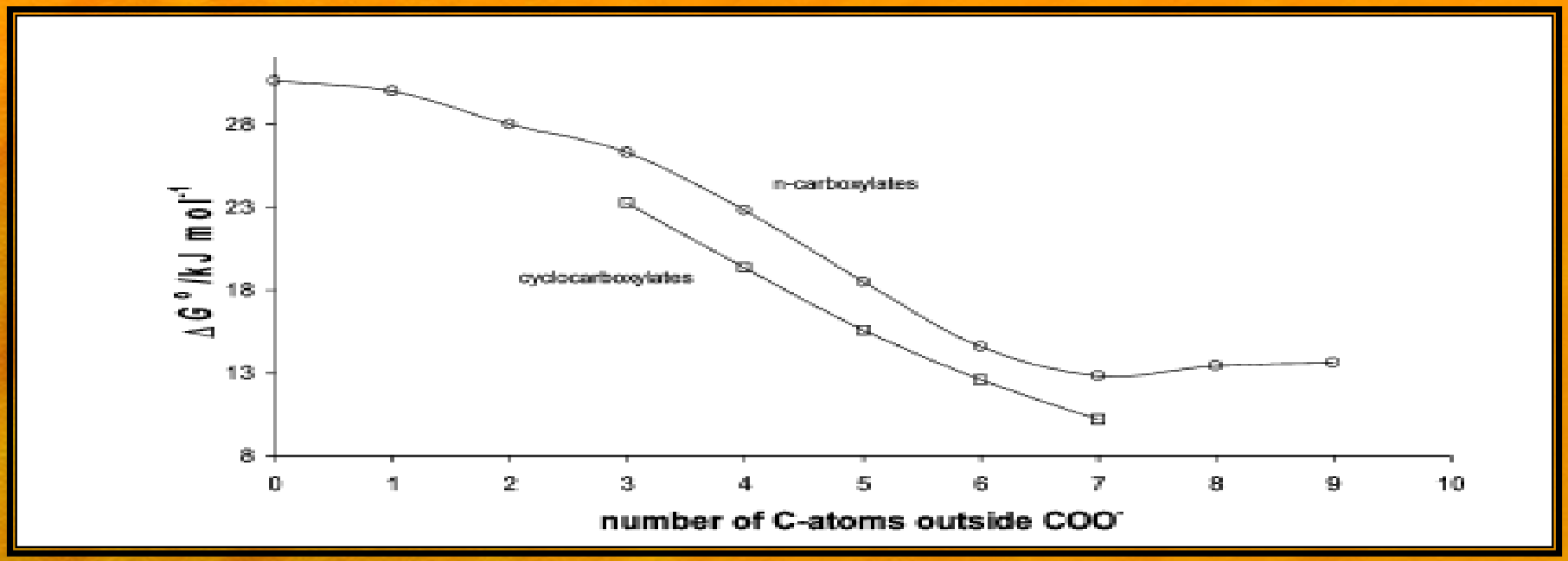
Influence of the charge delocalization effects to the lipophilicity of ions

For anions-presence of the groups with **negative inductive effect** {**NO_2, X, OH**} will produce **dispersion** of the negative charge throughout the structure of dissolved anions



Influence of the energy of making a cavity to the lipophilicity of the ions

$$E_{cav.} = 4\sigma_w^{o} A_i N_A$$



***Summary*:**

Ion transfer processes studied by ***three-phase electrodes:***

-common three-electrode setup

-simple, precise and fast determinations of

thermodynamic and kinetic parameters

-the approach applicable to different organic solvents (octanol(s), menthol, nitrobenzene, dichlorethan, nitrophenyl octyl ether, …)

-a huge data base of new determined standard Gibbs energies of transfer of various ions as well as of k_s values

-Potential applications as a sensor

and by the ion separation processes

-MD Simulations needed for molecular understanding

(N. Cordeiro, J. Miquel)

Acknowledgments

➢I thank **Prof. Natalia Cordeiro** and **Prof. Carlos Pereira** from **Porto University**

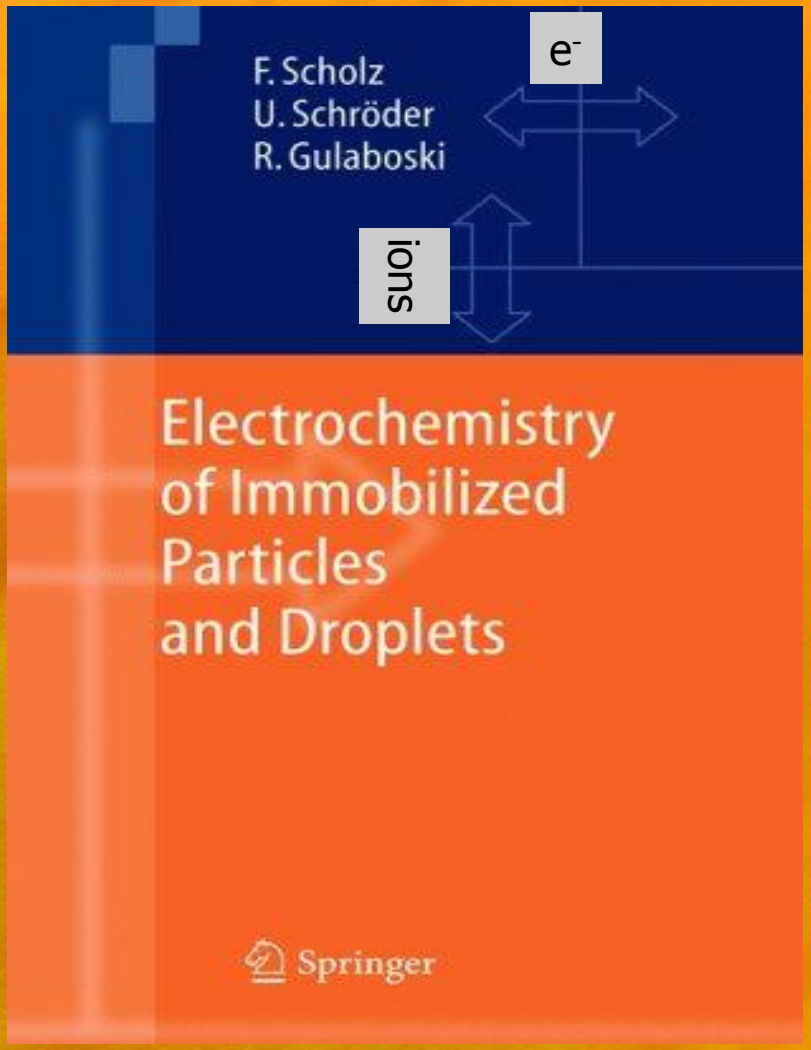
➢I thank my supervisor **Prof. Fritz Scholz** from Greifswald-University, Germany.

