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ELECTROQUIMICA
APLICADA

The cathodic reduction of disulphides: from voltametry to pre-industrial pilot plant

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Electrochemistry and Environment

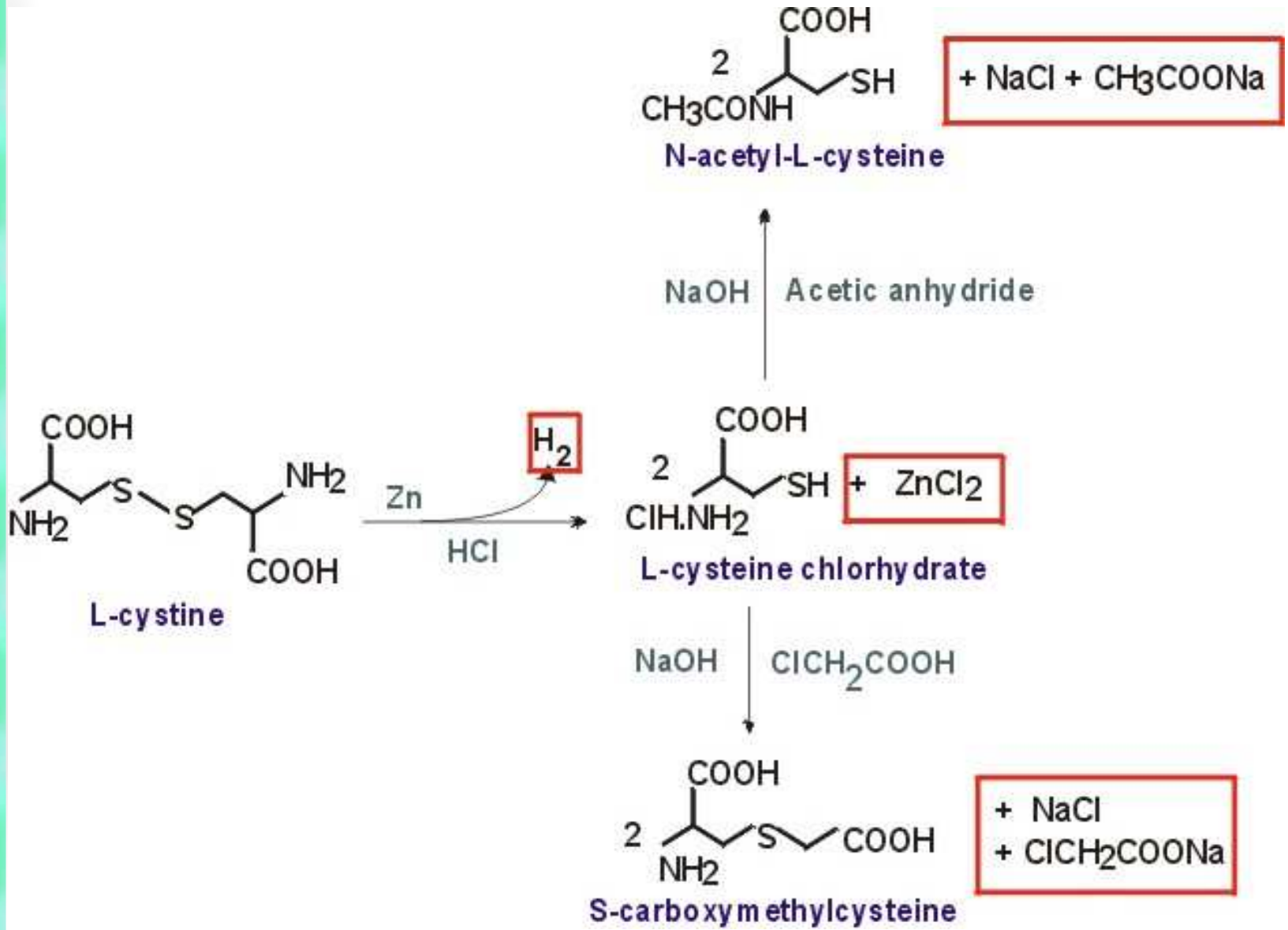
- **Cleaner generation of energy: Fuel Cells**
- **In situ chemical synthesis: Cl_2, H_2O_2...**
- **Improving water quality: O_3, ClO^-, Electrodialysis**
- **Efluent treatment: Heavy metals, salts..**
- **Improving atmospheres: SO_2, NO_x**
- **Sensors: O_2, CO, CO_2...**

Recycling process streams

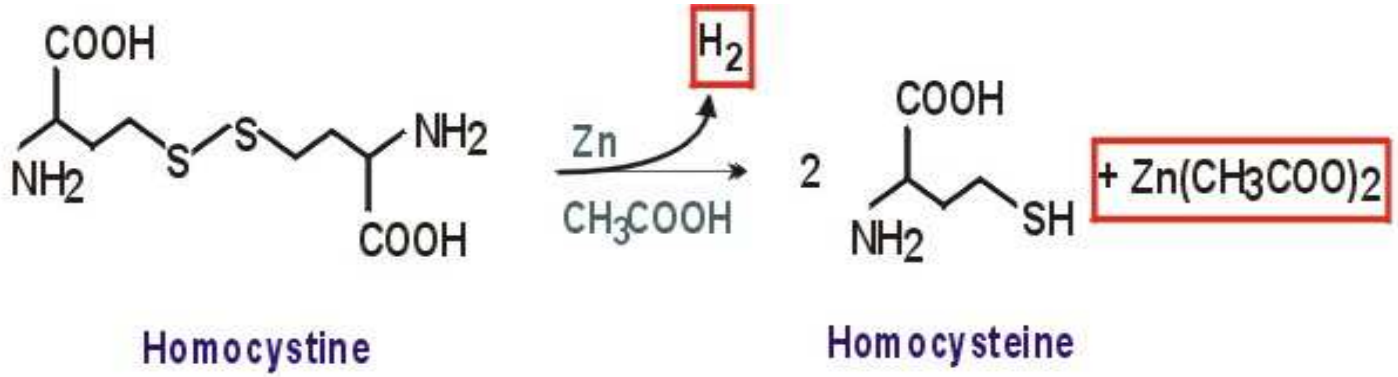
Cleaner and more selective synthesis

ELECTROCHEMICAL SYNTHESIS OF L-CYSTEINE DERIVATIVES

Classical synthesis of L-cysteine and derivatives

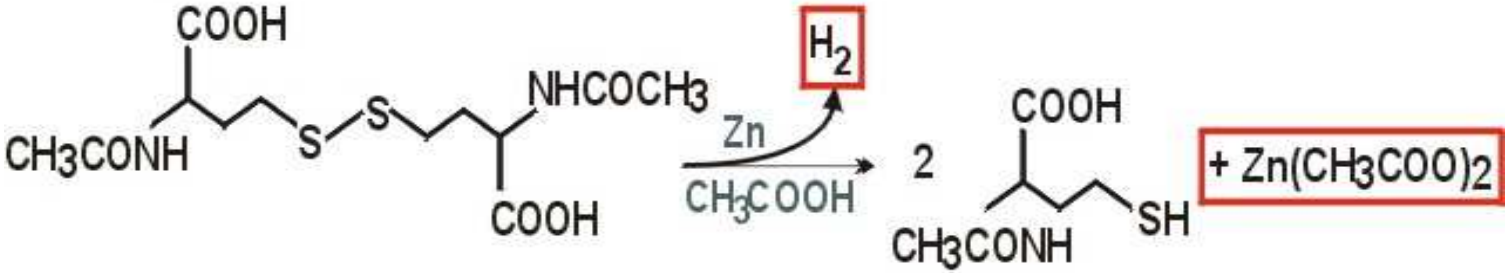


Classical synthesis of Homocysteine derivatives



Homocystine

Homocysteine



Acetylhomocystine

Acetylhomocysteine

Classical synthesis
(drawbacks)

- Production of large quantities of **hydrogen**
- Production of effluents containing **metallic salts** and **high salinity**
- Final product contaminated by **metallic ions**
- **Purification needs** due to high level of initial L-cystine
- **Exotermic** reaction
- Increase of the **complexity** and **cost** process

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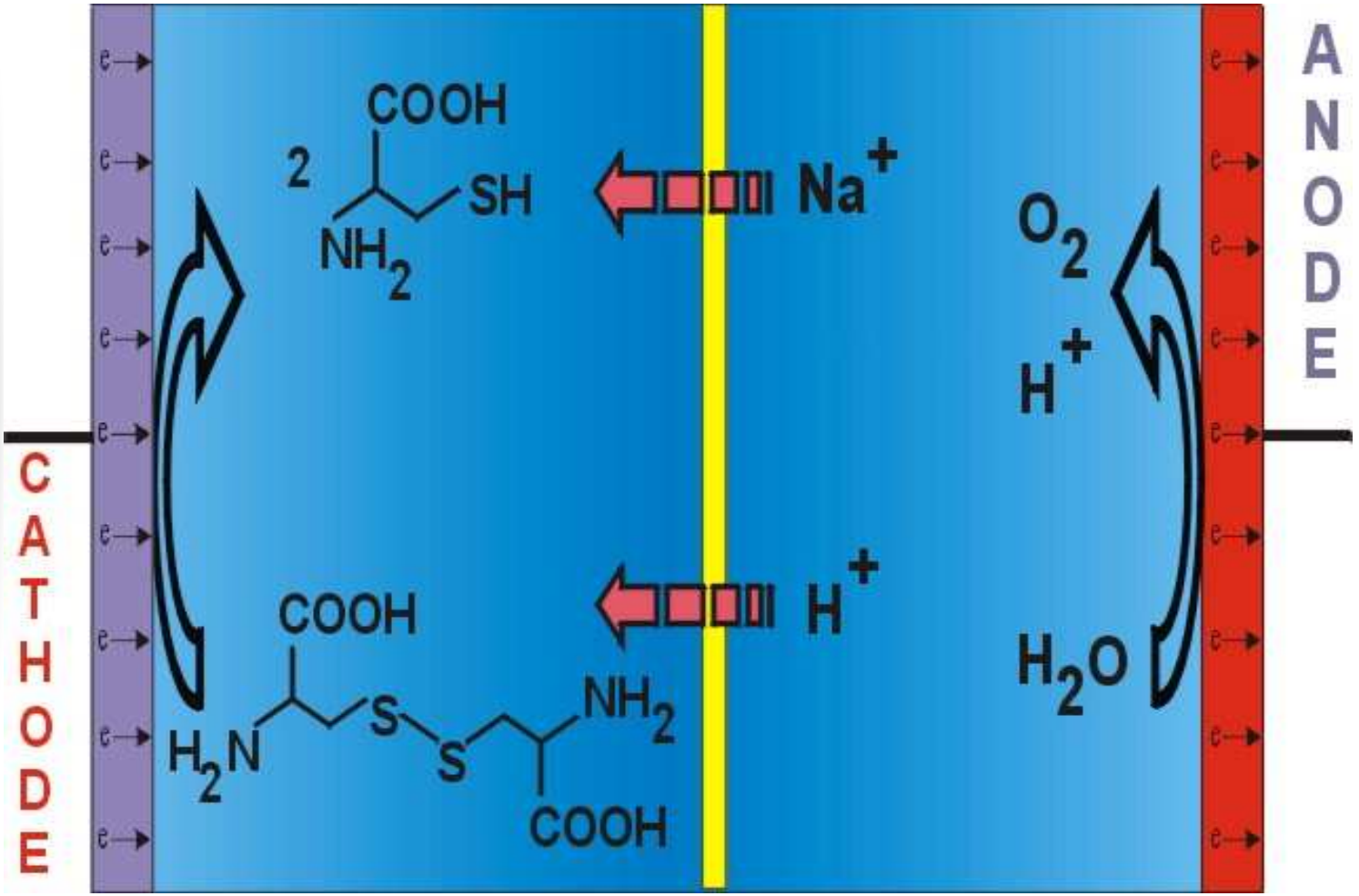
Electrochemical reduction of L-cystine



