AN INTRODUCTION TO MICROFLUIDICS :

Lecture n°4

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Outline of Lecture 1

1 - History and prospectives of microfluidics
2 - Microsystems and macroscopic approach.
3 - The spectacular changes of the balances of forces as we go to the small world.

Outline of Lecture 2

- The fluid mechanics of microfluidics
- Digital microfluidics

Outline of Lecture 3

1 - Basic notions on diffusive processes
2 - Micromixing
3 - Microreactors.

Outline of Lecture 4

1 - Electroosmosis, electrophoresis
2 - Miniaturisation of separation systems
3 - An example of a lab on a chip

Electrophoresis : Charged particles migrate

Electroosmose : Fluid is driven by charged layers close to the walls

Diélectrophoresis : Particles move under the effect a gradient of Electric field.

Using electric fields in miniaturized systems is easy because

$$E \sim V/l$$

A FEW THINGS TO KNOW ABOUT ELECTROKINETICS

1 - Electrophoresis

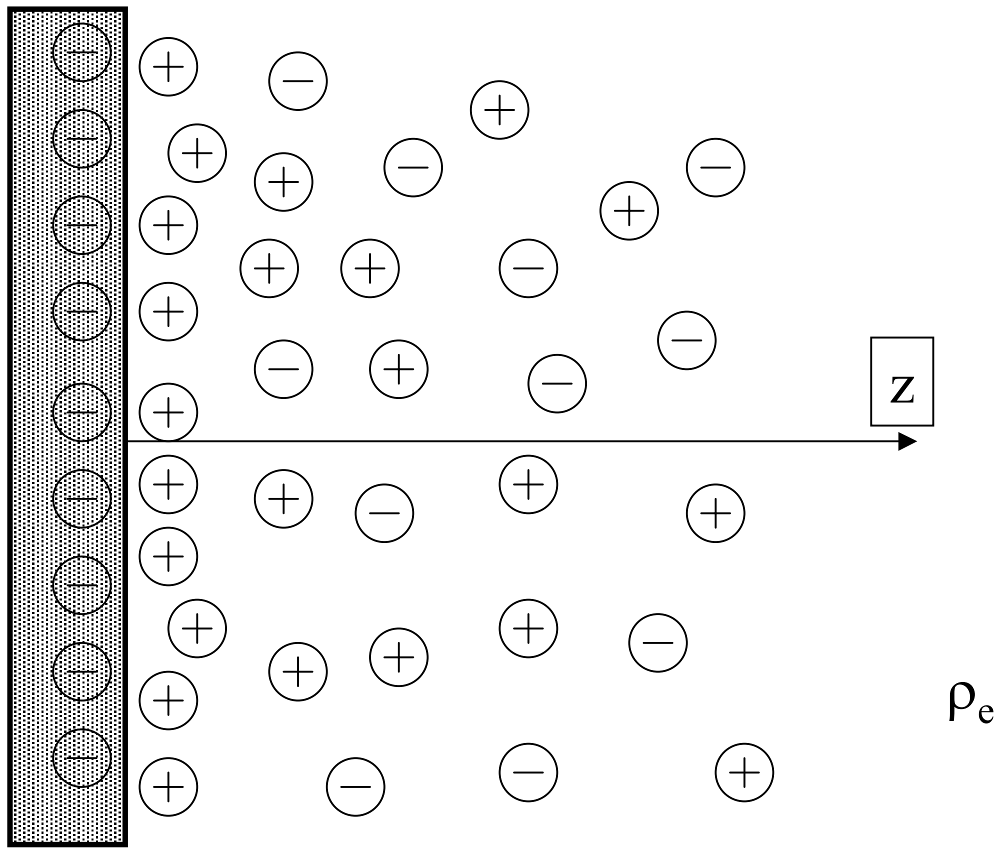
Coulomb law $$F = qE$$

In a fluid, the flow equations are

$$qE - F_v = m\frac{dV}{dt} \approx 0 \qquad F_V = 6\pi R\mu V$$

$$\boxed{V = \mu_e E} \quad with \quad \mu_e = \frac{q}{6\pi R\mu}$$

Double electric layer



CHARACTERISTICS OF THE DEBYE HUCKEL LAYER

Electrical Potential

$$\psi = \varsigma e^{-z/\lambda_D}$$

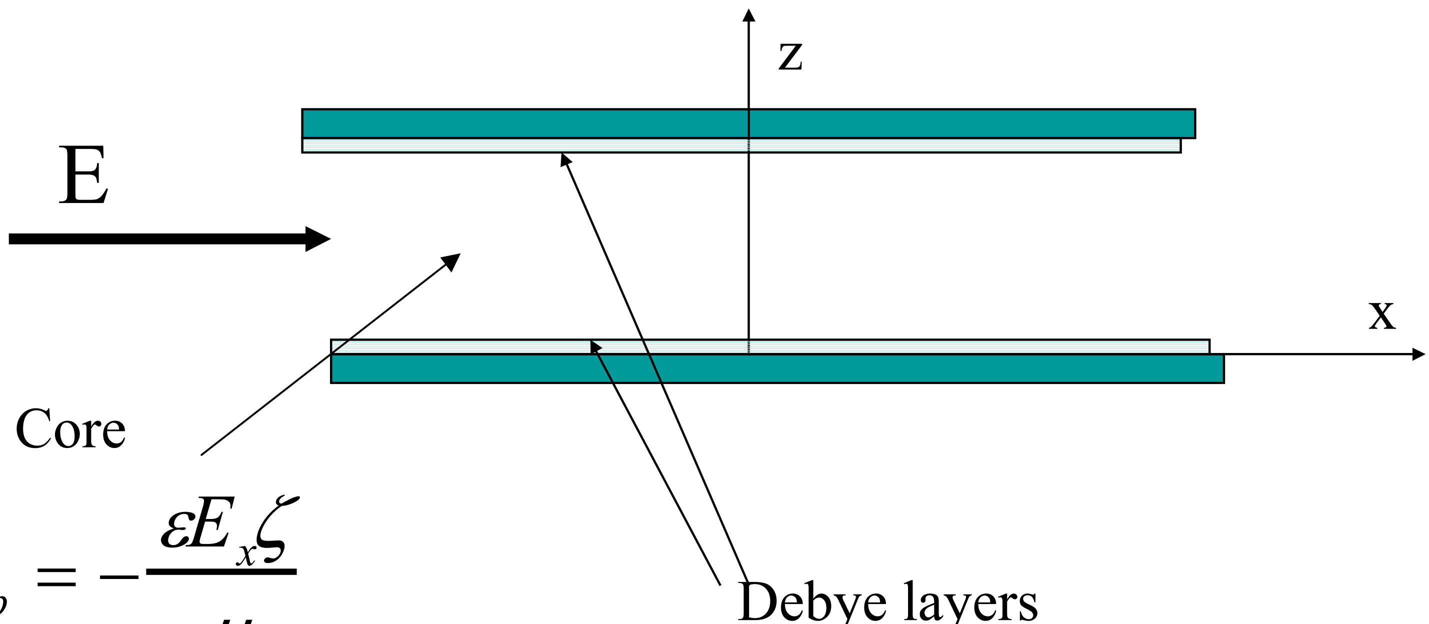
Thickness

$$\lambda_D = \sqrt{\frac{D\varepsilon}{\sigma}}$$

Debye-Huckel length

ELECTROOSMOSIS

3) <u>Electroosmosis</u> = Flow of an electrolyte produced by the presence of an electric field driving the charged layer close to the walls