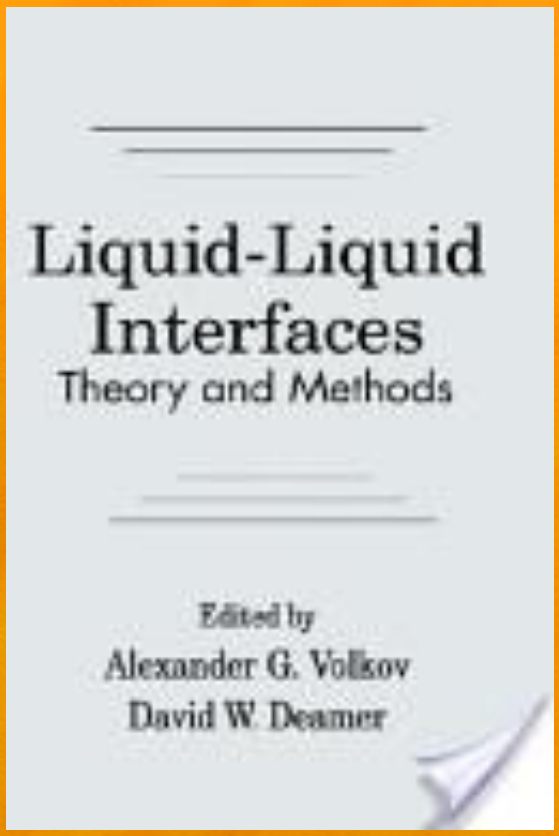
➢I thank my former Macedonian supervisor **Doc. Dr Valentin Mirčeski, Skopje University, MACEDONIA.**

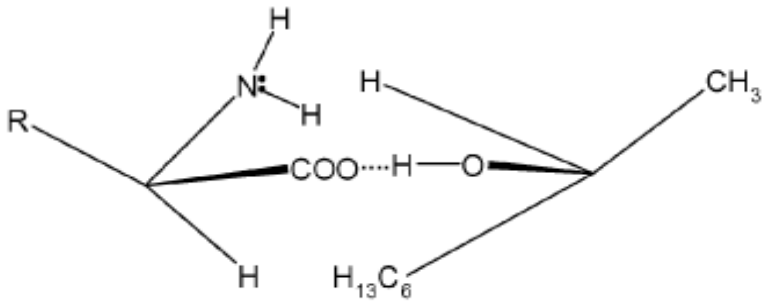
➢I thank **Prof. Šebojka Komorsky-Lovrić** and **Prof. Milivoj Lovrić** , **Zagreb, Croatia.**

➢I thank **Dr. Jorge Miguel** and **Prof A. F. Silva, M. Chirea**

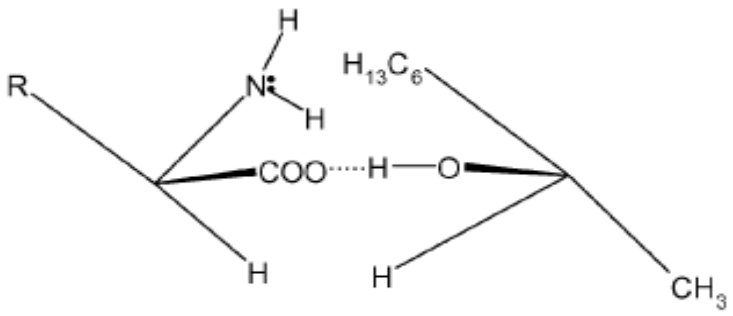
15. **Electrochemistry of Immobilized Particles and Droplets**-F. Scholz, U. Schröder, **R. Gulaboski**,
Springer, Heidelberg, Berlin 2005.







D-ion/D-solvent



D-ion/L-solvent

Limitations of the 4-electrode voltammetry at ITIES:

- **Narrow potential windows**
- **Applicable to few organic solvents only, mainly to 1,2 dichlorethan and Nitrobenzene**

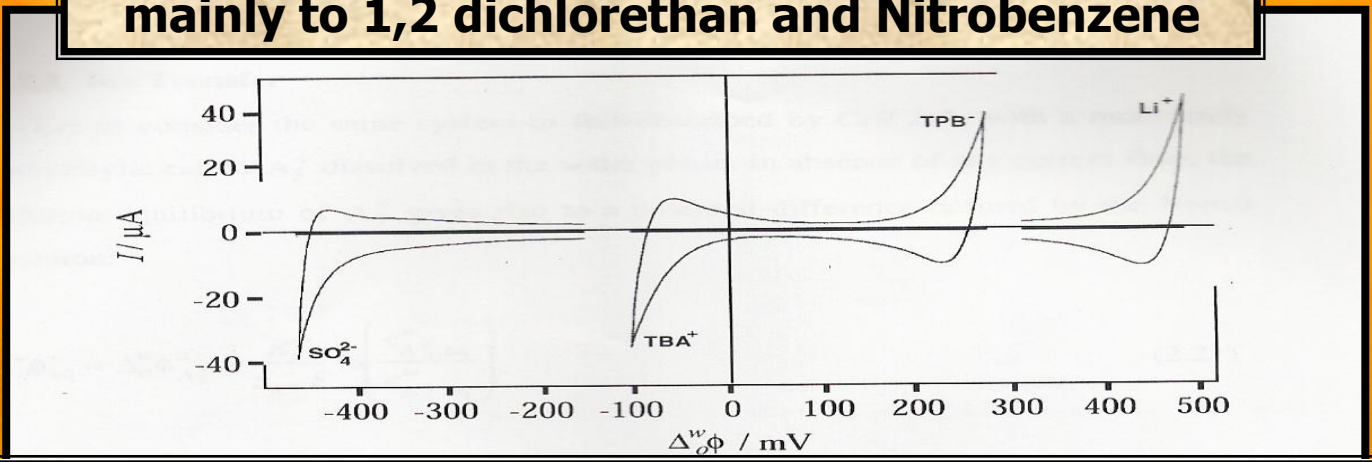
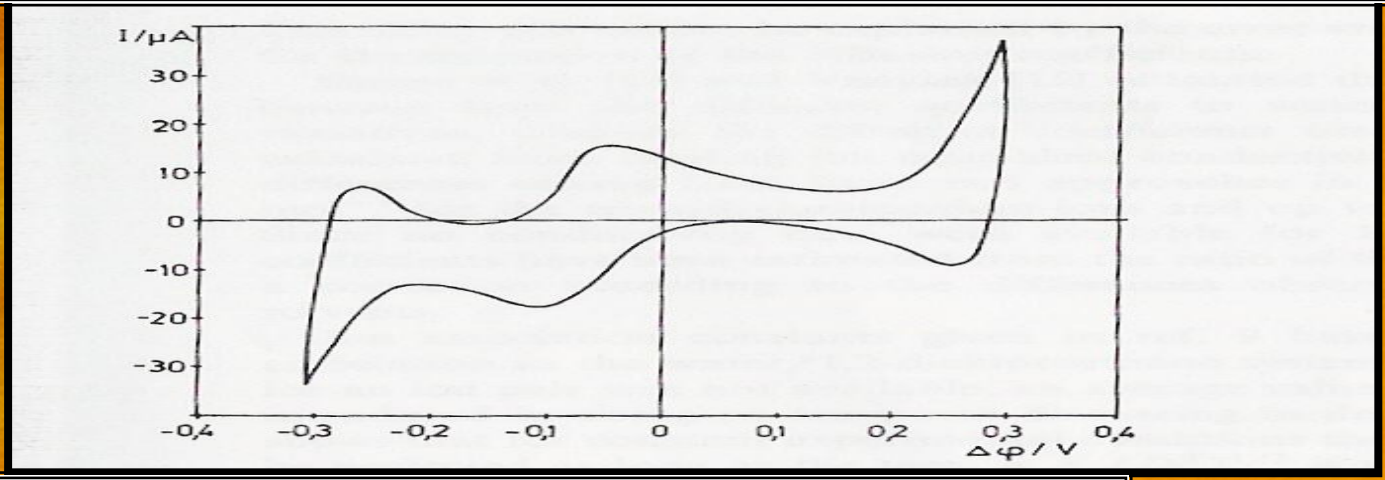