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Electrochemical synthesis
(Pros and cons)

- Electrochemical processes are very selective
- Electrochemical processes are normally carried out at room temperature and atmospheric pressure
- They are safe processes
- From a energetic point of view they are very cheap

The main reactant, the electron, is always available, cheap and does not need to be stoked

- It is a green technology, the pollution caused is very low and can be eliminated using electrochemical routes

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Electrochemical synthesis
(Pros and cons)

- It is wiewed as a new tecnology in organic chemistry in spite of the fact the Kolbe synthesis was carried out in the XIX century
- An electrochemical reactor is not a simple system compared to classical vessel reactors
- It is an unknown technology in the organic industry
- Electrochemistry is hardly feature as a subject in the chemistry curriculum. This makes the chemist in chemical industry very reluctant to use this technology

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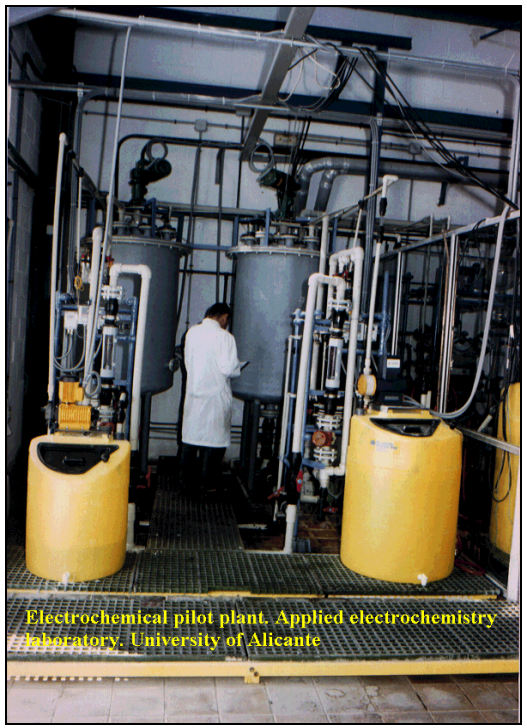
Applied Electrochemical Group

(Different scales)

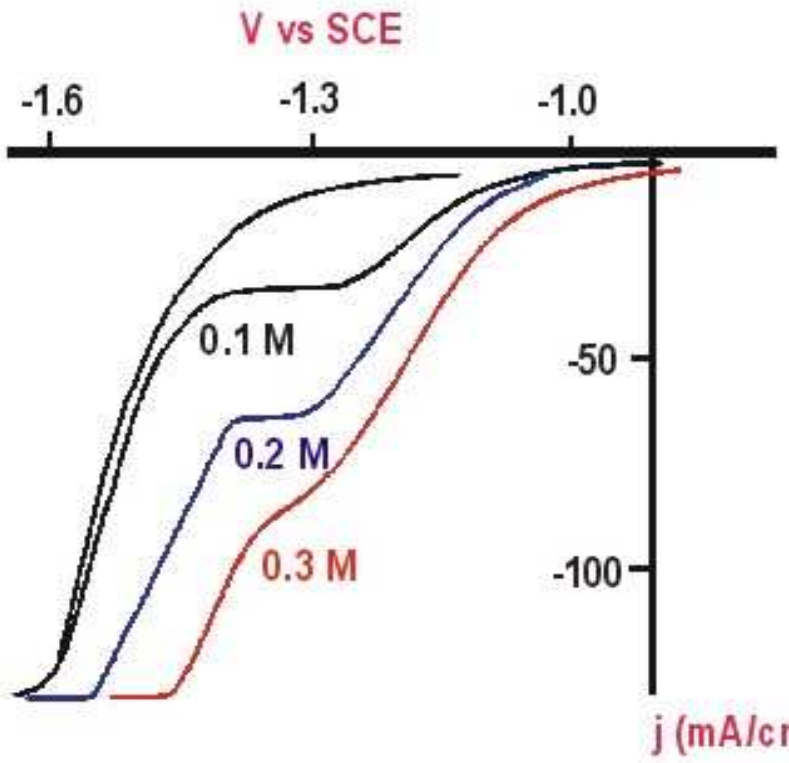


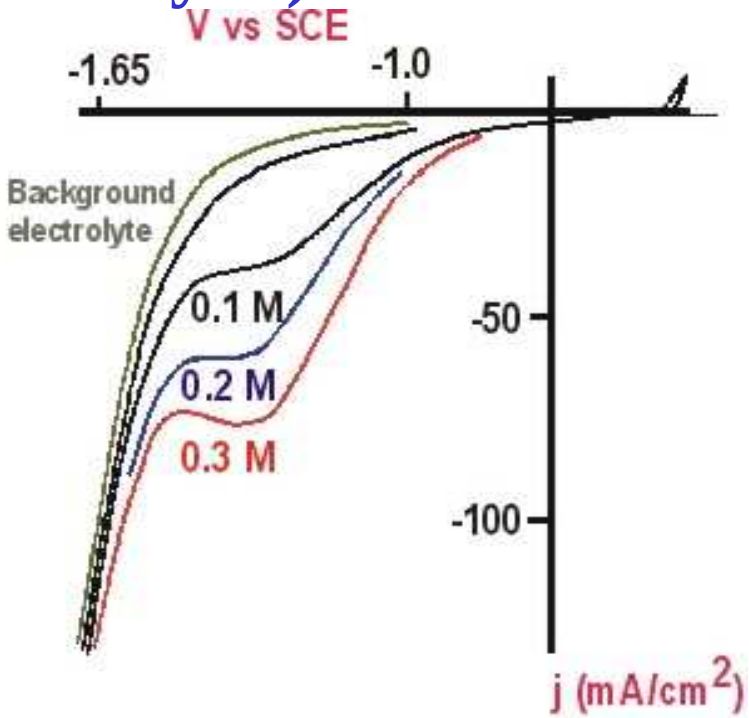
Electrochemical pilot plant. Applied electrochemistry laboratory. University of Alicante

Electrochemical reduction of L-cystine

(Voltammetric analysis)

Voltammograms of L-cystine in HCl 1.5M on a lead electrode. v=100 mV/s. T=20ºC





Voltammograms of L-cystine in H_2SO_4 1.5 M on a lead electrode. v=100 mV/s. T=20ºC

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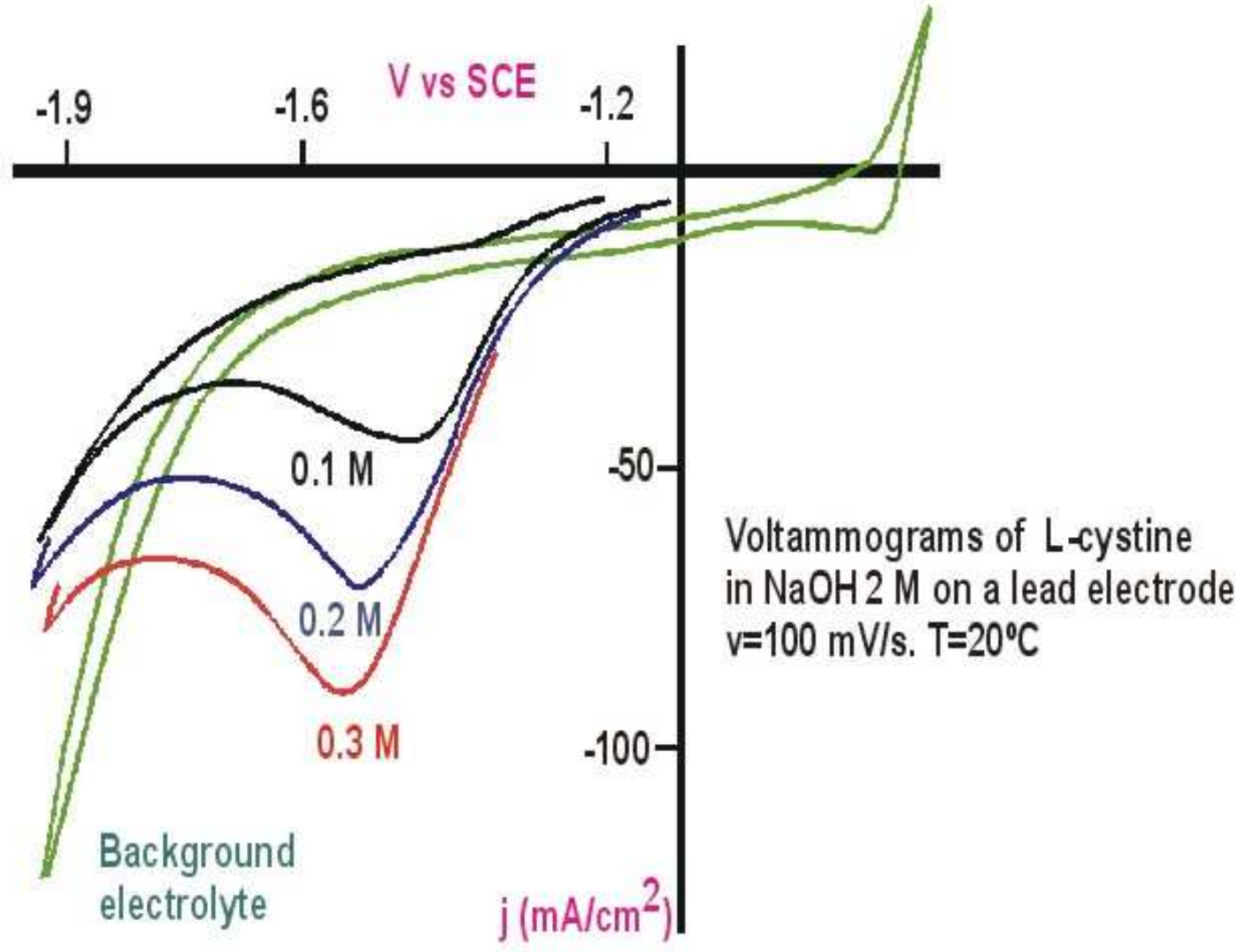
Electrochemical reduction of L-cystine