$$u_p = -\frac{\varepsilon E_x \zeta}{\mu}$$

$$u_p = -\frac{\varepsilon E_x \zeta}{\mu}$$

Vitesse de Smoluchowsky

STREAMING POTENTIAL

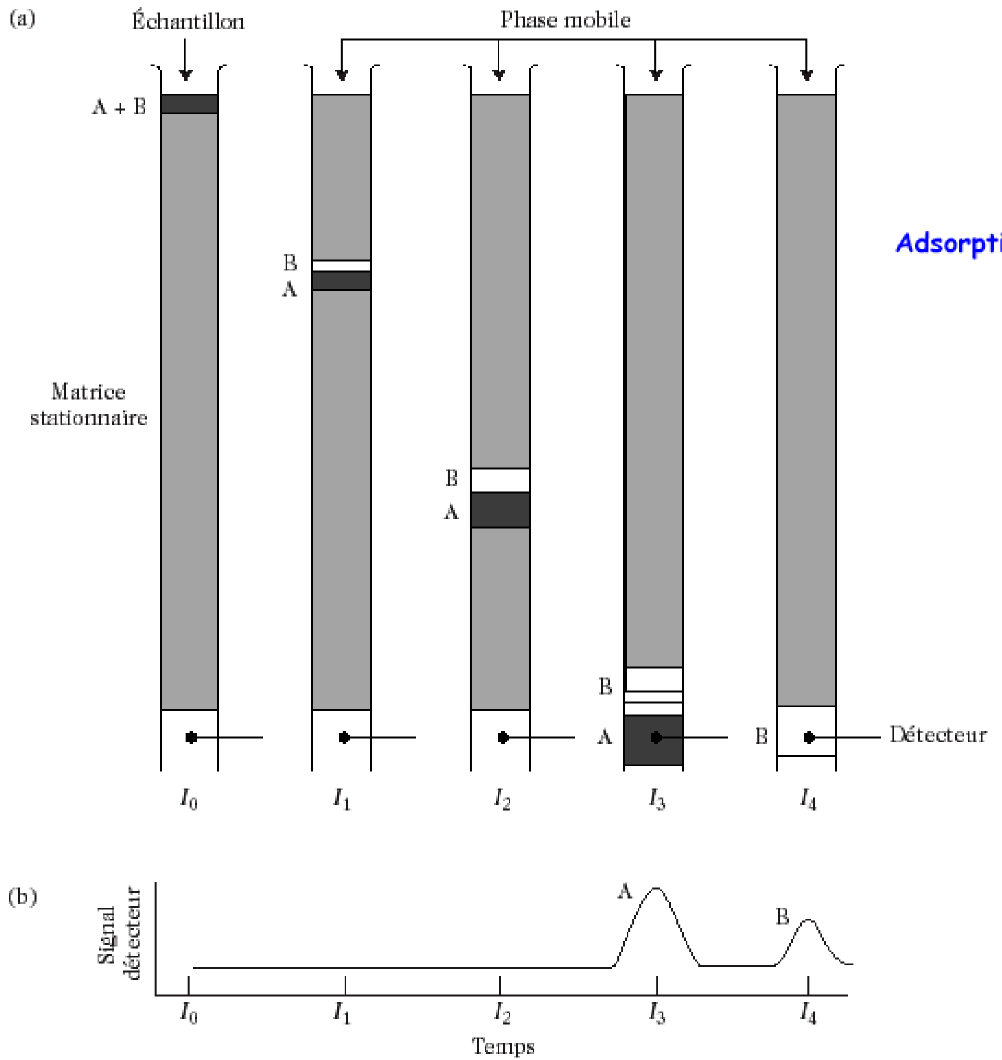
The inverse effect of electroosmosis

A flow generates an electric field

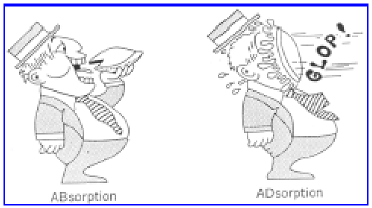
Various fields requiring separation sciences

- Pharmaceutical and other various industries
- Public health
- Food security (involves environment, agriculture, fishing, food prodution industry, packaging...)
- Environmental protection
- Safety of manufactured products (ex: toys for infants)
- Frauds and counterfeiting
- Doping
- Historical heritage, archeology