Figure: blank voltammograms obtained by four-electrode measurements

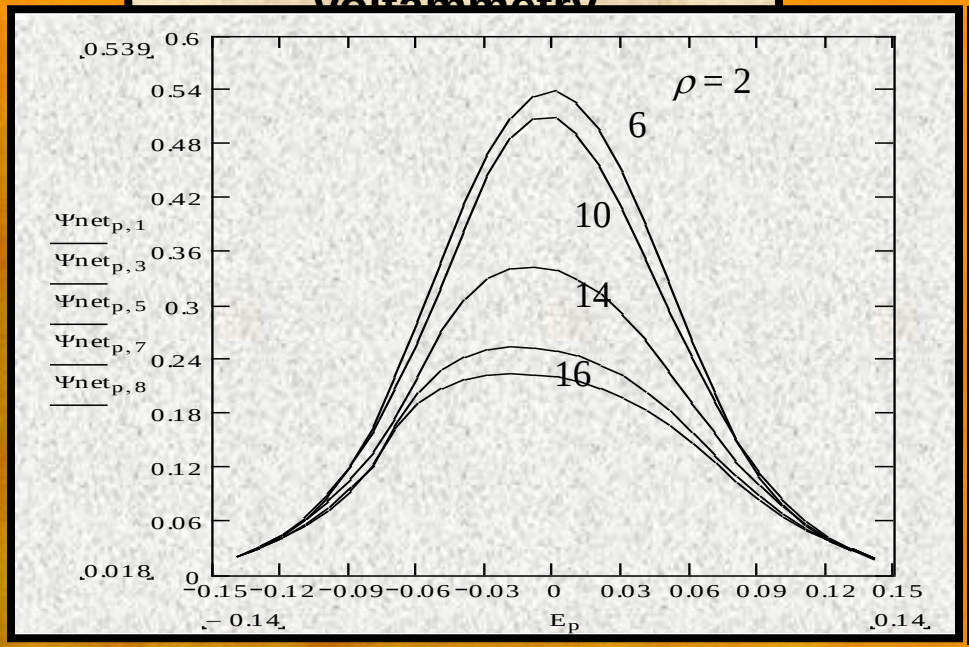


Transfer of perchlorate across water/NB interface

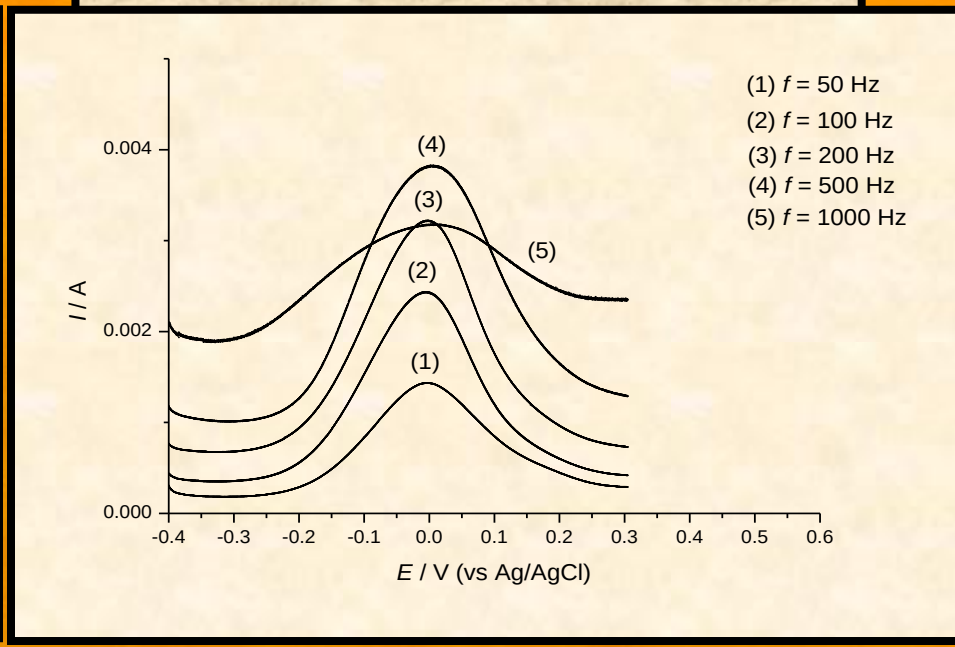
Influence of the uncompensated resistance in the square-wave thin-film voltammetry