(Voltammetry study)



Voltammograms of L-cystine in NaOH 2 M on a lead electrode v=100 mV/s. T=20ºC

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Electrochemical synthesis
(Preliminary study)

GLOBAL ASPECTS OF THE PROCESS
- Electrocatalysis: electrode materials
- Type of process controlling the current density
- Reversibility: necessity or not of a divided cell
- Interference with other reactions
- Identification of products (electrochemical synthesis)

TECHNIQUES EMPLOYED
- Current density-potential curves using a RDE
- Voltammetry
- Electrolisis at controlled potential and/or controlled current

CONCLUSIONS
- Cathodic material
- Value of the current density
- Type of the cell: divided or undivided
- Purity of the product: interferences with other cathodic processes
- Feasibility of the synthesis

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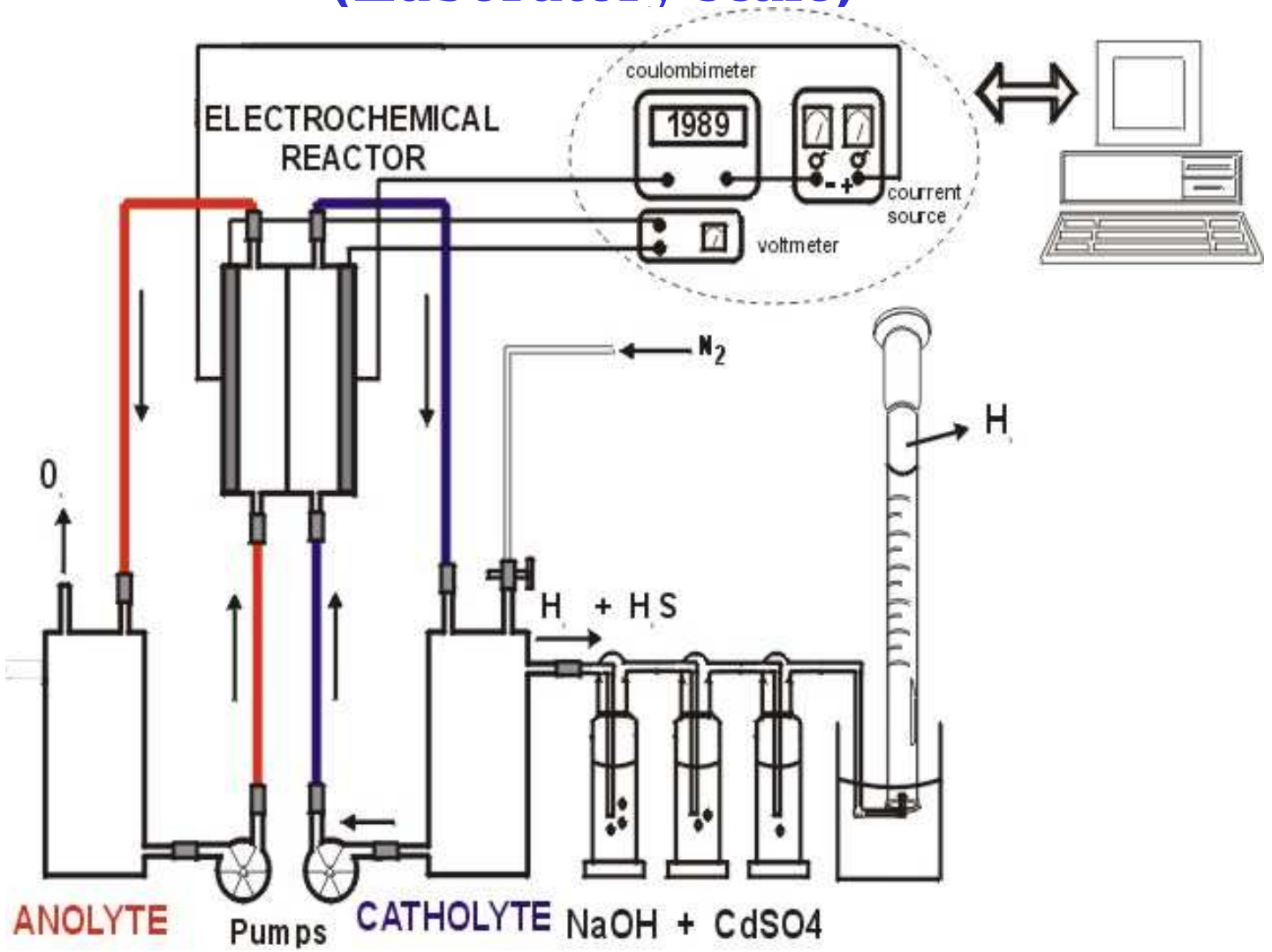
Electrochemical reduction of L-cystine

(Laboratory scale)



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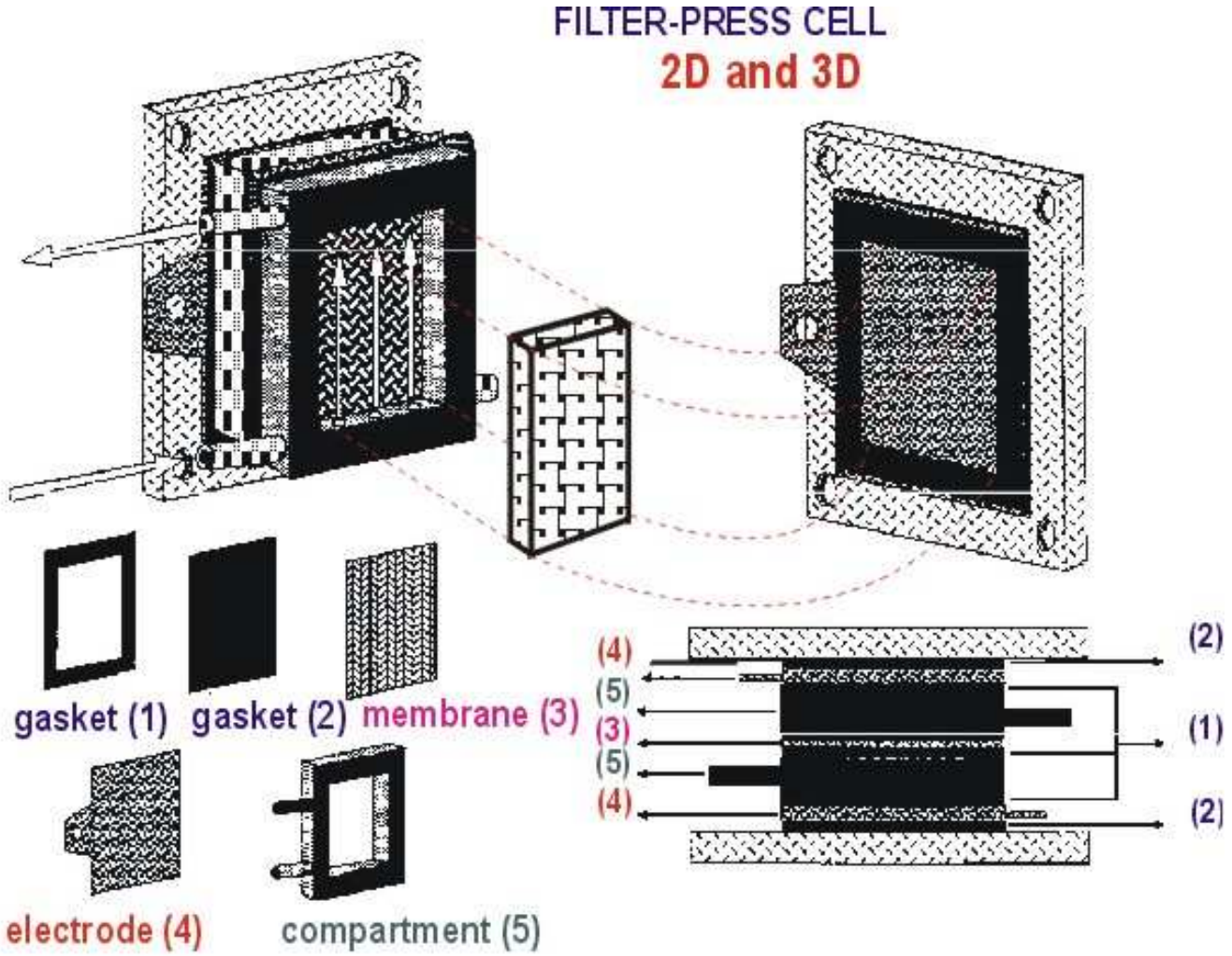
Electrochemical reduction of L-cystine

(Laboratory reactor UA16-UA20)