Principle of chromatography

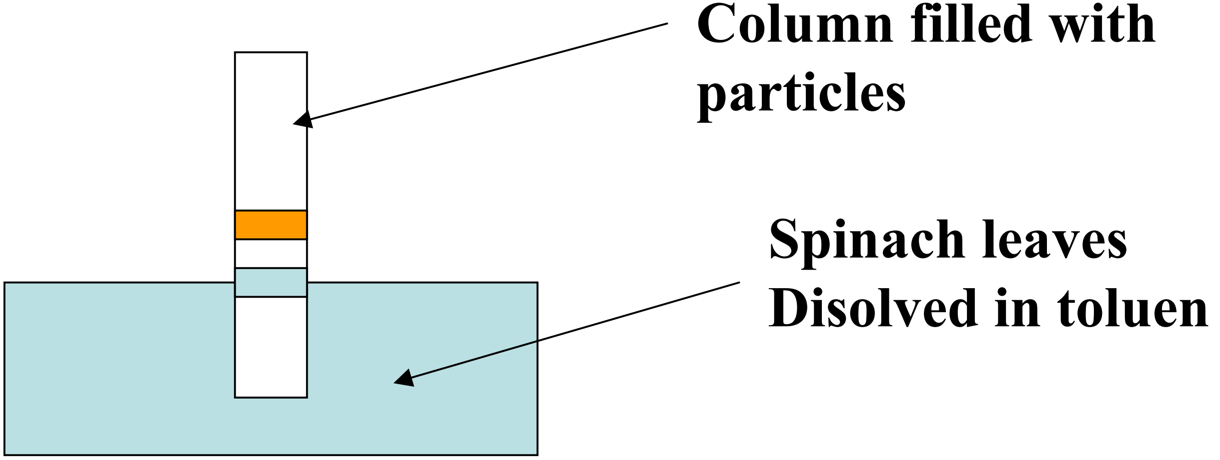


Adsorption chromatography

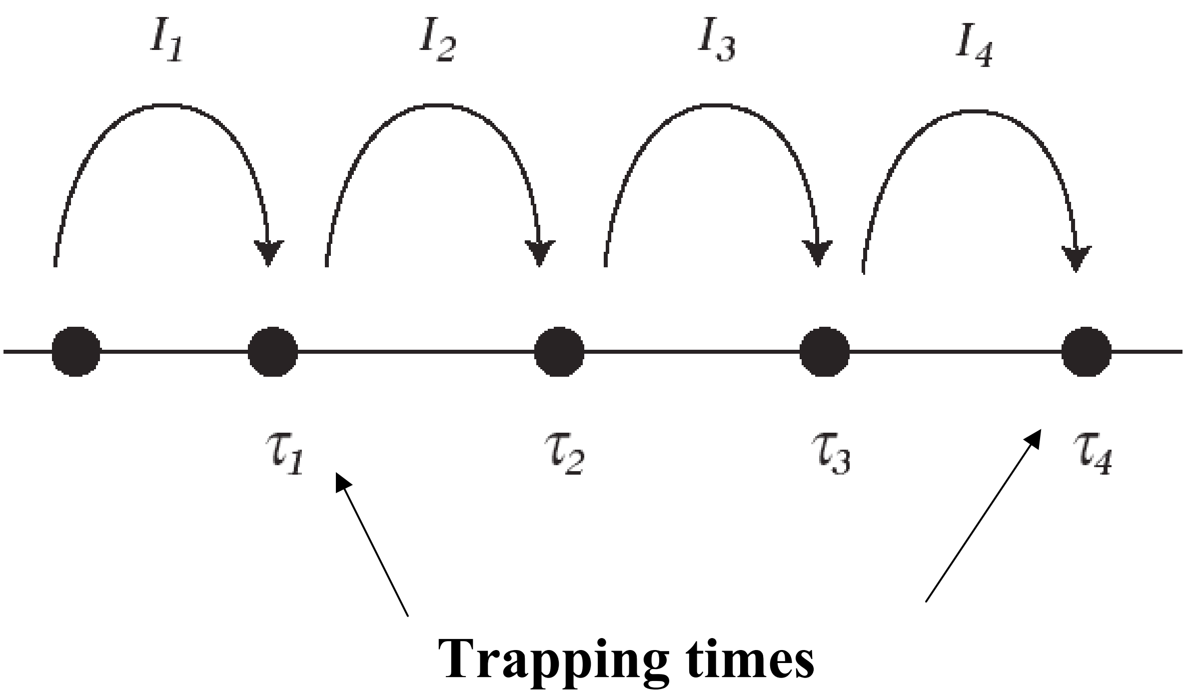


Microfluidics and separation techniques

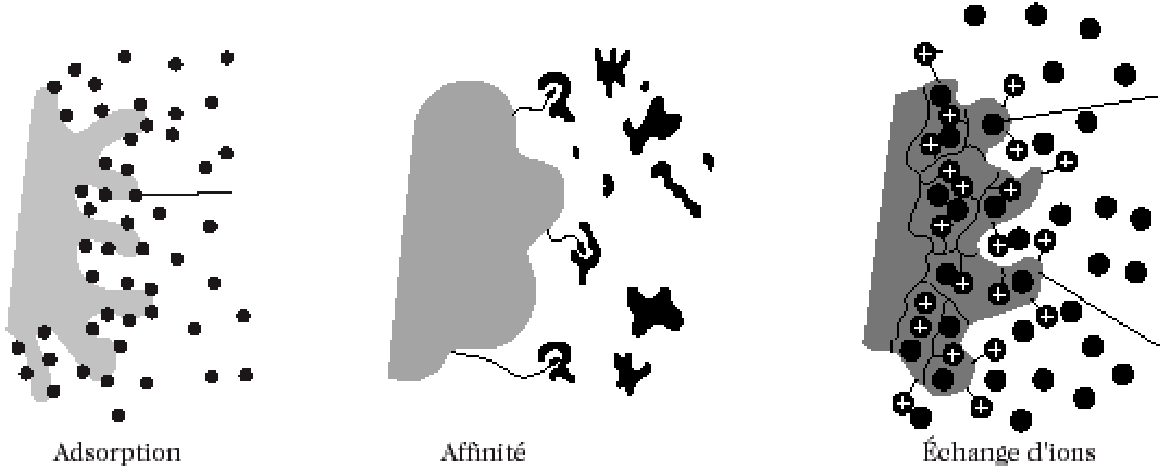
The first separation experiment was done by Tswett (1902)
This led to the discovery of chlorophylle.



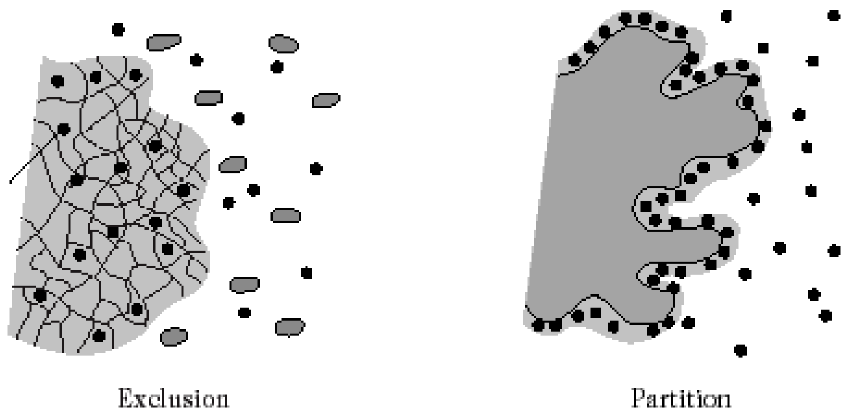
Statistical model for chromatography



5 fundamental types of chromatography

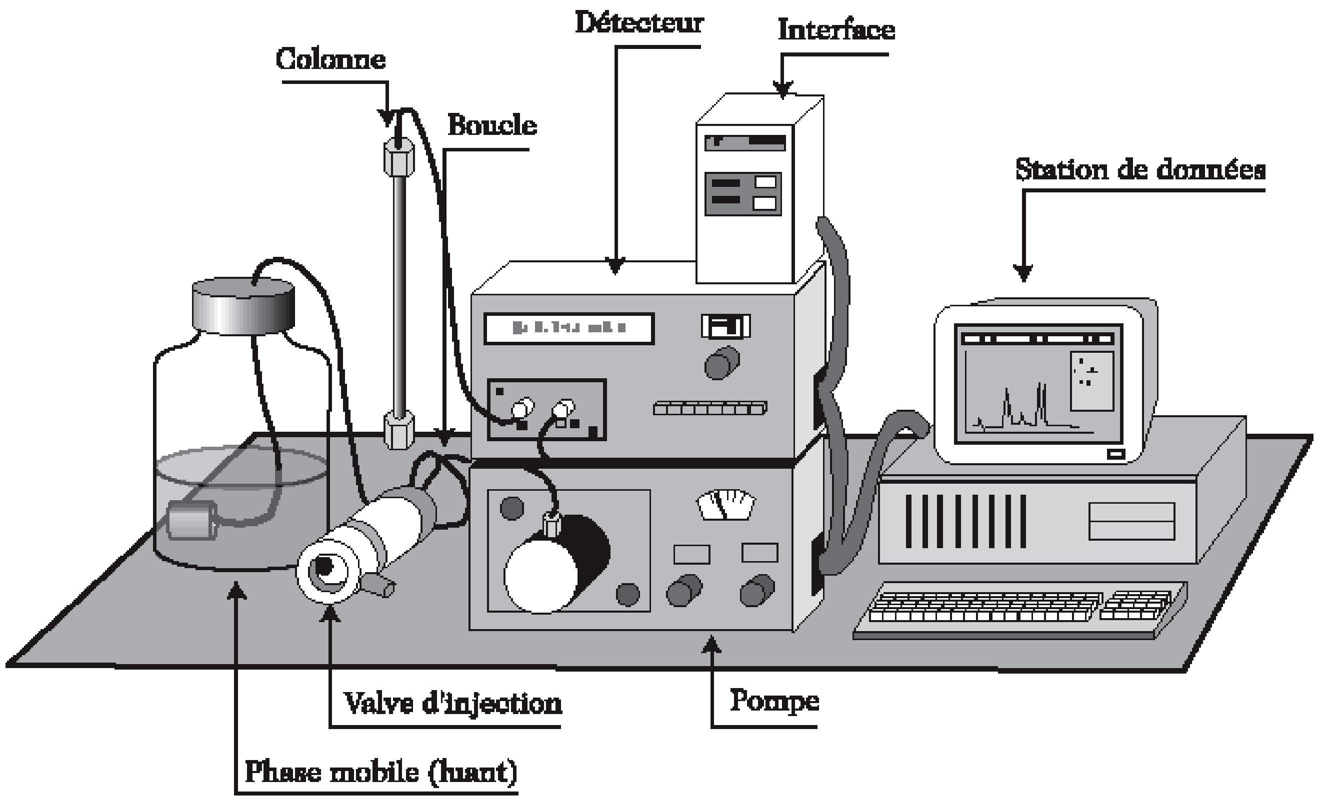


(a)