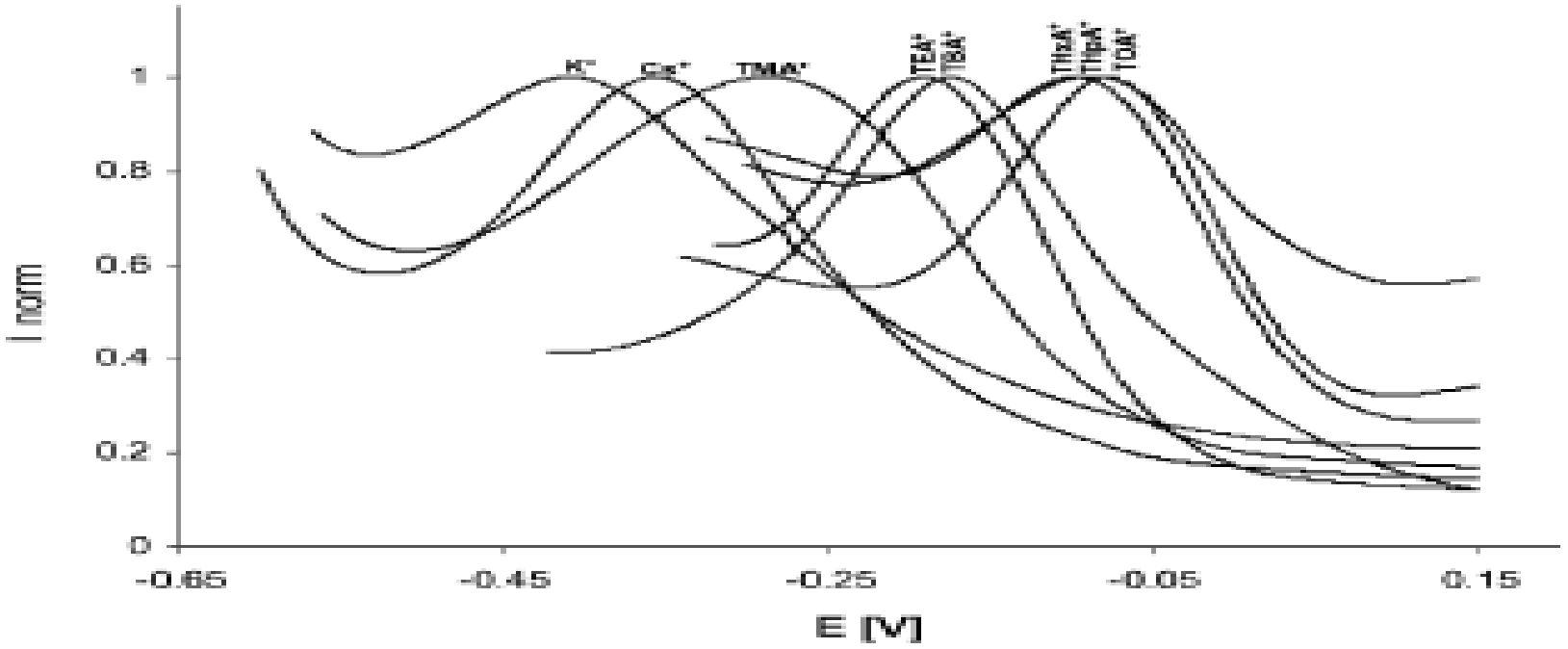
$$\rho = \frac{n^2 F^2 S \sqrt{D} c_{Ox} R_\Omega \sqrt{f}}{RT}$$

Effect of the Uncompensated Resistance in Thin-Film Voltammetry



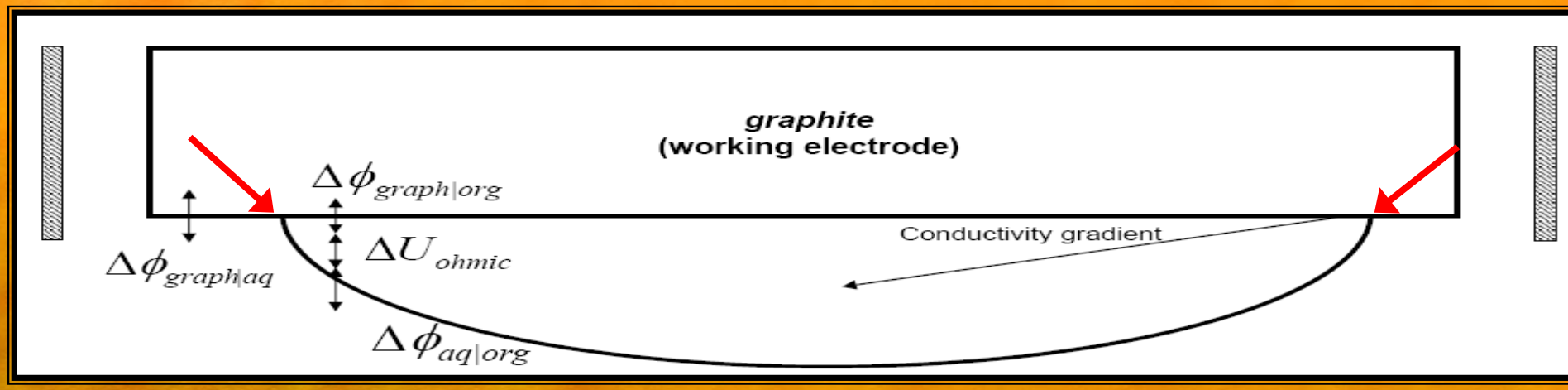
Effect of the SW frequency on the voltammetric response of DMFC





SW voltammograms showing transfer of some monocations across the w|nitrobenzene interface

Mechanistic view of the processes occuring at three-phase electrode



➢INITIALLY-NO ELECTROLYTE IN THE ORGANIC PHASE

➢How (and where) can the reaction in organic phase start?

-The natural partition of the electrolyte from aq. phase enables enough conductivity at the edges of organic phase

$$dmfc(o) + A^-(w) \Leftrightarrow dmfc^+(o) + A^-(o) + 1e^-$$

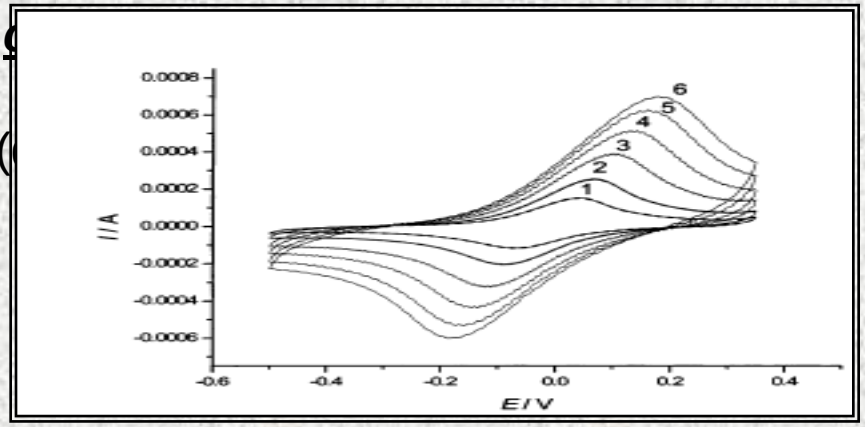
-Once the reaction in the organic phase starts, then significant ammount of ions is being created in the organic phase

The Ionic content in organic solvent
at potential that is 250 mV more negative
than the formal potential of the redox system
(i.e. at $E(<0) - E^o = -250$ mV):

$$c(\text{dmfc+X-})o = c(\text{Salt})w * \varepsilon/2\ [-1+(1+(4*c(\text{dmfc})o/e*c(\text{salt})w)^{0.5}]$$

$$\varepsilon = \exp(F(E(<0) - E^o)/RT)$$

(for $c($



I. A-B. Standard Gibbs energies of transfer of some inorganic anions and monoanions of various carboxylic acids

Table 1: Peak potentials E_p, slope of E_p versus concentration of anions in aqueous phase, standard deviation of peak potentials, standard Gibbs energies of ion transfer ΔG^o, and standard deviation of Gibbs energies of all studied anions.