Electrode area 20 cm^2

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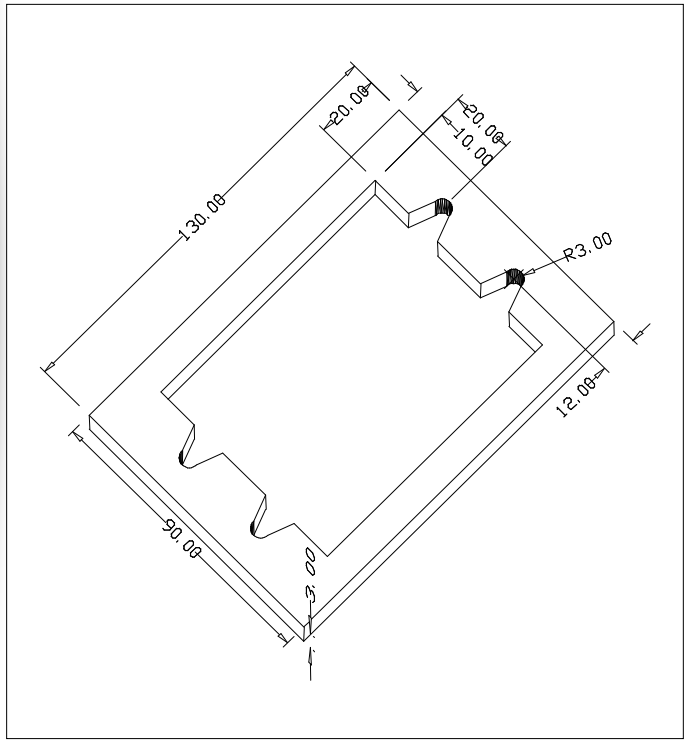
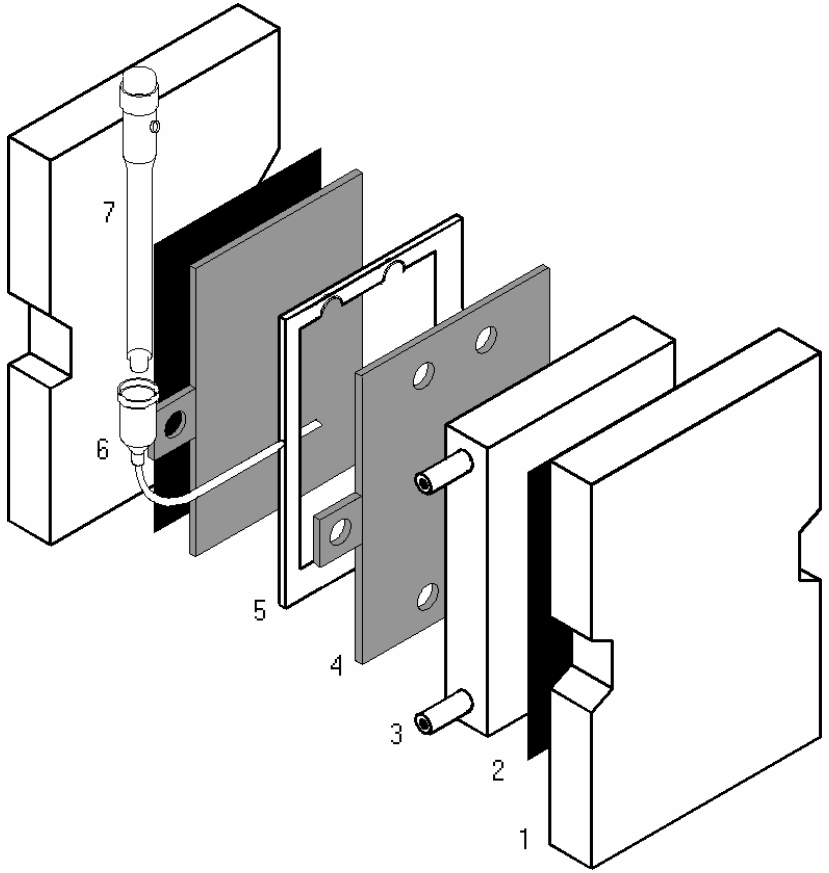
Electrochemical reduction of L-cystine

(Laboratory scale reactor UA63.03)





Electrode area 63 cm^2

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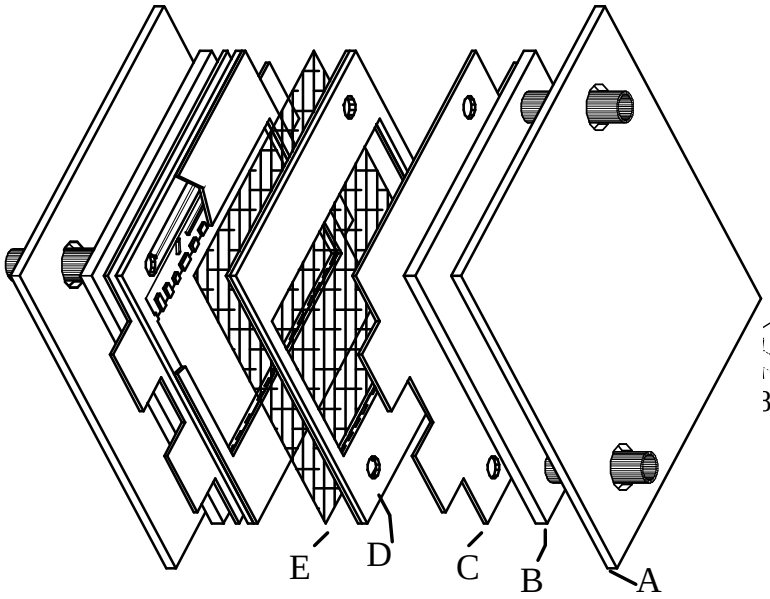
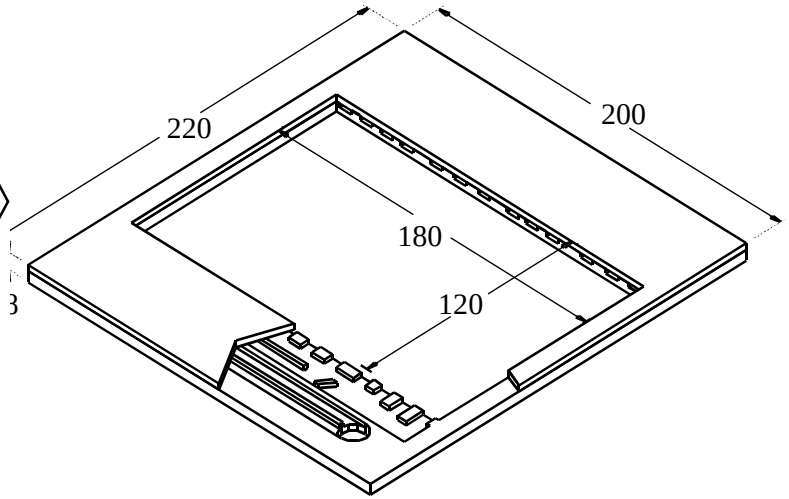
Electrochemical reduction of L-cystine

(Pre-Pilot reactor UA200.08)



Electrode area 200 cm^2



A=backplate, B=portplate C=electrode, D=compartment, E= membrane

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Electrochemical synthesis

(Laboratory and pre-pilot scale)

REACTOR:

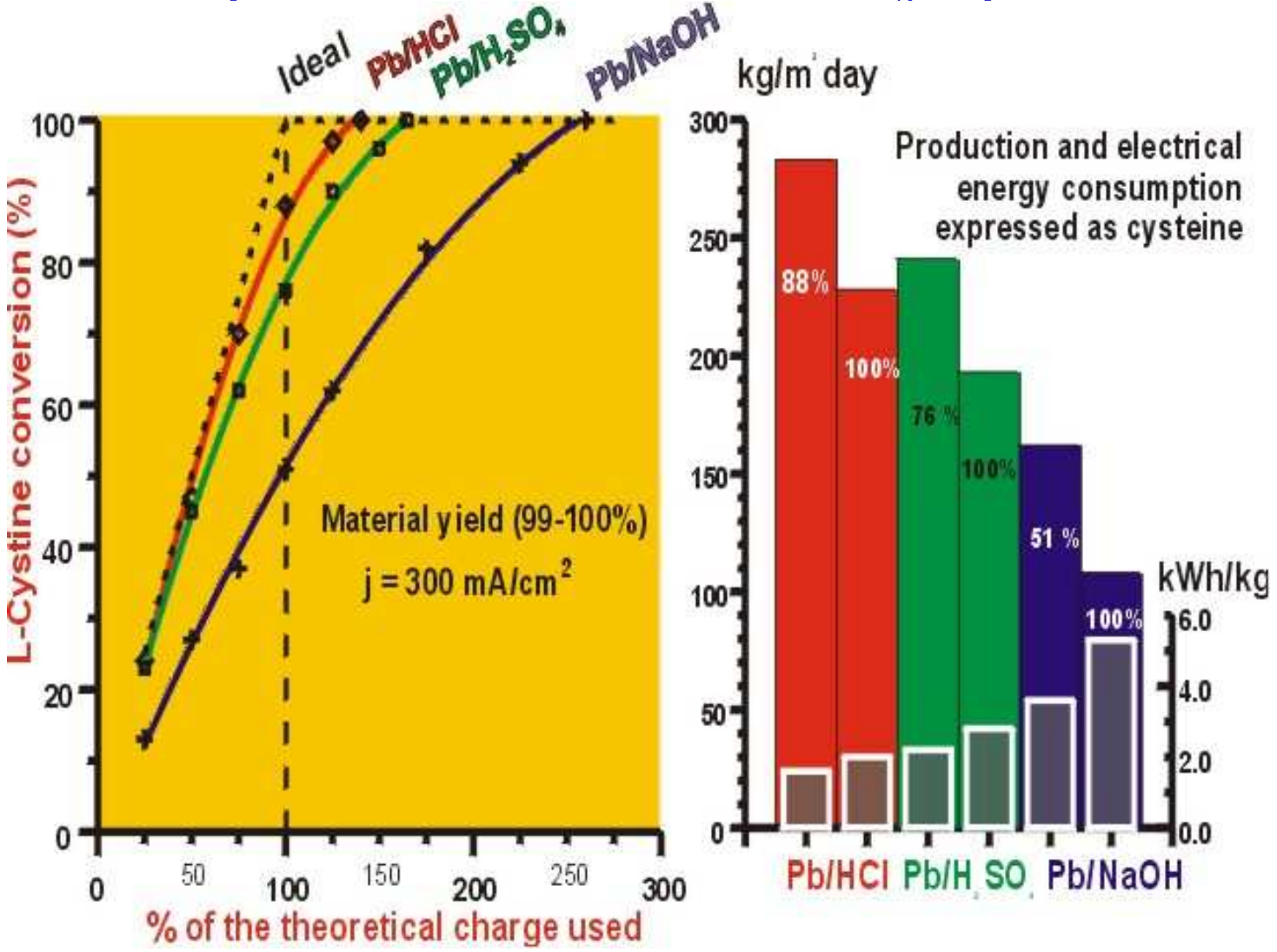
Divided filter-press reactors, provided with two 20 cm^2 (lab scale) and 200 cm^2 (pre-pilot scale) electrodes

PARAMETERS ANALYZED:

- **Current efficiency and material yield**
- **Cathodic and anodic materials**
- **Anodic reaction**
- **Applied current density and type of separator**
- **Influence of initial concentration of L-cystine and pH**
- **Purity of the final product**
- **Energetic cost (kWh/kg)**
- **Production vs current density used (kg/m^2 day)**
- **Preliminary conclusion about economical viability**

Electrochemical reduction of L-cystine

(Influence of the electrolyte)