(b)

A typical equipment for HPLC



Electrophoretic separation

For an isolated particle of charge q, mass m, Coulomb force reads :

$$F = qE$$

In a fluid, the charged particle move according to the law :

$$qE - F_v = m\frac{dV}{dt} \approx 0 \qquad F_V = 6\pi R\mu V$$

Viscous friction

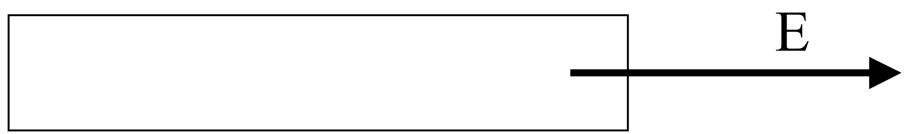
Therefore

$$V = \mu_e E \quad where \quad \mu_e = \frac{q}{6\pi R\eta}$$

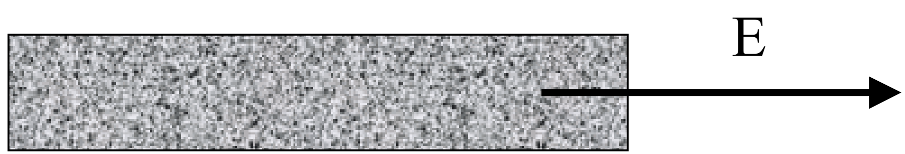
Seperation is feasible, because ions with different ratio q/R will migrate at different speeds

Separation techniques using electric fields

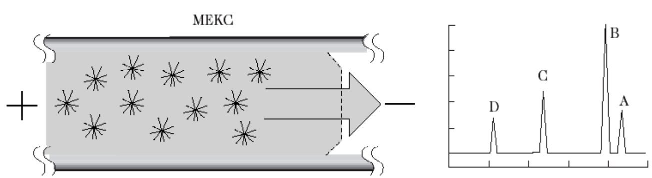
– FSCE : Electrophoresis in a free medium



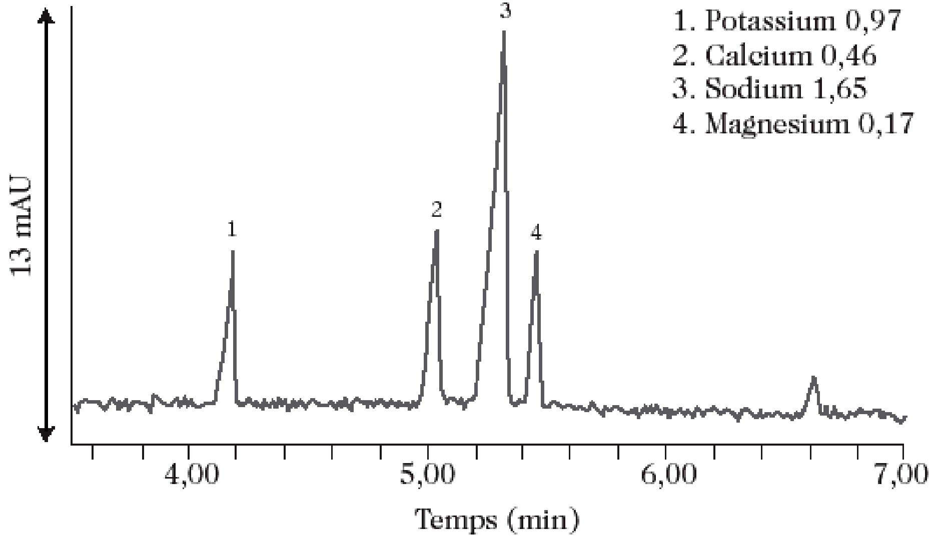
- CEC : Capillary Electro Chromatography (a gel is used)



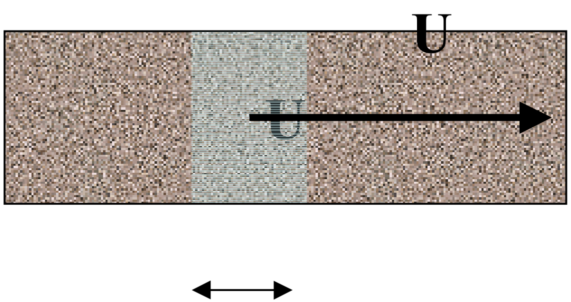
- MEKC : Micellar ElectroKinetic chromatography



Un example of an electrochromatogram



How much the bands spread ?



$\delta = \sqrt{D_{eff} t}$

Taylor
Aris estimate

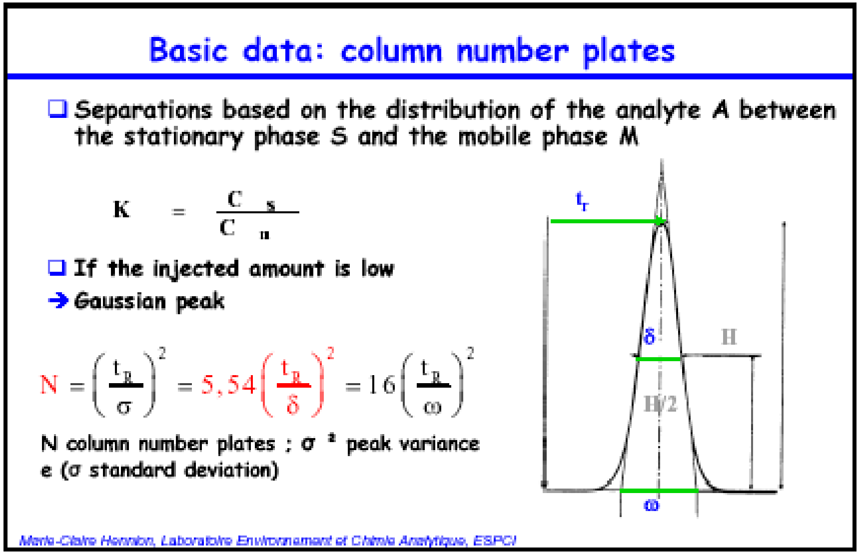
$D_{eff} \sim Pe^2 D \sim U^2 b^2 / D$

SOME IMPORTANT QUANTITIES USEFUL FOR THE CHARACTERIZATION OF THE PERFORMANCES OF THE SEPARATION TECHNIQUE

The number of theoretical plates

$$N = \left(\frac{\text{distance parcourue par la bande}}{\text{largeur diffusive de la bande}} \right)^2$$

$$N \sim \frac{L^2}{D_{eff}(L/U)} \sim \frac{UL}{D_{eff}}$$



(From M.C.Hennion (2004))