anion	E_p / mV	slope E_p vs. log (c) /mV	$s(E_p)$ / mV	ΔG^o / kJ mol^{-1}	s (ΔG^o) / kJ mol^{-1}
ClO_3^-	2	-55.3	6.43	25.40	0.64
BrO_3^-	60	-58.7	7.17	30.90	0.71
IO_3^-	74	-54.3	8.08	32.40	0.80
IO_4^-	-132	-56.4	2.00	12.50	0.19
OCN^-	45	-50.5	2.45	29.50	0.23
$SeCN^-$	-136	-43.0	5.30	11.80	0.53
CN^-	41	-58.1	4.43	29.60	0.45
N_3^-	14	-52.1	3.44	26.80	0.35
Monofluoro acetate	44	-54.4	5.48	29.90	0.54
Difluoro acetate	34	-48.5	3.90	28.90	0.38
Trifluoro acetate	-2	-60.1	1.79	25.30	0.18
Monochloro acetate	36	-51.5	4.73	29.10	0.48
Dichloro acetate	9	-58.0	1.15	26.40	0.10
Trichloro acetate	-66	-60.1	1.97	18.80	0.20
Monobromo acetate	12	-39.3	3.44	26.70	0.35
Dibromo acetate	-7	-59.0	2.00	24.80	0.20
Tribromo acetate	-94	-59.8	1.03	16.00	0.10
Monoiodo acetate	0	-54.6	1.20	25.10	0.10
$HCOO^-$	58	-56.4	2.40	30.60	0.23
H_3CCOO^-	52	-58.0	1.50	30.10	0.13
$H_3CCH_2COO^-$	29	-54.6	0.80	27.98	0.10
$H_3C(CH_2)_2COO^-$	11	-53.1	2.20	26.25	0.21
$H_3C(CH_2)_3COO^-$	-31	-63.5	2.80	22.30	0.26
$H_3C(CH_2)_4COO^-$	-75	-60.3	1.40	18.10	0.12
$H_3C(CH_2)_5COO^-$	-115	-55.2	1.80	14.20	0.16
$H_3C(CH_2)_6COO^-$	-125	-57.4	4.20	12.64	0.40
$H_3C(CH_2)_7COO^-$	-120	-52.9	3.20	13.40	0.30
$H_3C(CH_2)_8COO^-$	-118	-58.4	2.50	13.60	0.24
Cyclopropane carboxylate	-20	-60.0	1.10	23.25	0.10
Cyclobutane carboxylate	-61	-57.8	1.40	19.30	0.12
Cyclopentane carboxylate	-100	-63.2	1.60	15.54	0.15
Cyclohexane carboxylate	-131	-56.8	2.80	12.54	0.26
Cycloheptane carboxylate	-155	-55.4	2.00	10.22	0.19

- 6 measurements have been performed for one concentration of each anion

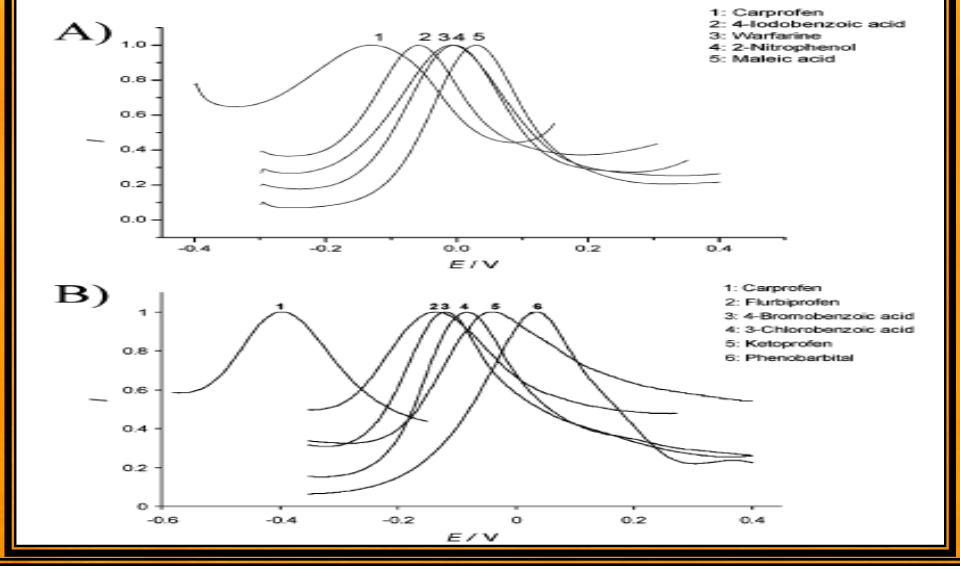
s (E_p) is the standard deviation of SW peak potential

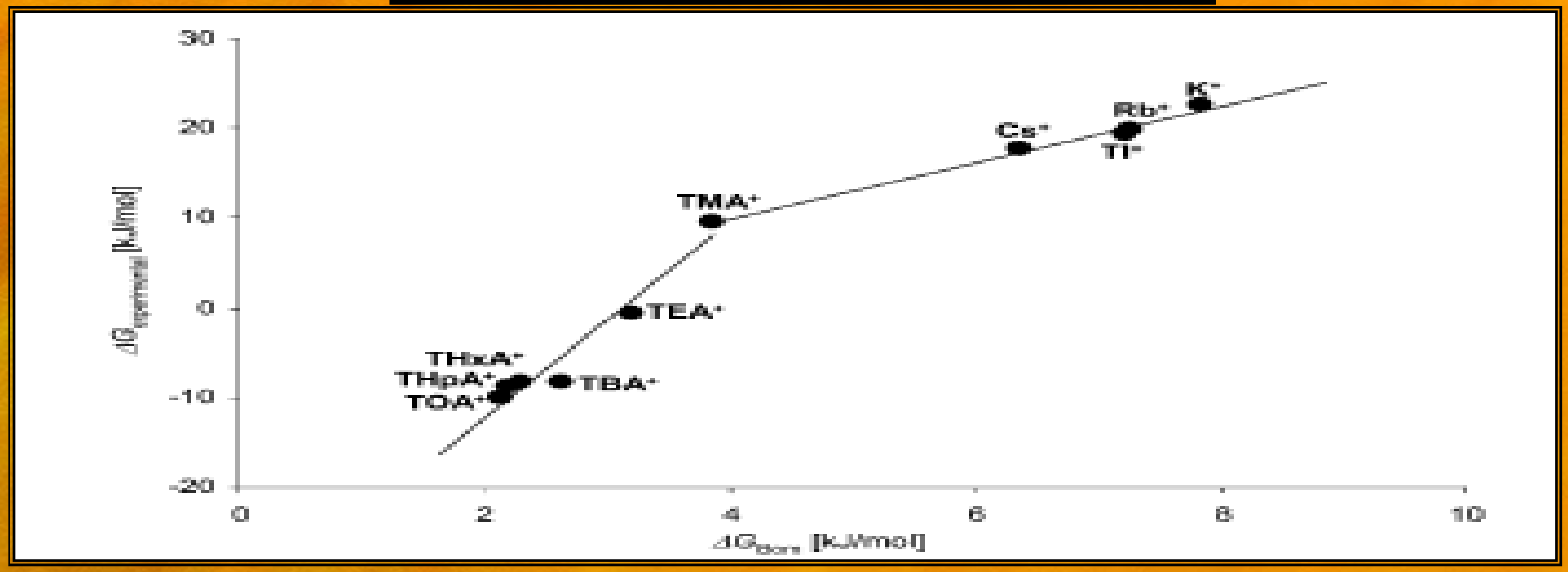
s (ΔG^o) is the standard deviation of Gibbs free energy