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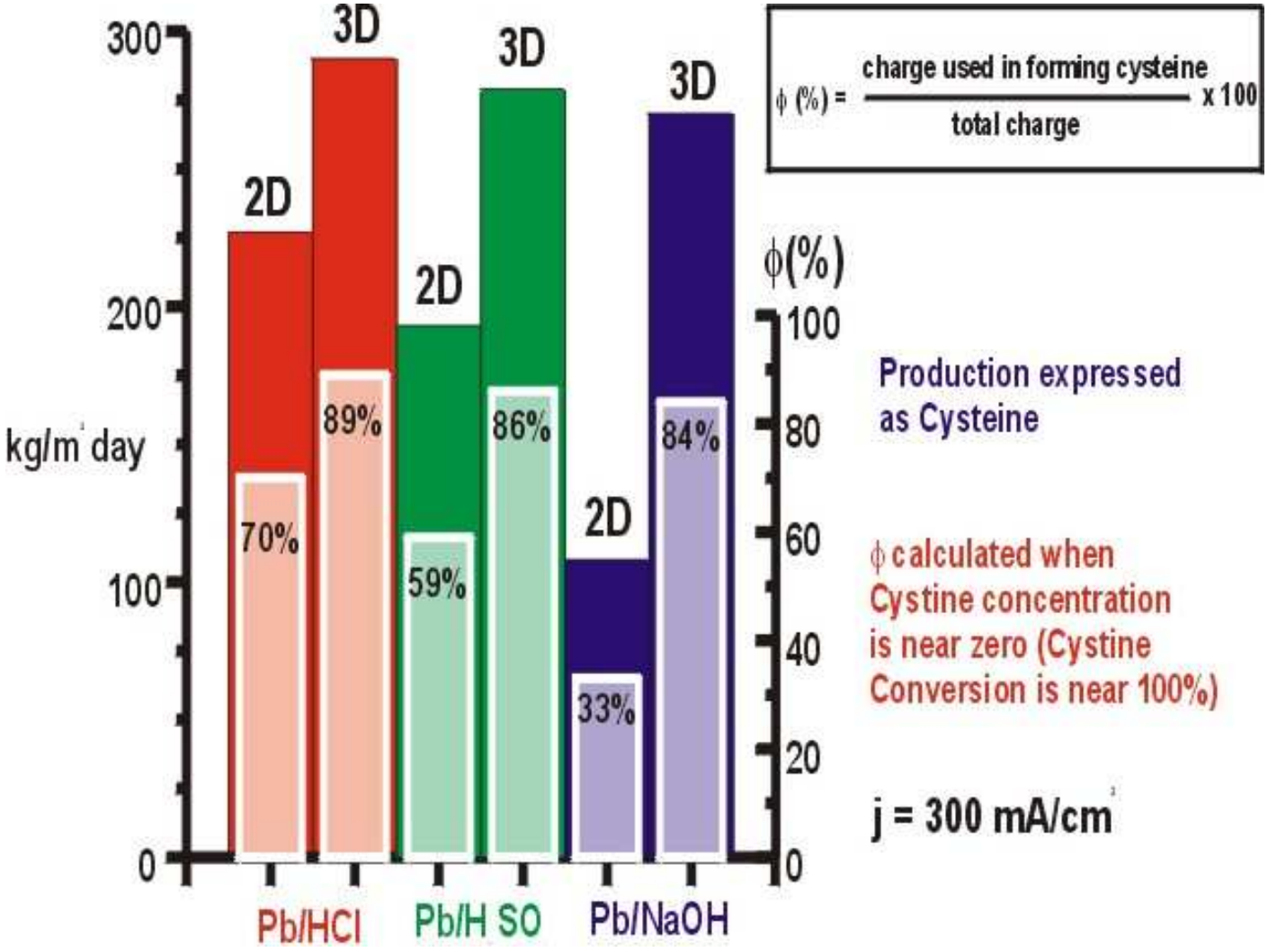
Electrochemical reduction of L-cystine

(Electrodes 2D vs 3D)



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Electrochemical synthesis

(Pre-industrial scale)

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REACTOR:

Divided filter-press cell with n electrodes of 1000 cm^2 and 3000 cm^2 geometric area

PARAMETERS STUDIED:

Electrical aspects

- **Monopolar vs bipolar stacks**
- **Serie or parallel electrical feed**

Long-term electrolysis

- **Components stability**
- **Final product quality**
- **Influence of the purity of the initial products**
- **Stops and events effects**
- **Treatment of the effluents**
- **Economical aspects of the process**
- **Book process**
- **Training of the future workers**

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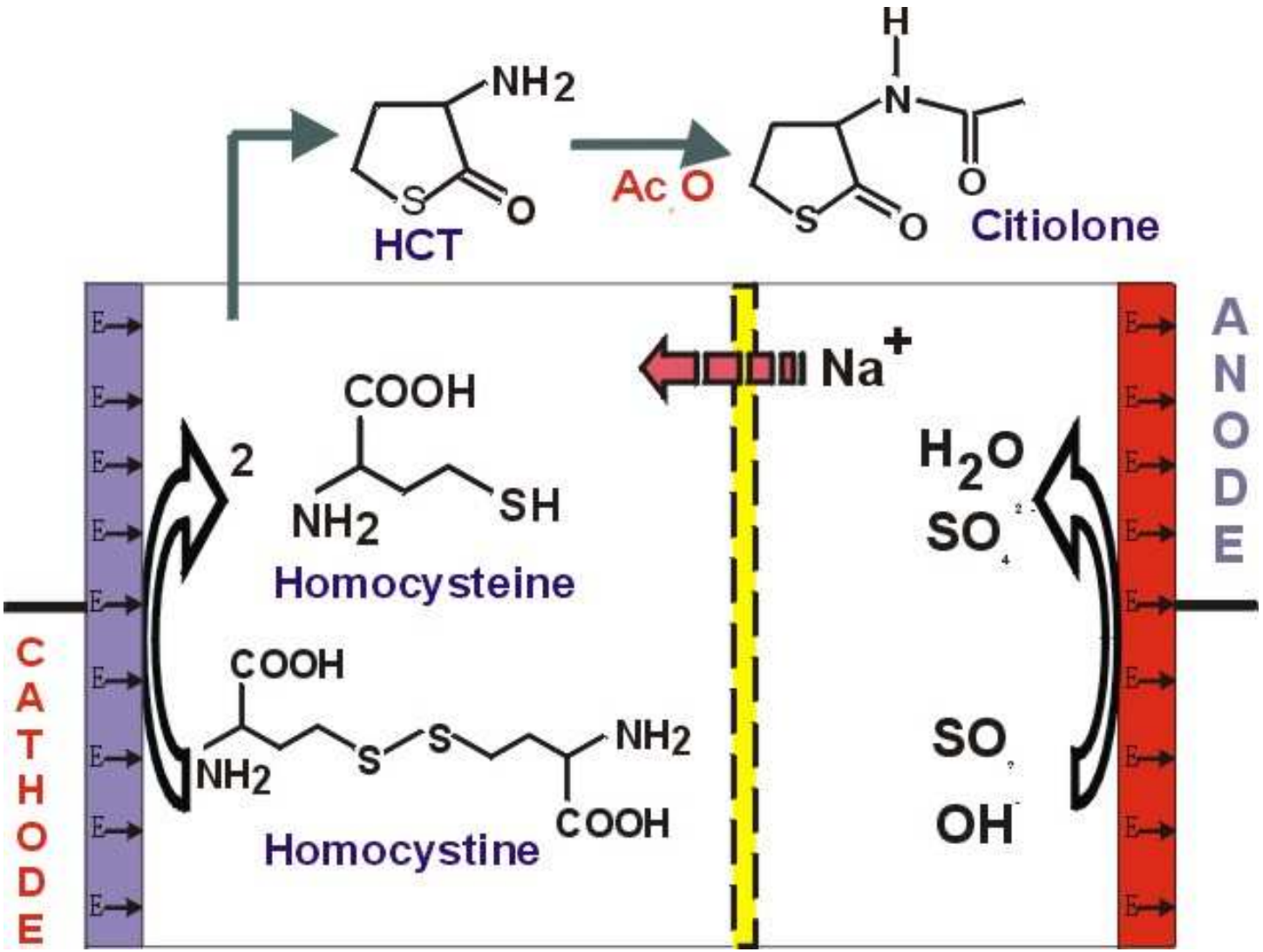
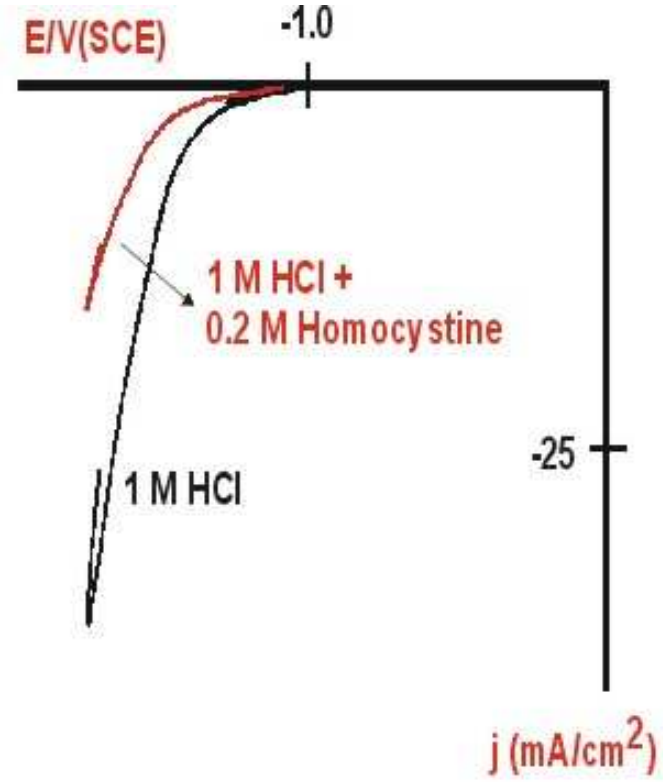
Electrochemical reduction of Homocystine