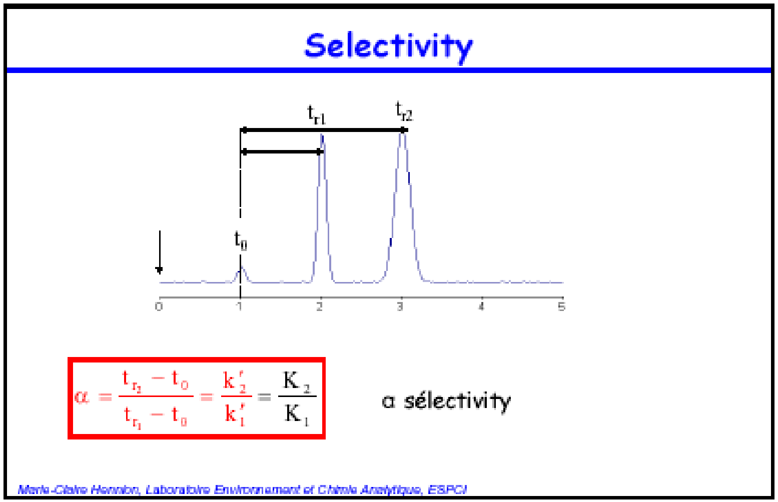
One infers

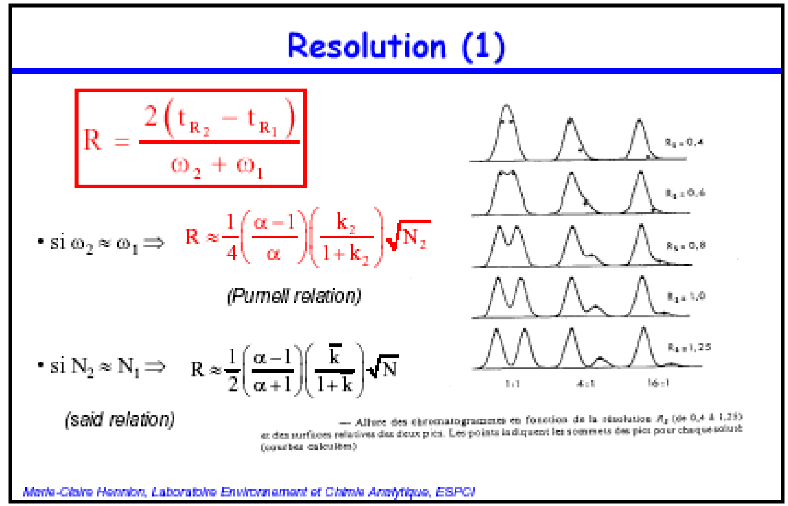
Retention time in the column

$$N \sim \frac{UL}{D_{eff}} \sim \frac{ULD}{U^2 b^2} \sim \frac{LD}{Ub^2} \sim \frac{t_R D}{b^2}$$

Number of theoretical plates

OTHER QUANTITIES OF INTEREST





(From M.C.Hennion (2004))

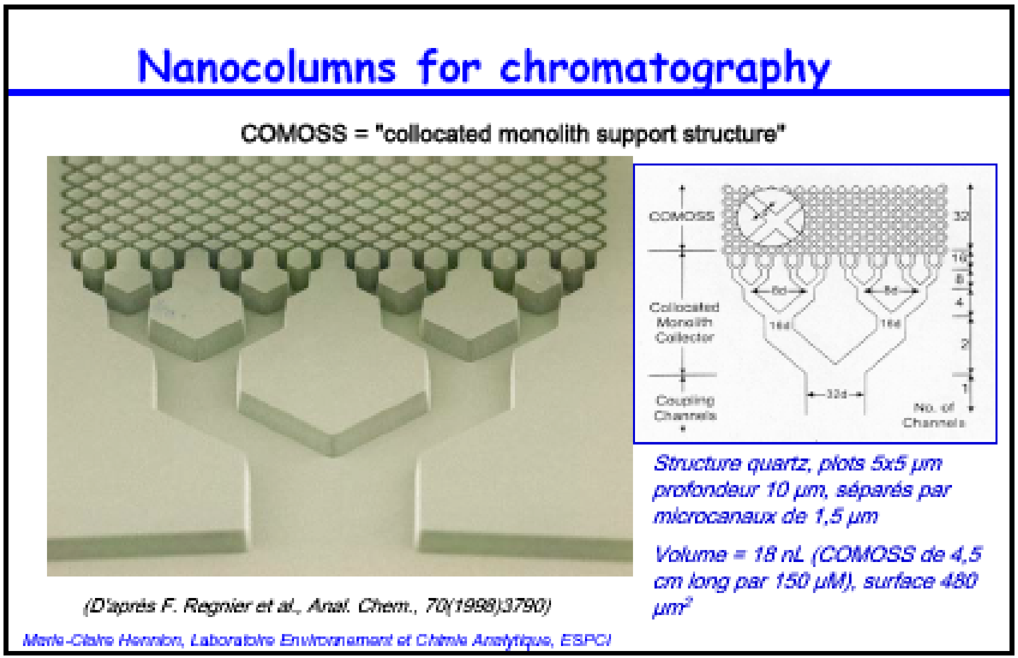
IS MINIATURIZATION ADVANTAGEOUS ?

1) **NON ELECTRICAL SEPARATION TECHNIQUES**

- Small samples
- Intégration possible
- Parallelism possible

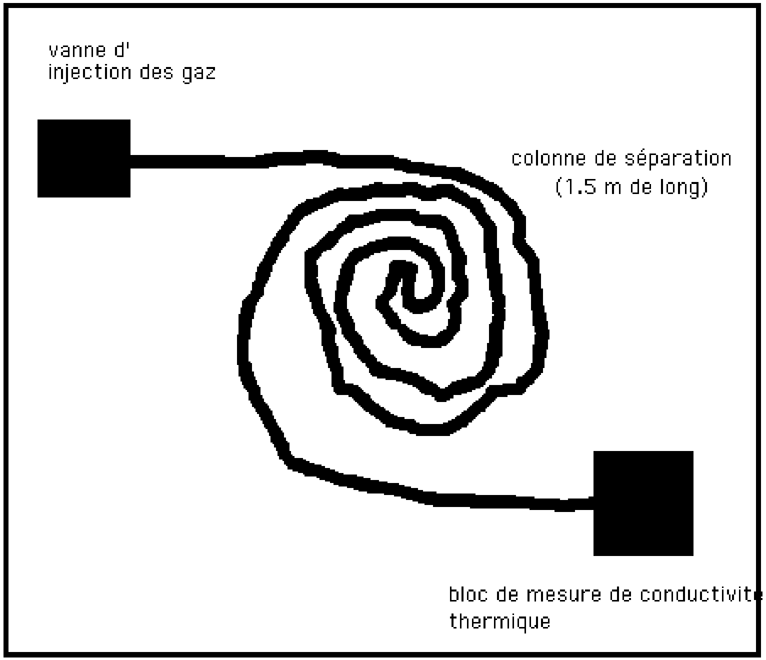
But no improvement of the analytical performances

$$N \sim \frac{t_R D}{b^2} \sim l^0 \qquad t_R \sim l/U \sim l^0$$



(From M.C.Hennion (2004))