TABLE 1: Data of the Lipophilicities of the Investigated Peptides

peptide anions	$\Delta\phi^{o}$/V[a]	ΔG^{o}/kJ mol^{-1}[b]	log P[c]	slope E_p vs log[c]/mV[d]
		(A)		
Trp^{-}[e]	0.115	10.80	−1.90	−64
Trp-Ala^{-}	0.165	15.75	−2.75	−80
Trp-Gly^{-}	0.162	15.60	−2.73	−73
Trp-Val^{-}	0.120	11.60	−2.05	−75
Trp-Leu^{-}	0.100	9.50	−1.66	−73
Trp-Tyr^{-}	0.075	7.40	−1.30	−65
Trp-Phe^{-}	0.055	5.30	−0.93	−77
Trp-Trp^{-}	0.05	4.80	−0.85	−70
Trp-Gly-Gly^{-}	0.165	15.80	−2.75	−75
Trp-Gly-Tyr^{-}	0.155	15.00	−2.65	−74
Trp-Gly-Gly-Tyr^{-}	0.160	15.50	−2.70	−74
		(B)		
Leu-Leu^{-}	0.245	23.70	−4.15	−71
Leu-Leu-Ala^{-}	0.293	28.20	−4.95	−57
Leu-Leu-Gly^{-}	0.290	28.00	−4.91	−80
Leu-Leu-Leu^{-}	0.240	23.20	−4.05	−80
Leu-Leu-Tyr^{-}	0.205	19.70	−3.45	−56
Leu-Leu-Phe^{-}	0.180	17.50	−3.05	−64
Leu-Gly-Phe	0.275	26.50	−4.65	−65
		(C)		
Gly-Phe^{-}	0.260	25.00	−4.40	−59
Gly-Phe-Ala^{-}	0.285	27.50	−4.80	−75
Gly-Phe-Gly^{-}	0.265	25.60	−4.50	−63
Gly-Phe-Tyr^{-}	0.210	20.20	−3.55	−72
Gly-Phe-Phe^{-}	0.208	20.15	−3.53	−70
Phe-Gly-Gly^{-}	0.300	29.00	−5.10	−55
		(D)		
Gly-Gly^{-}[e]	0.280	27.00	−4.75	−49
Gly-Gly-Val^{-}	0.275	26.40	−4.60	−57
Gly-Gly-Leu^{-}	0.280	26.80	−4.70	−56
Gly-Gly-Tyr^{-}	0.300	29.00	−5.10	−57
Gly-Gly-Phe^{-}	0.270	26.00	−4.55	−58
Gly-Gly-Trp^{-}	0.195	19.00	−3.35	−56
Gly-Leu-Gly^{-}	0.280	27.00	−4.75	−49
Gly-Trp-Gly^{-}	0.165	15.80	−2.75	−48
Gly-Tyr-Gly^{-}	0.280	27.10	−4.75	−48
Gly-Leu-Tyr^{-}	0.245	23.40	−4.10	−71
Gly-Leu-Phe^{-}	0.270	26.20	−4.60	−60
Gly-Ala-Phe^{-}	0.285	27.40	−4.80	−70
		(E)		
Tyr-Ala-Gly^{-}	0.260	24.90	−4.40	−48
Tyr-Ala-Gly-Phe-Leu^{-}	0.175	16.60	−2.90	−50
Tyr-Ala-Gly-Leu-Arg^{-}	0.175	17.10	−3.00	−78
Tyr-Ala-Gly-Phe-Met^{-}	0.190	18.40	−3.30	−61
Tyr-Ala-Gly-Met-Phe-Glycinol^{-}	0.260	24.90	−4.40	−48
Tyr-Lys-Thr^{-}	0.255	24.60	−4.30	−59
Lys-Tyr-Thr^{-}	0.310	30.00	−5.25	−58
		(F) Amino Acid Anions[e]		
Gly^{-}	0.275	26.60	−4.65	−54
Ala^{-}	0.285	27.50	−4.80	−58
Val^{-}	0.278	26.80	−4.70	−52
Leu^{-}	0.245	23.90	−4.20	−66
Phe^{-}	0.215	21.00	−3.70	−60
Tyr^{-}	0.220	21.20	−3.72	−64
Met^{-}	0.255	24.50	−4.30	−56
Trp^{-}	0.115	10.80	−1.90	−64
Lys^{-}	0.283	27.30	−4.78	−48
Pro^{-}	0.305	29.50	−5.20	−59
His^{-}	0.29	27.70	−4.85	−63

[a] Standard potential differences at the W|NB interface ($\Delta\phi^{o}$). [b] Standard Gibbs energies of ion transfer (ΔG^{o}). [c] Logarithm of the ion partition coefficients (log P). [d] Slopes of the dependencies of the peak potentials vs logarithm of the concentration of peptide anions in the water phase (E_p vs log[c]) evaluated from the square-wave voltammetric responses of dmfc at the three-phase electrode. [e] Data taken from ref 16.





Comparison between experimentally determined and the estimated values by using the electrostatic Born theory

$\Delta G^{NB^{\circ}}_{W^{\circ}Cat^{+}}$

The Ionic content in organic solvent
at potential that is 250 mV more negative
than the Standard redox potential
(i.e. at $E(<0) - E^o = -250$ mV):

$c(\mathrm{dmfc^+X^-})_o = c(\mathrm{Salt})_{w*}\varepsilon/2\ [-1+(1+(4*c(\mathrm{dmfc})o/\varepsilon*c(\mathrm{salt})_w)^{0.5}]$