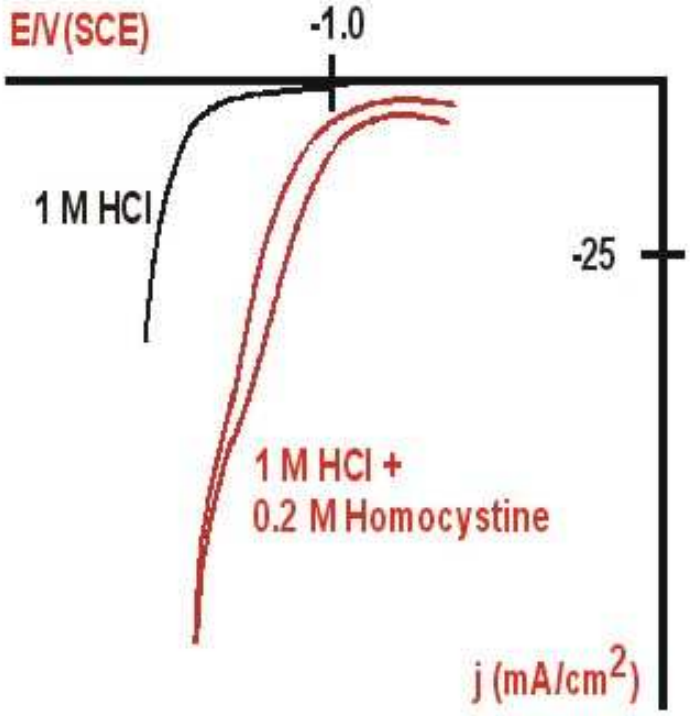
Electrochemical reduction of Homocystine

(Voltammetric study)



Voltammogram of Homocystine in HCl on a vitreous carbon electrode. v=50 mV/s. T=25°C

Voltammogram of Homocystine in HCl on a lead electrode. v=50 mV/s. T=25°C



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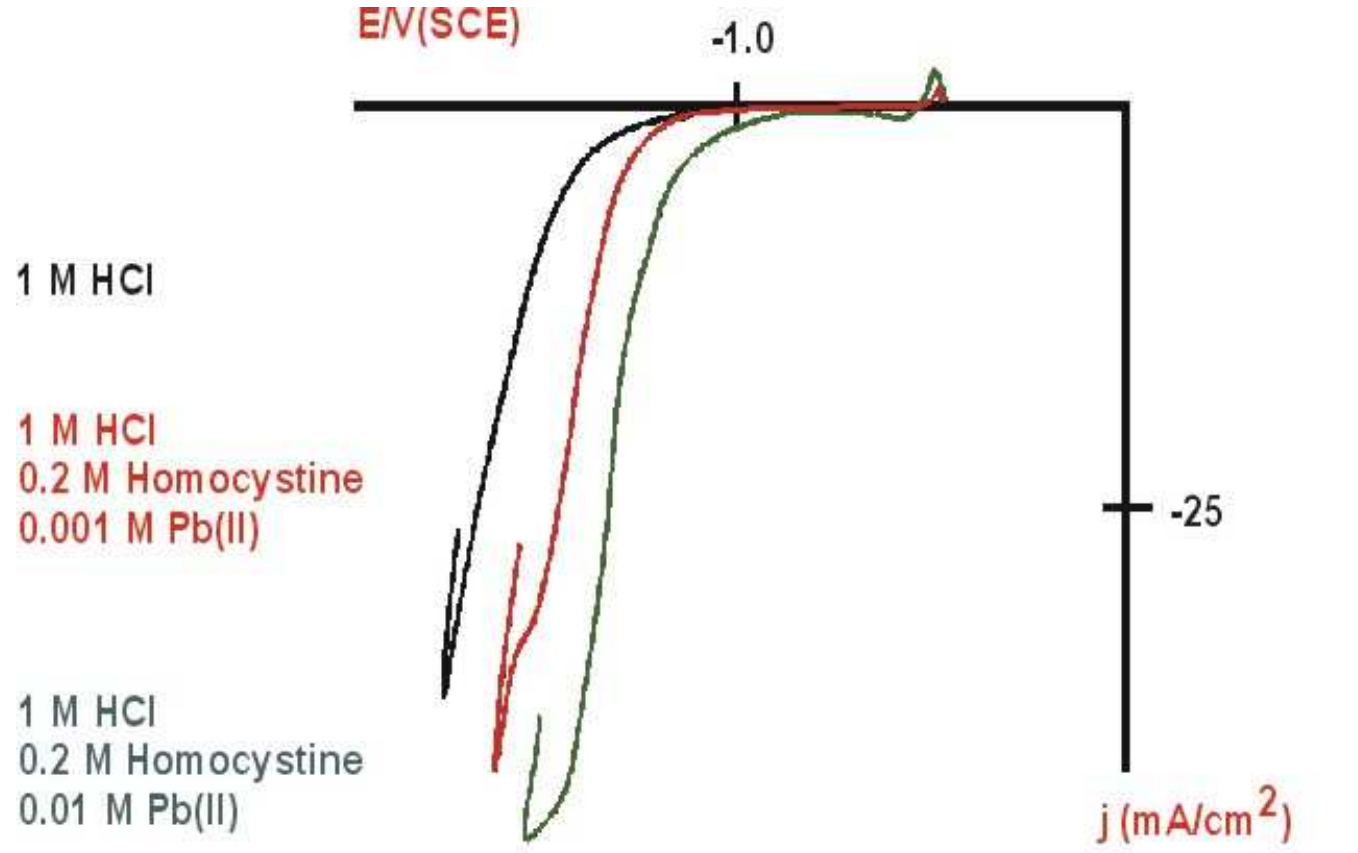
Electrochemical reduction of Homocystine

(Voltammetric study)



Voltammogram of Homocystine in HCl on a vitreous carbon electrode.
v=50 mV/s. T=25ºC

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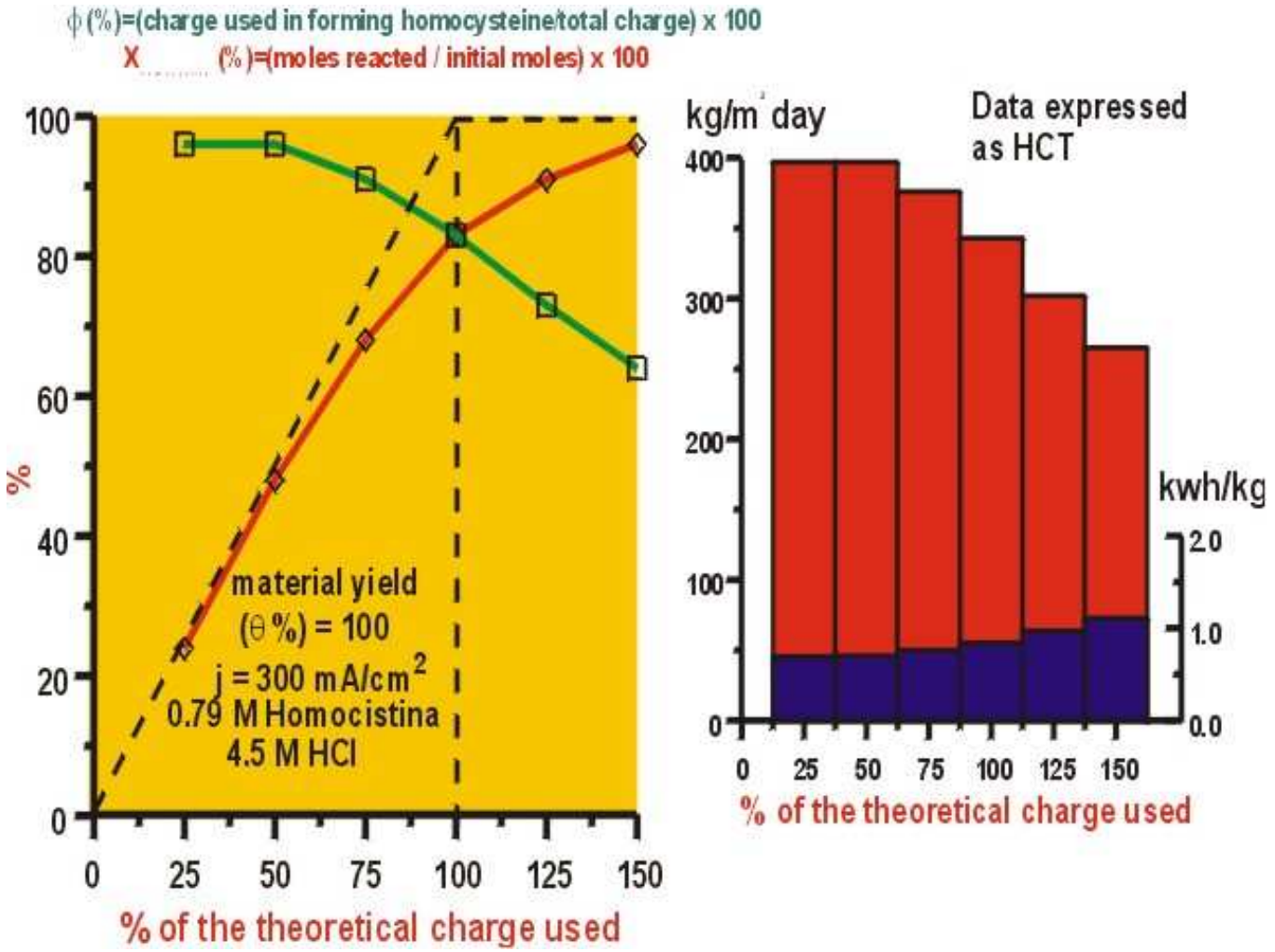
Electrochemical reduction of Homocystine

(Best conditions)