Le premier lab on a chip était une colonne chromatographique à gaz (Terry, 1975)



2)Electrical separation techniques

$$N \sim \frac{\mu_{EOF} EL}{D}$$

Number of theoretical plates

Maximum electrical field that can be applied

$$Q \sim K\Delta Tl \sim K\sigma E^2 l^3$$

Therefore

$$E \sim l^{-1}$$

Thereby

$$N \sim l^0$$

The number of plates remains the same, while the retention time becomes :

$$t_R \sim L/V \sim l^2$$

Conclusion : it is tremendously advantageous

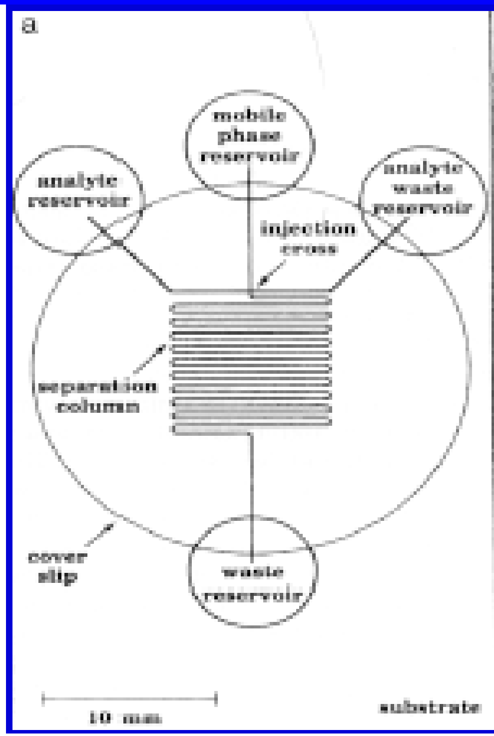
-Same performances, must smaller times

-(800 μs, Jacobson et al)

Miniaturization in this case thus leads to :

- Small volumes
- Intégration and parallélization possible
- Conservation of the efficiency of the column
- Considerable gain of time

The first chip electrochromatography



- Glass structure
- 5 cm x 2,5 cm (serpentine 1 cm x 1 cm)
- Channel : 165 mm long, 10-µm deep, 90-µm wide at surface, 70 µm at the bottom
- Peak broadening due to the U-turns
- Reproducibility of injection (≈90 pL in pinched mode and ≈ 300 pL en gating mode)

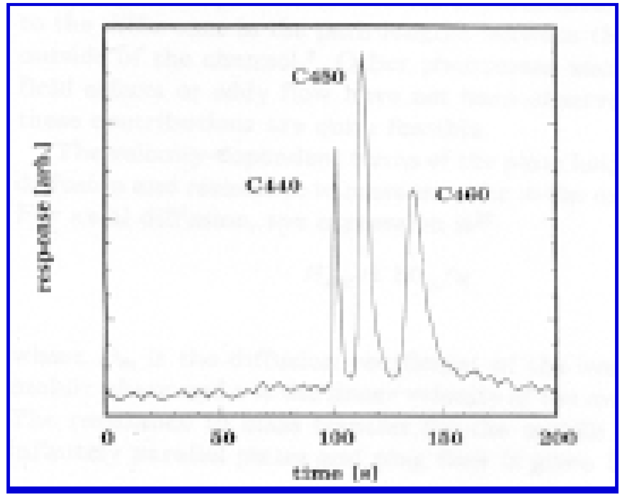
(D'après M. Ramsey, Anal. Chem. 66(1994)1107)

Marie-Claire Hennion, Laboratoire Environnement et Chimie Analytique, ESPCI

(From M.C.Hennion (2004))

The first chip electrochromatography

- In situ bonding of the canal surface with octadecylsilane
- Electroosmotic flow for both injection and separation
- Plate number : 11700 for C440, 2950 for C450 and 1290 for C460
- Peak broadening due to the serpentine shape



Separation of 3 coumarines, tétraborate buffer, pH 9,2, 10mM with 25% acétonitrile, u=0,65 mm/s (V= 138V/cm)

(S.Jacobson et al, Anal.Chem., 66(1994)2369)

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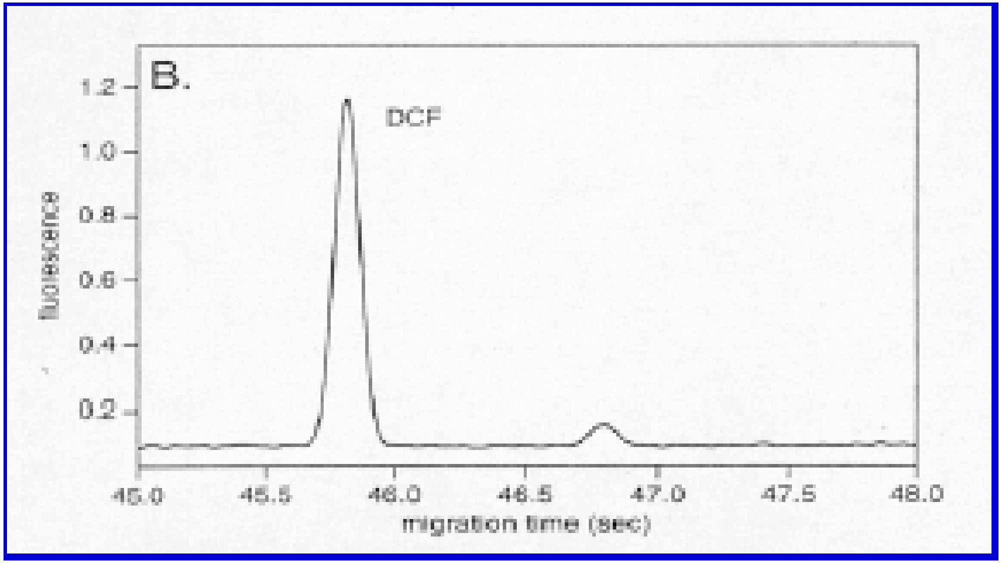
(From M.C.Hennion (2004))

More than 1 million plates within 46 seconds



Electrophoregramme of dichlorofluoresceine and impurity

1170 V/cm, 22,2 cm spiral, boric acid 20mM with TRIS buffer 100mM

N= 1 100 000 plateaux

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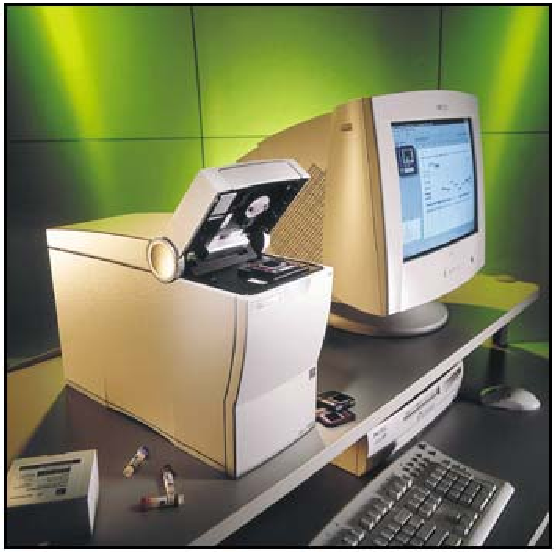
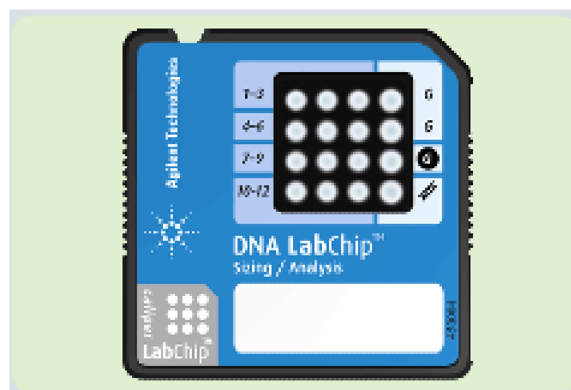
(From M.C.Hennion (2004))