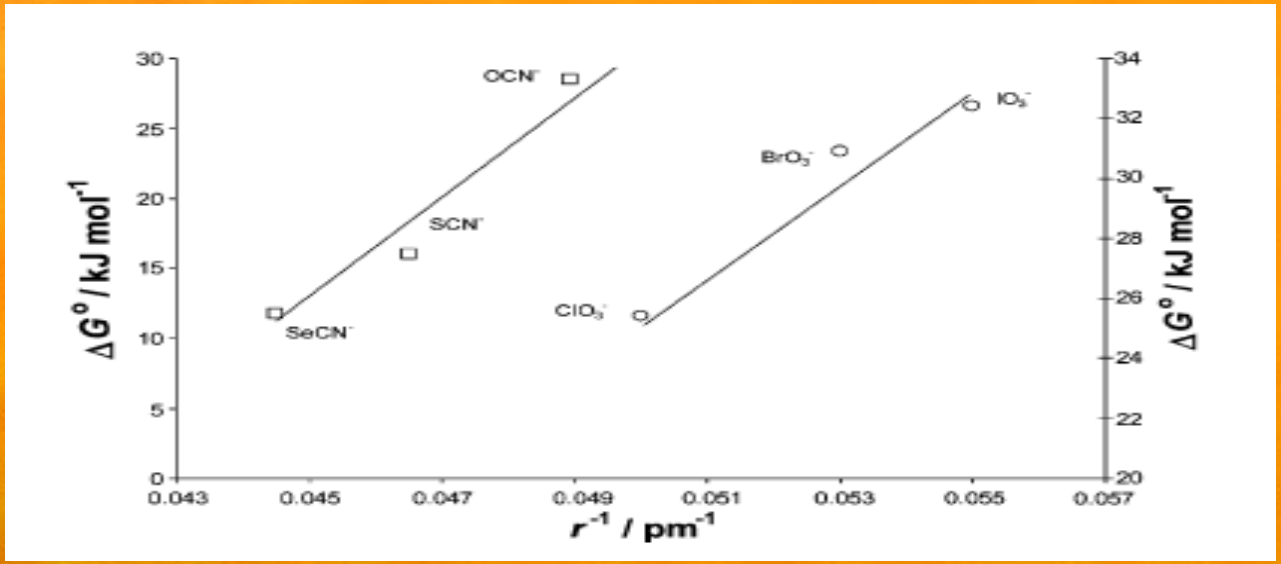
$\varepsilon = \exp(F(E(<0) - E^o)/RT)$

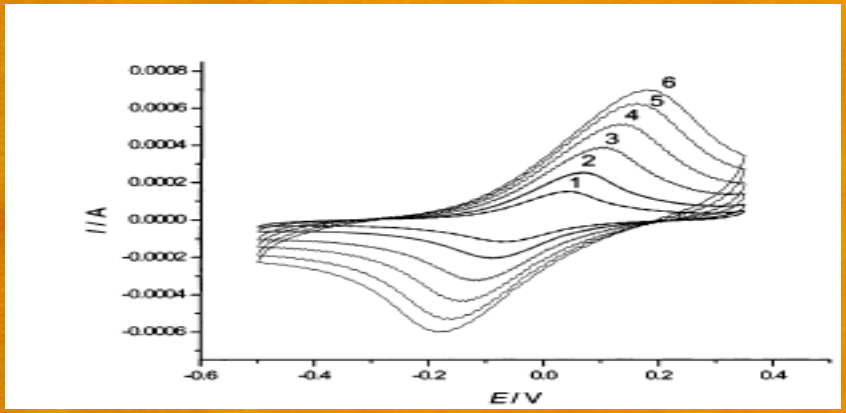
$c(\mathrm{dmfc^+X^-})_{\text{org. phase}} = 5$ mM!!!

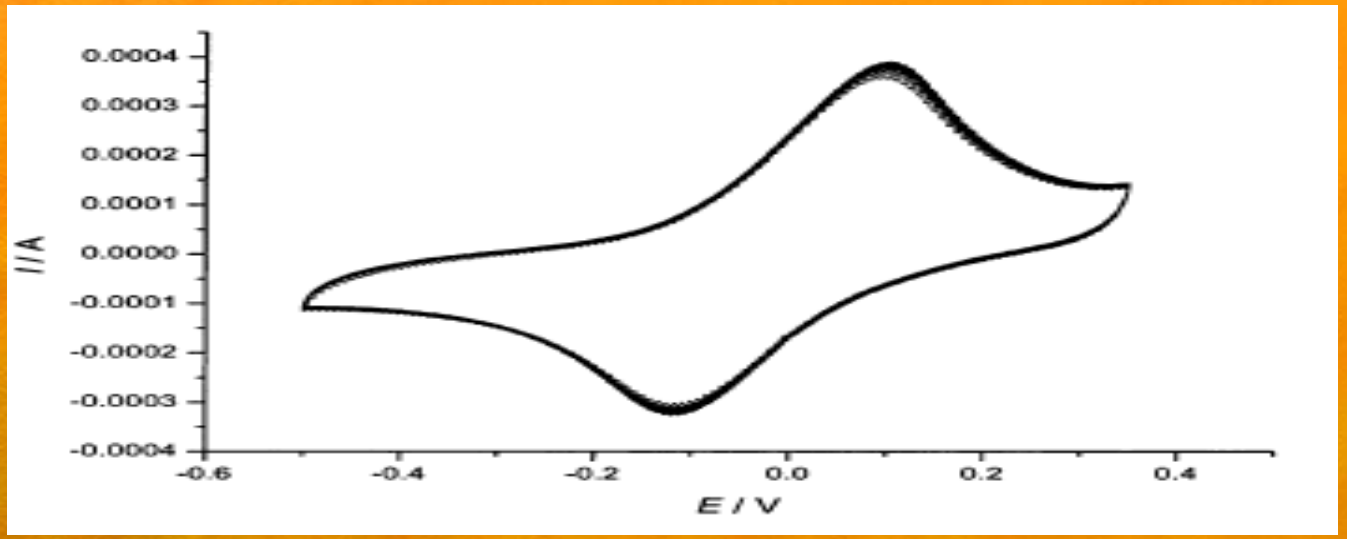
(for $c(\mathrm{dmfc})_o = 0.05$ M, and $c(\mathrm{salt})_w = 0.5$ M)