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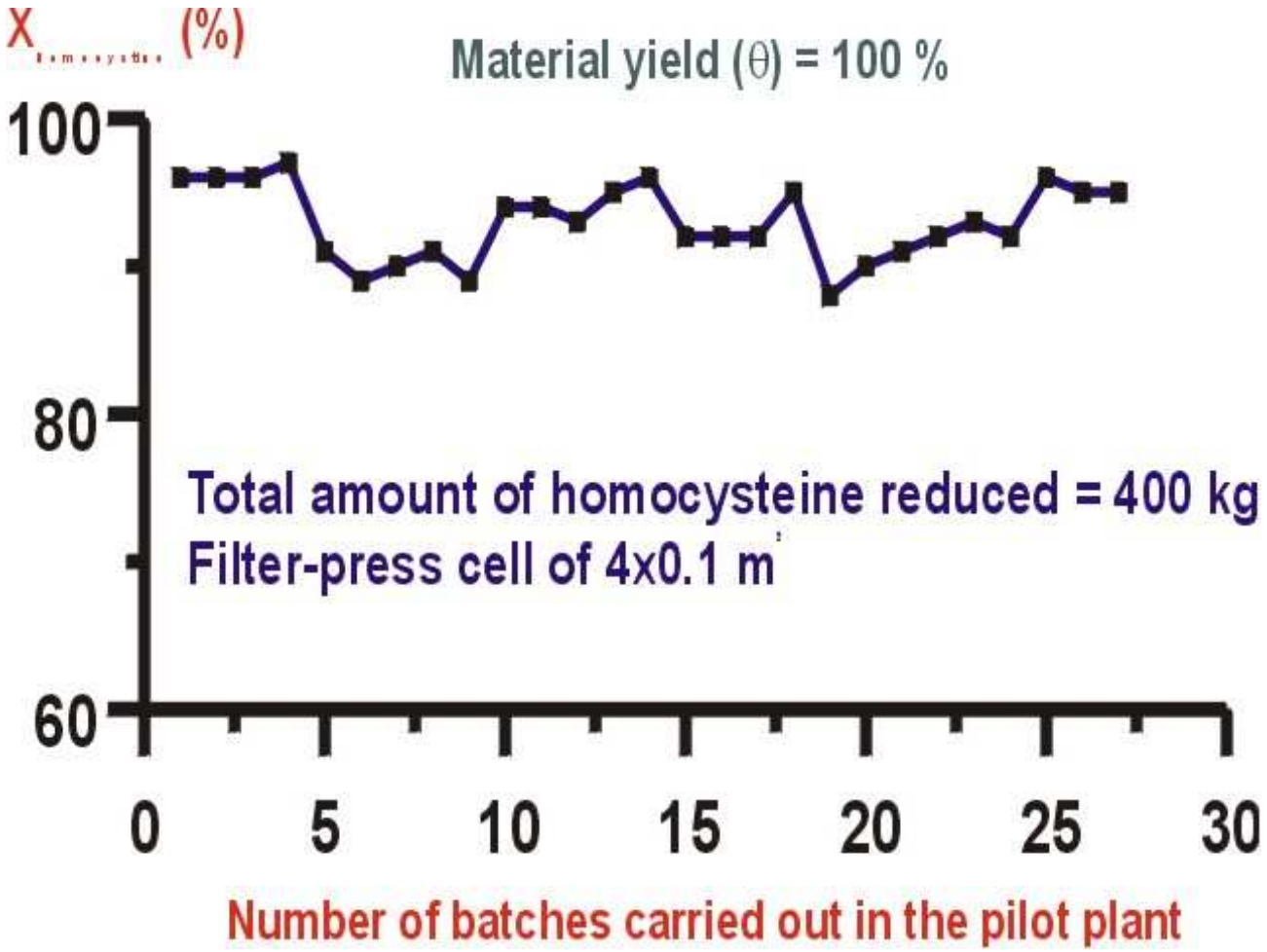
Electrochemical reduction of Homocystine

(Pilot plant)



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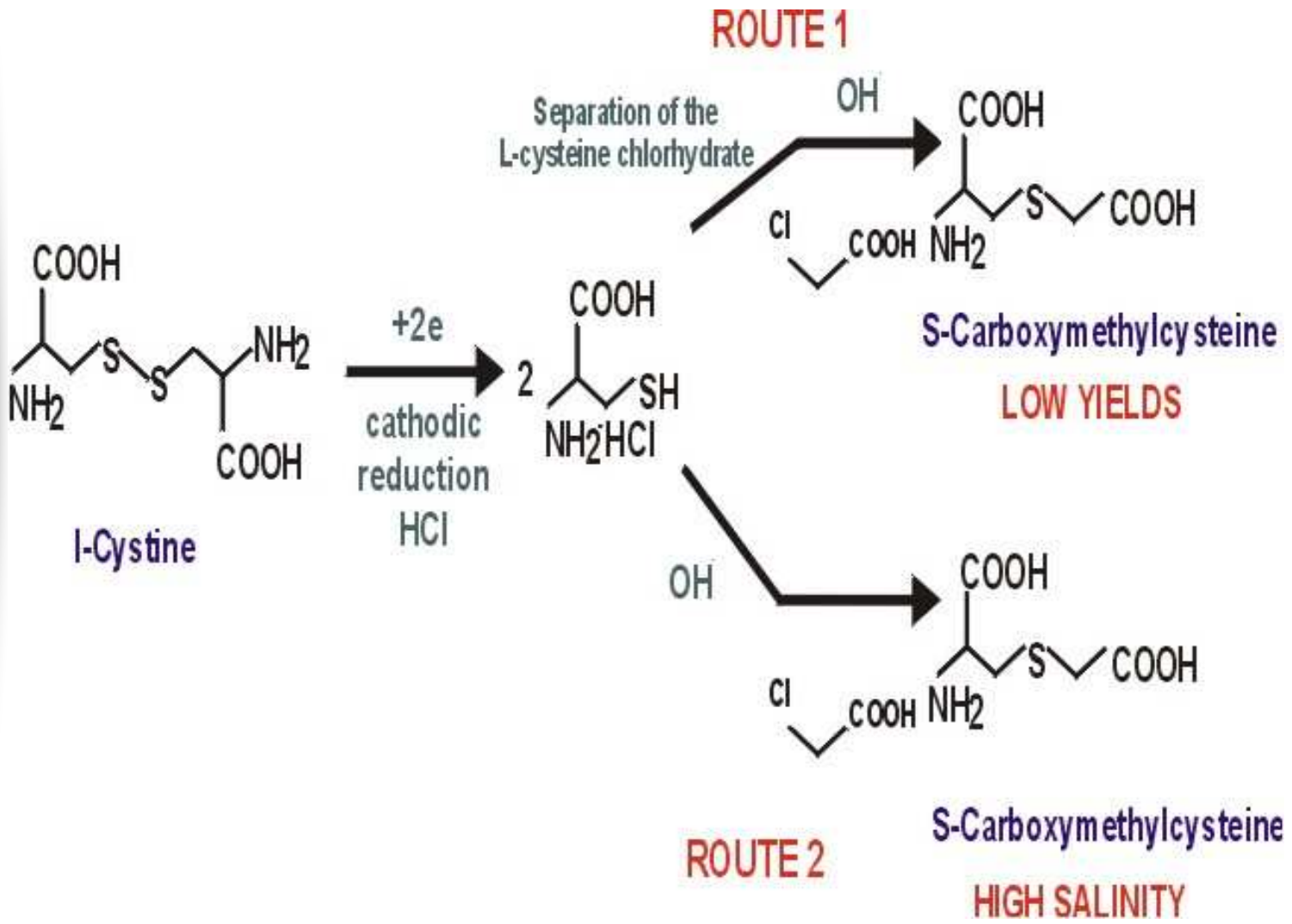
Electrochemical synthesis of S-carboxymethyl-L-cysteine

(Classical routes)



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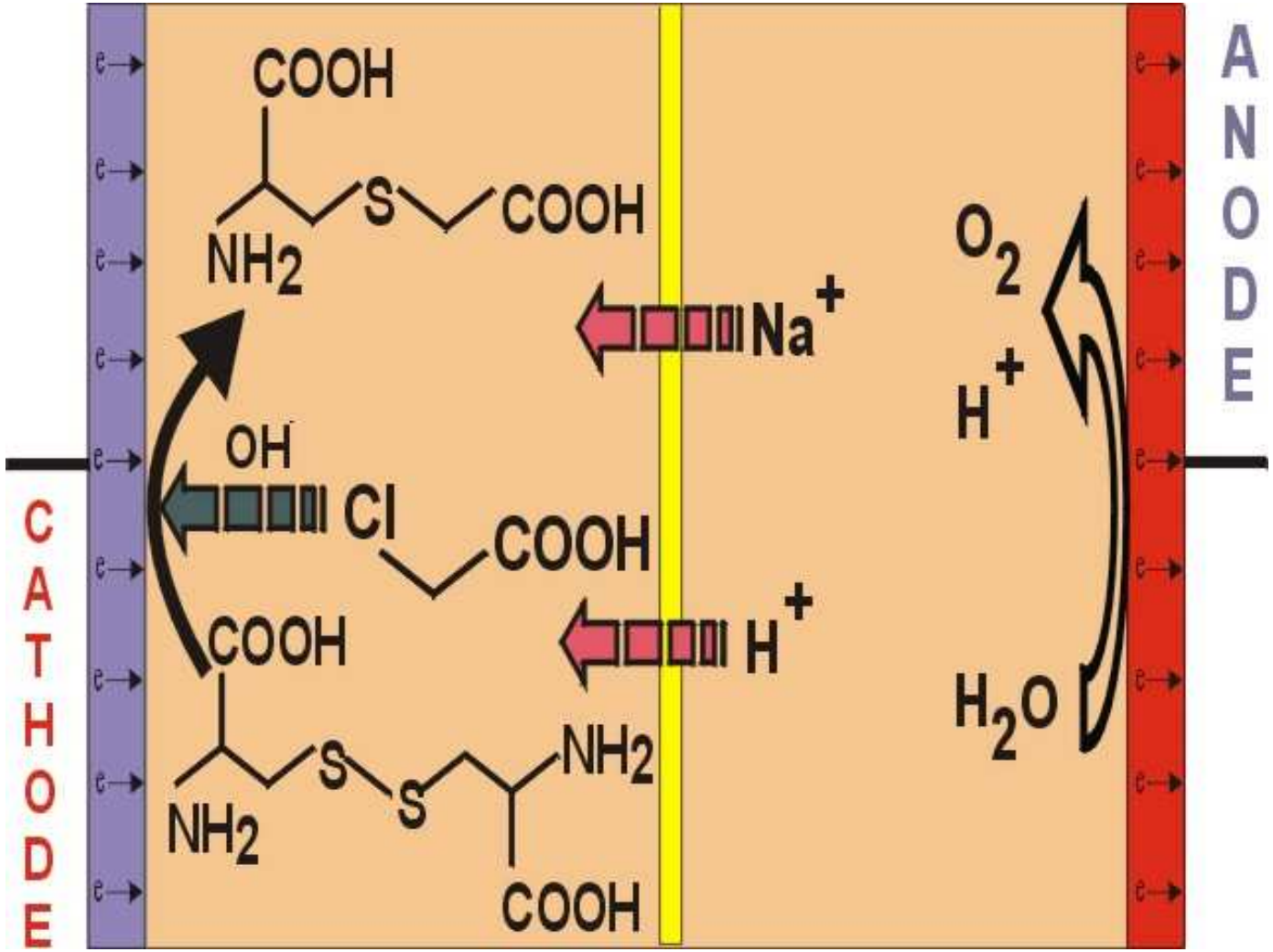
Electrochemical synthesis of S-carboxymethyl-L-cysteine

(Electrochemical route)



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Electrochemical synthesis of S-carboxymethyl-L-cysteine

(Best conditions)

CATHODE: Modified carbon felt electrode for obtaining high current efficiency

ANODE: Dimensionally stable anode (DSA)

CATHOLYTE: (0.8-1.3)M L-cystine in NaOH(pH ε[8-13.5])