A microfluidic system for DNA separation



From Agilent-
Caliper

Allow to characterize DNA Fragments with excellent Resolution, and in a small time



Miniaturization of electrophoretic separation systems

Caliper

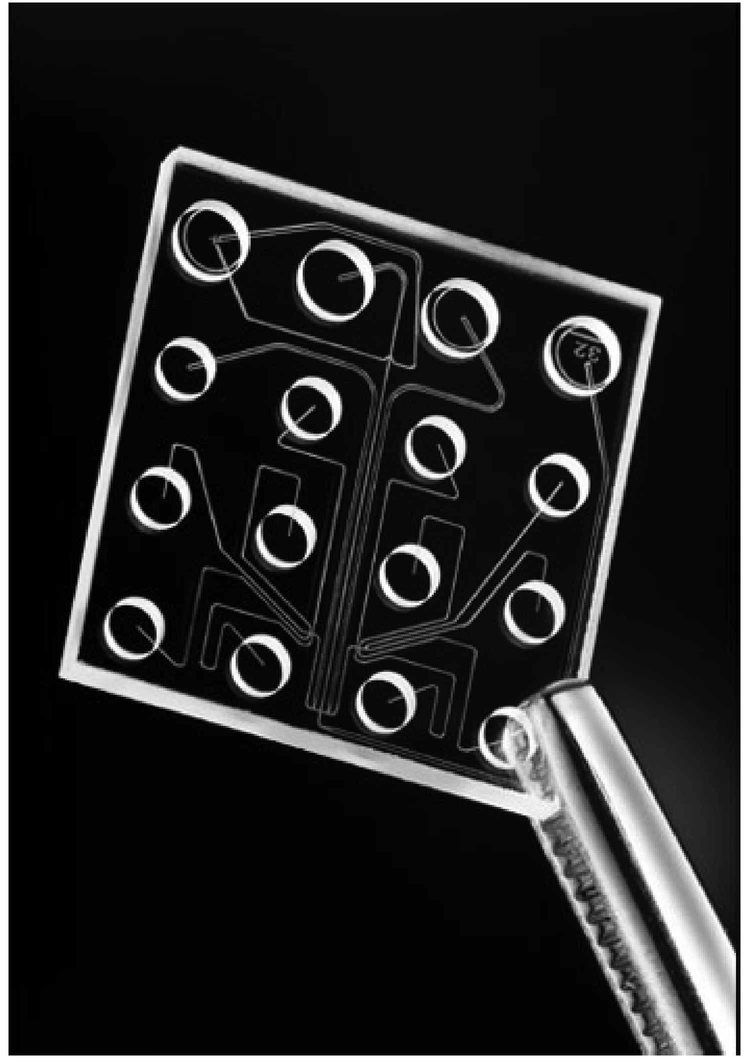
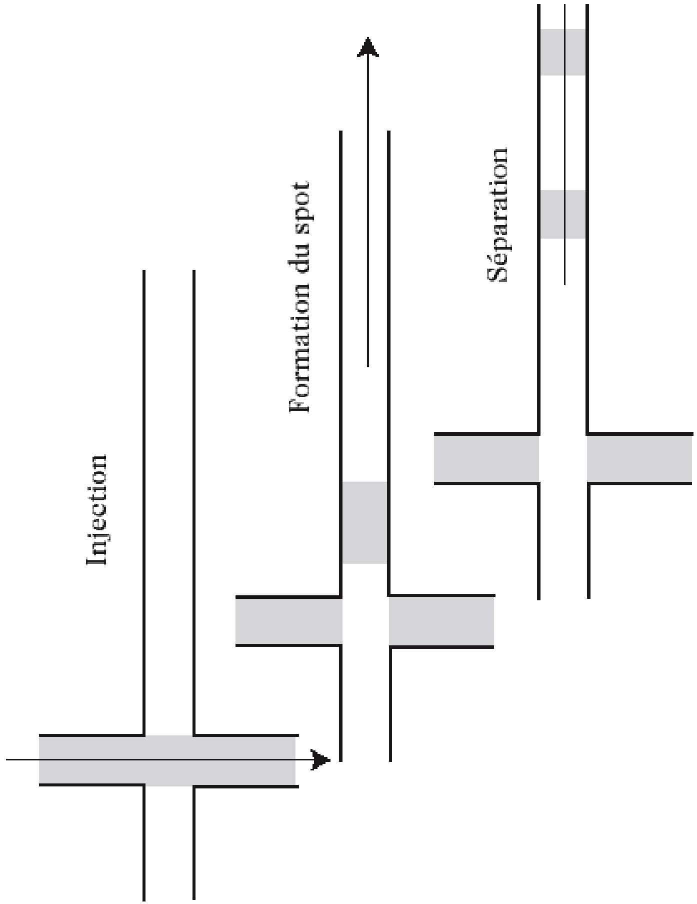
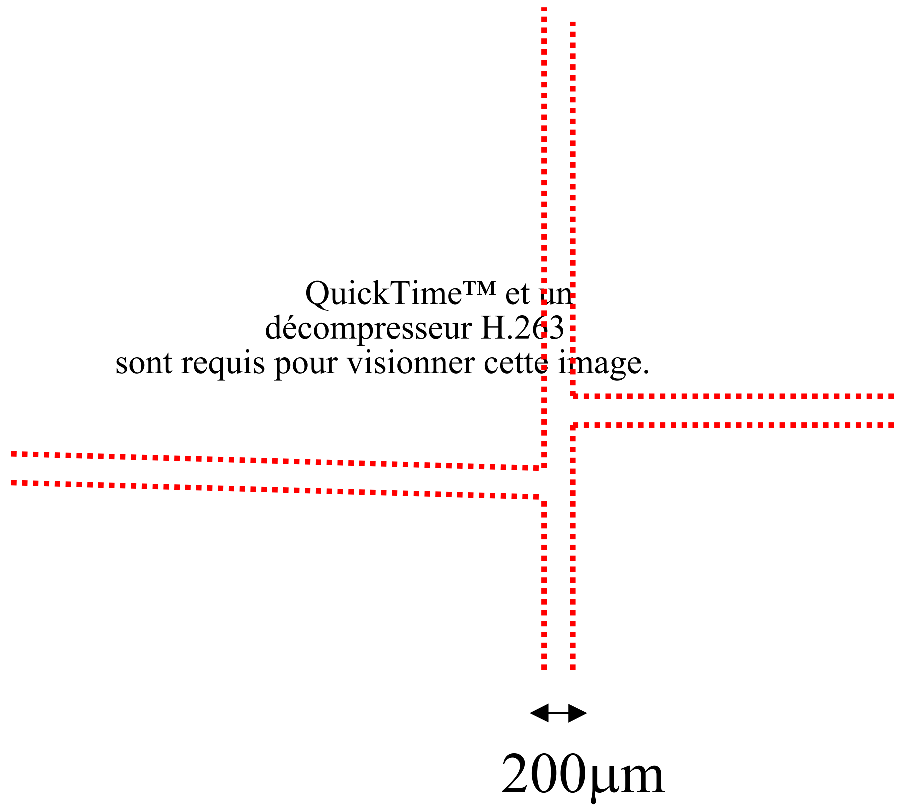


Figure 4.9. Puce commercialisée par la société Caliper permettant une séparation par électrophorèse. Les micro-canaux ont été remplis d'un liquide coloré permettant de les visualiser.