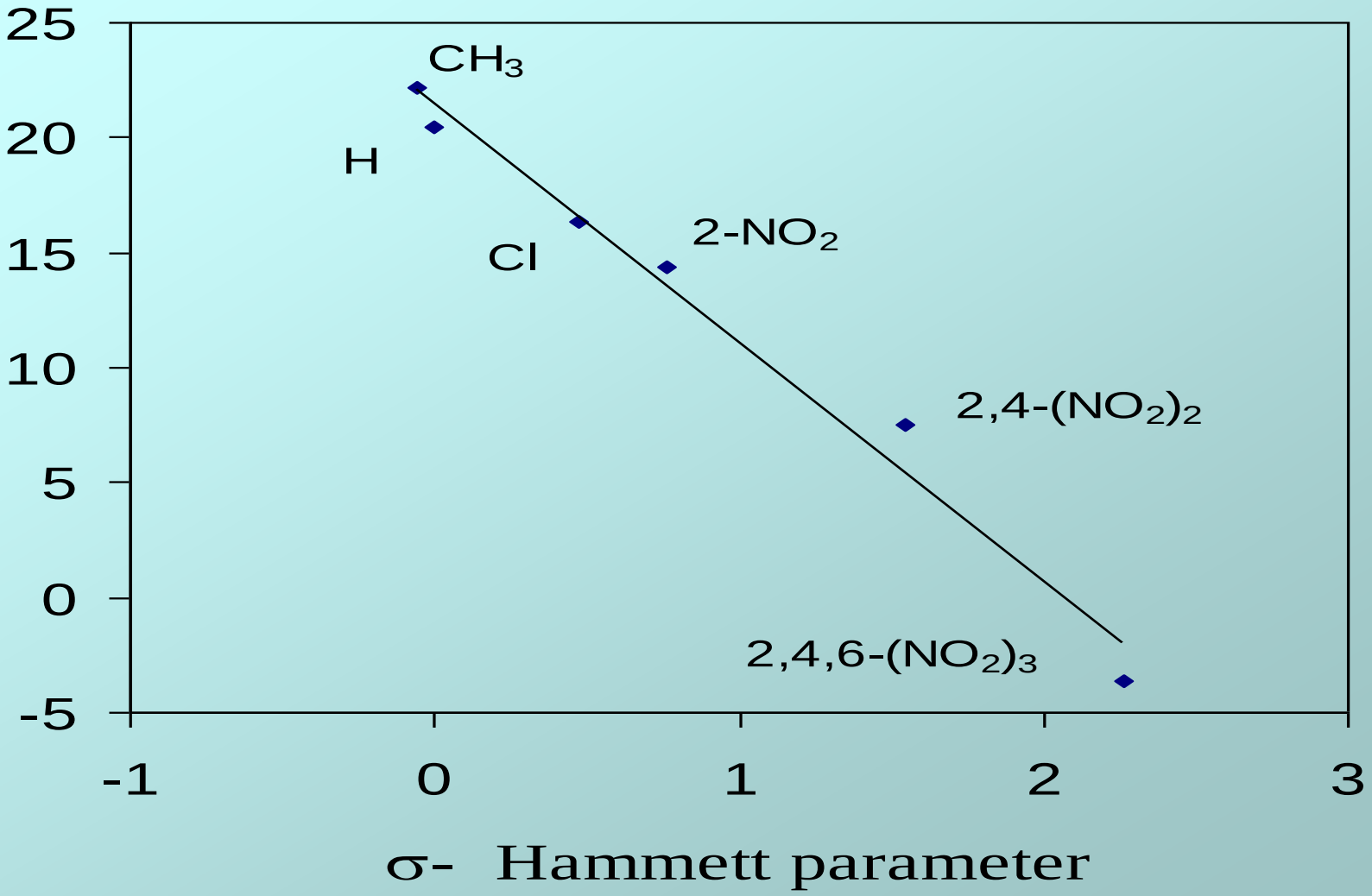
Distance that can be reached by diffusion:

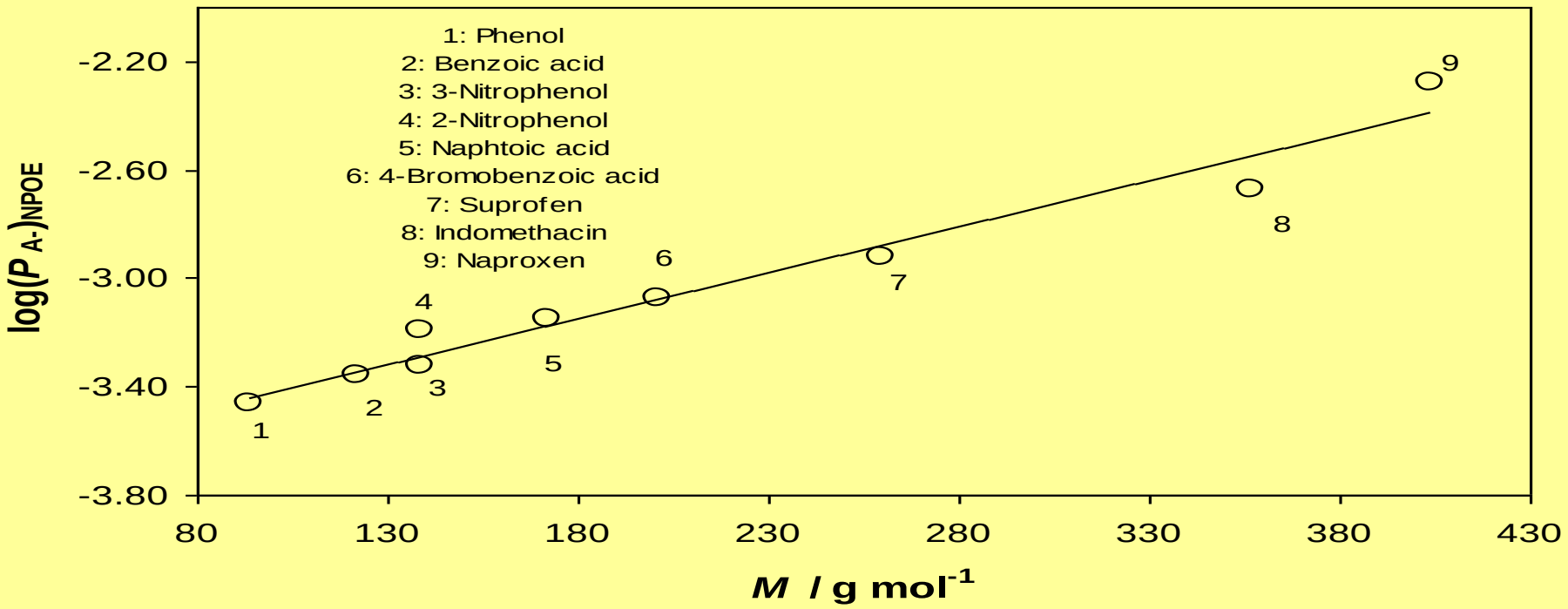
$L = (Dt)^{0.5}$


ΔG° / kJ mol⁻¹
r⁻¹ / pm⁻¹
OCN⁻
SCN⁻
SeCN⁻
ClO₃⁻
BrO₃⁻
IO₃⁻


I / A
E / V


0.0004
0.0003
0.0002
0.0001
0.0000
-0.0001
-0.0002
-0.0003
-0.0004
I / A
-0.6
-0.4
-0.2
0.0
0.2
0.4
E / V


25
20
15
10
5
0
-5
-1
0
1
2
3
CH3
H
Cl
2-NO2
2,4-(NO2)2
2,4,6-(NO2)3
σ- Hammett parameter


1: Phenol
2: Benzoic acid
3: 3-Nitrophenol
4: 2-Nitrophenol
5: Naphtoic acid
6: 4-Bromobenzoic acid
7: Suprofen
8: Indomethacin
9: Naproxen
log(P A-)NPOE
-2.20
-2.60
-3.00
-3.40
-3.80
80
130
180
230
280
330
380
430
M / g mol-1