ANOLYTE: Aqueous solution of Na_2SO_4

SEPARATOR: Cationic membrane: Neosepta CMX

TEMPERATURE: 40-50ºC

CURRENT DENSITY: 250-2000 A/m^2

Final point of electrolisis: 115-125% of the theoretical charge (2F/mol)

L-cystine in the final catholyte: <0.5%

Energetic cost: 1.0 kWh/kg

Production: 190 kg/m^2 day

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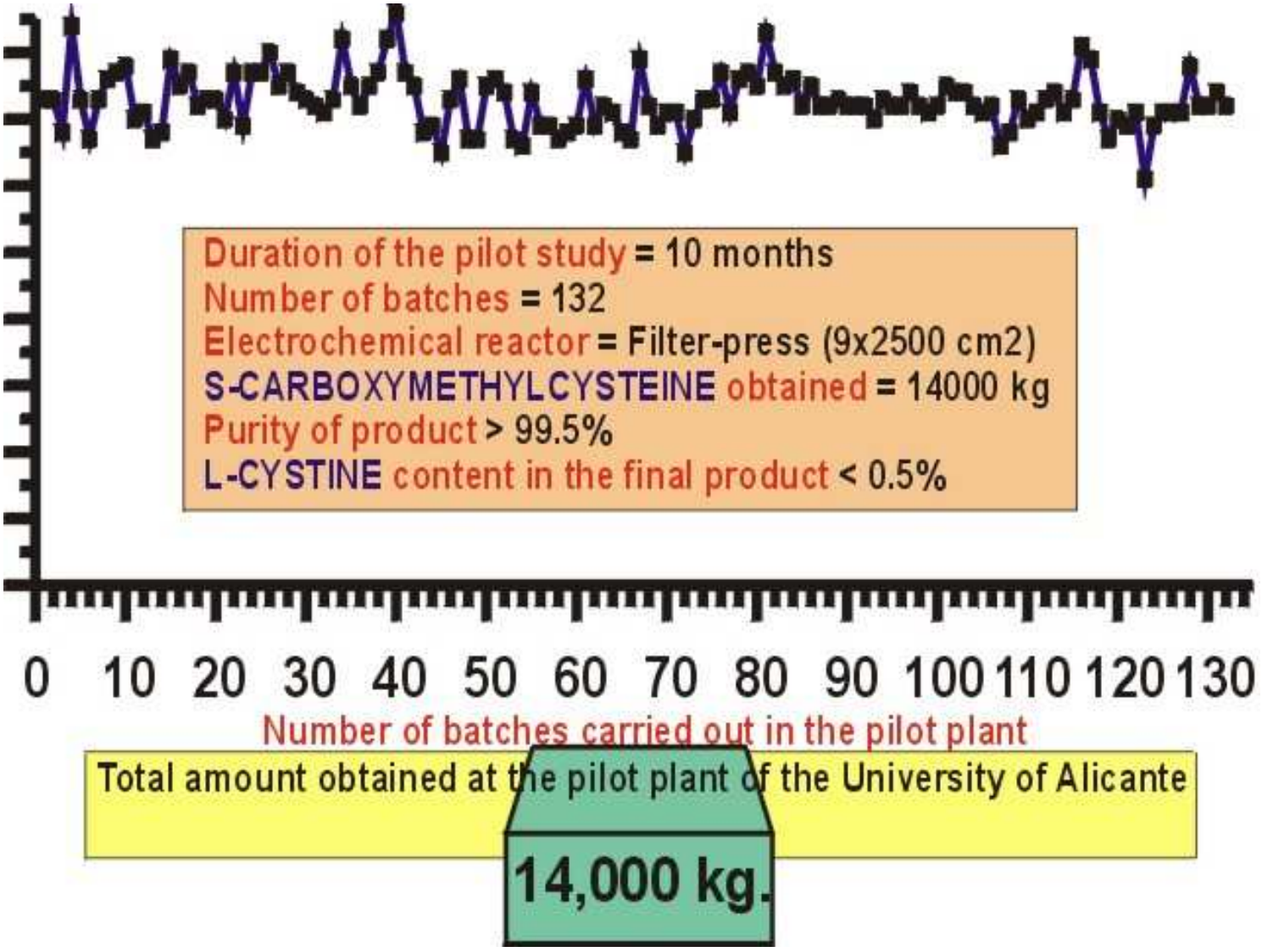
Electrochemical synthesis of S-carboxymethyl-L-cysteine

(Pre-industrial scale)



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Electrochemical synthesis of S-carboxymethyl-L-cysteine

(Final Conclusions)

QUALITY OF THE FINAL PRODUCT

Contents:	**>98.5%**
Specific rotation :(c=10%, pH=6,3)	**-33.0 - -35.0**
Clarity:	**transparent**
Residue on ingintion:	**<0.30%**
Chloride level:	**<0.15%**
Cystine level:	**≤0.5%**
Heavy metals:	**<10 ppm**

CONCLUSIONS

The use of the electrochemical technology has permitted the development of a new procedure for obtaining a very interesting pharmaceutical product S-Carboxymethyl-L-cysteine avoinding the inconvience of using metals reductans and improving the purity of the final product.

It has been demostrated that is possible, starting from the voltammetric study to scale up an elecrochemical process to the industrial level and to carry out the synthesis of 14,000 kg of a pharmaceutical product in a University laboratory with the help and collaboration of a Company

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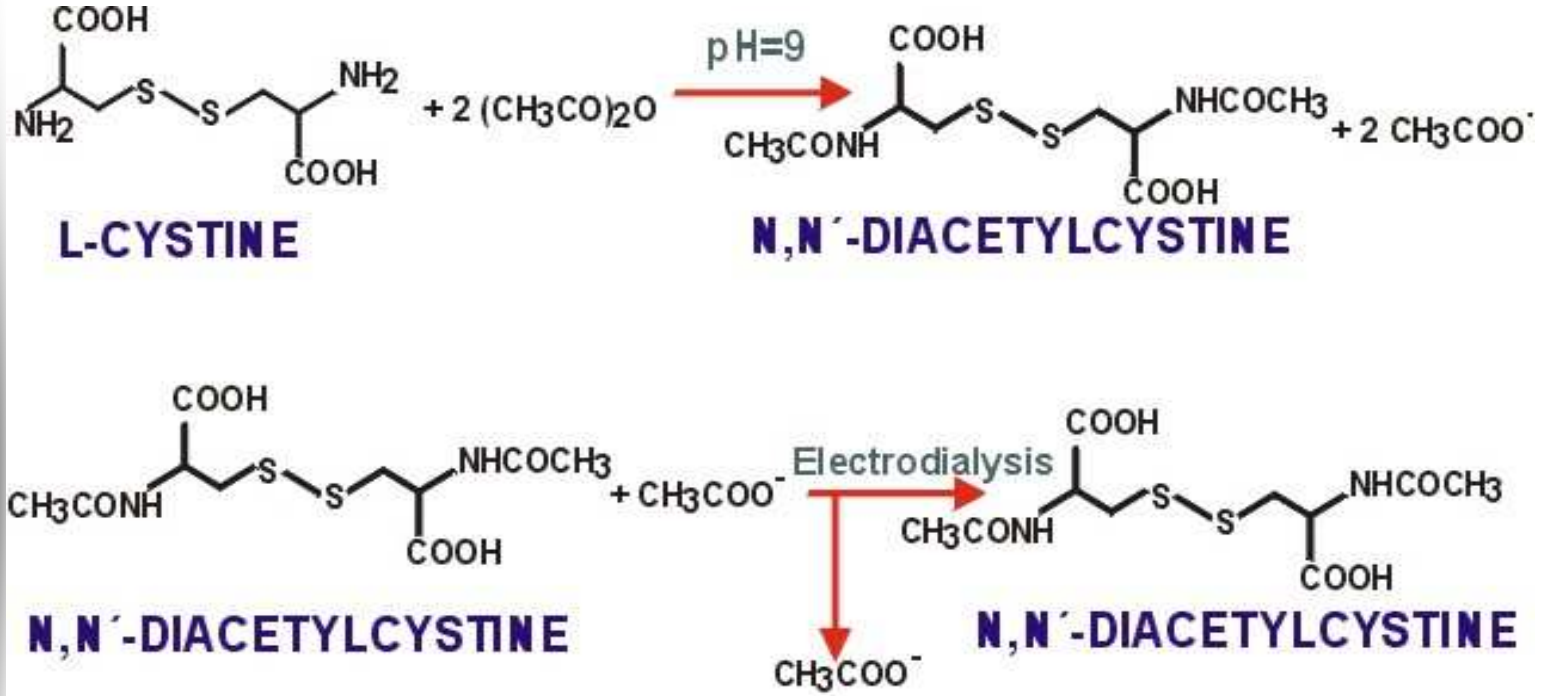
Electrochemical synthesis of N-acetyl-L-cysteine

(Electrochemical route)



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Electrochemical synthesis of N-acetyl-L-cysteine

(Simultaneous reduction and removal of salts)

REACTOR:	**Four compartments Area 200 cm^2**
CATHODE:	**Modified carbon felt electrode for obtaining high current efficiency**
ANODE:	**Dimensionally stable anode (DSA)**
Catholite/diluate:	**Stream coming from acetylation step**
Anolyte/Concentrate:	**0.1 M $NaCH_3COO$**
SEPARATORS:	**Cationic membrane:Nafion 117**
	Anionic membrane: Tokuyama ACS
CURRENT DENSITY:	**250-2000 A/m^2**

QUALITY OF THE FINAL PRODUCT

Contents:	**88.2-100.2%**
Specific rotation:	**+21º - +27º**
Residue on ignition:	**<0.5%**
Loss on drying:	**<1,0%**
Heavy metals:	**<10ppm**
Arsenic:	**< 5ppm**

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Electrochemical synthesis

(Main advantages)

- Avoid the use of reducing agents (powder metals)
- High selectivity and yield
- Isolation of intermediates are not required
- Small amount of undesired products
- Non or very low environmental impact
- Safety in handling of reactants and products (neither hydrogen nor metals ions formed)
- Better quality of the final product
- Electron is always available

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Group Members

(1988-?)

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- Dr. Vicente García García
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- Dr. Guillermo Codina Ripoll
- Dr. Ángel José Frías Ferrer
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Lda. Verónica Sáez Bernal
Ldo. José Ramón Pérez Mallol
Ldo. Jesús Menéndez Fuello
Ing. Francisco Gallud Martínez

- D. Miguel Ángel Pastor Durá
- D. Javier Medina Ruiz
- Dña. Dolores García Bezares

AKNOWLEDGEMENTS

- Prodesfarma S. A.
- Almu S. A.
- DSM Deretil
- I.D. Electroquímica S.L.