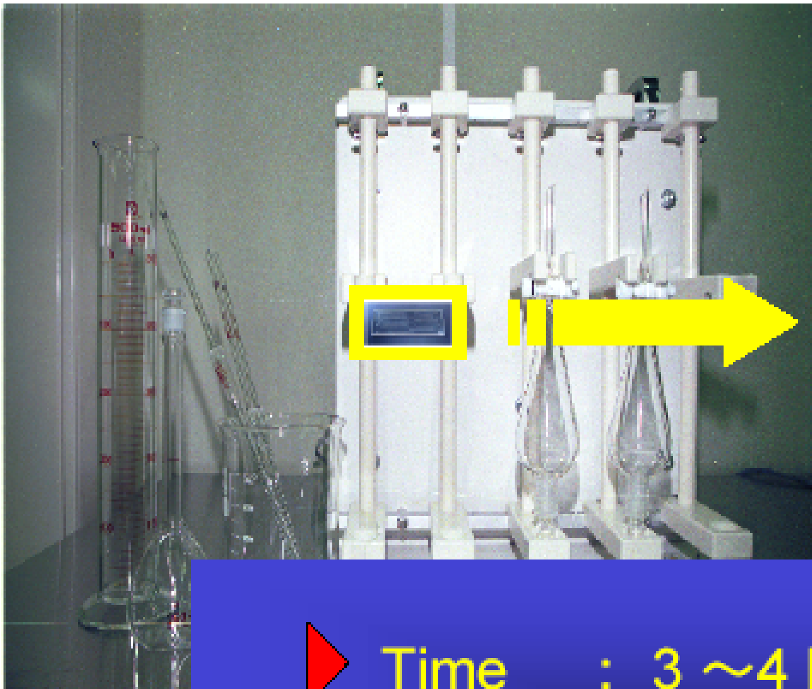
Miniaturization of electrophoretic separation systems

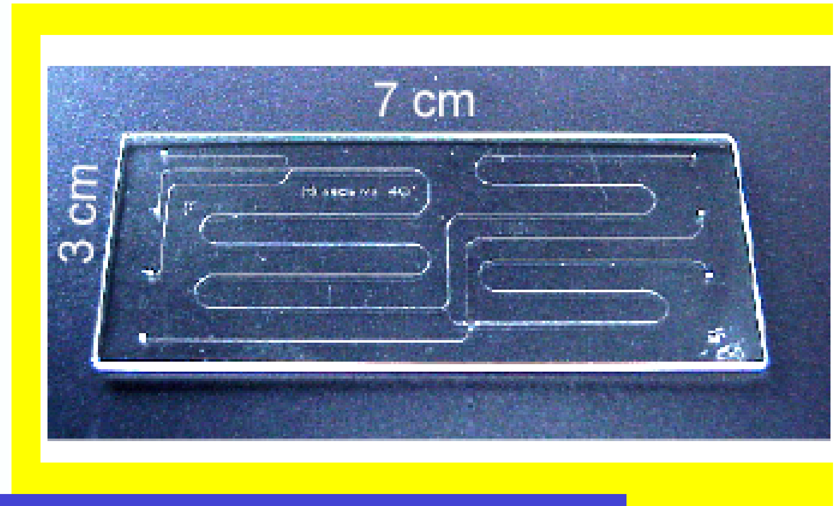




Experiment done by E. Brunet (MMN)

μ-Wet Analysis System
Environmental Heavy Metal (Co) Analysis Chip



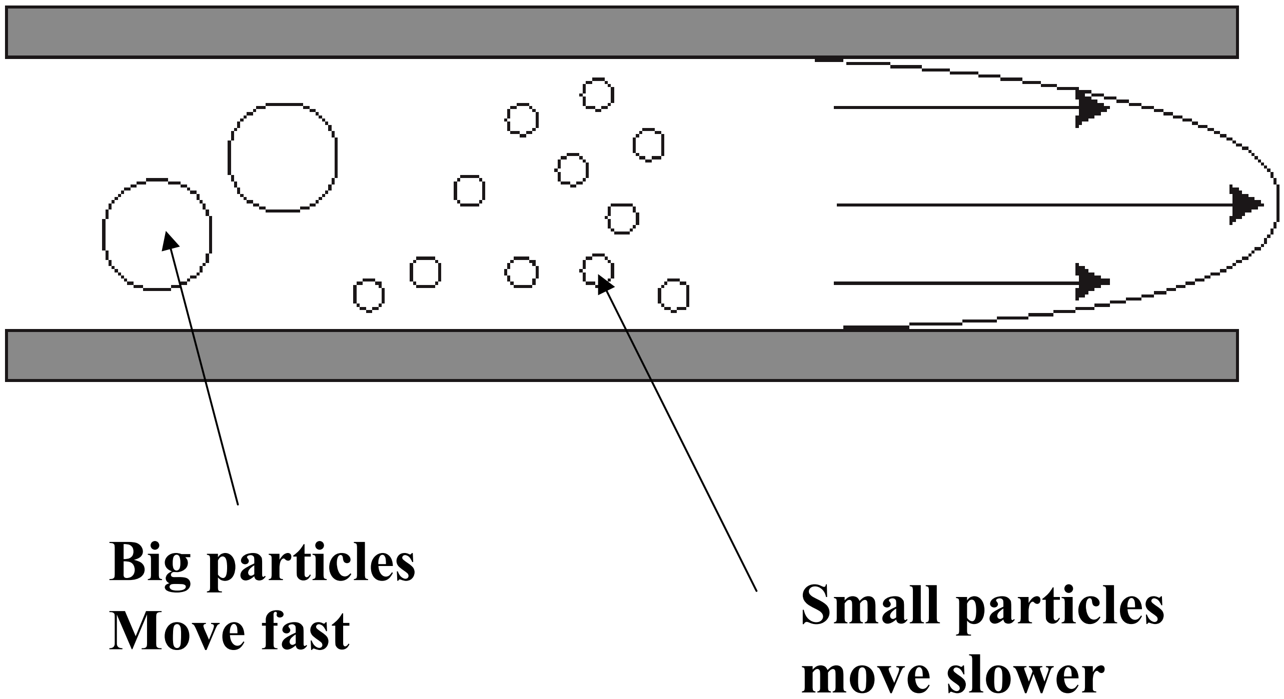


- Time : 3 ~4 hours → 50 sec
- Quantity : 1 kg → 1 μg
- Sens. : pmol → 0.08 zmol
  48 atom

(From Kitamuri (2004))

SOME DEVELOPMENTS OF MICROFLUIDIC SYSTEMS DEDICATED TO SEPARATION

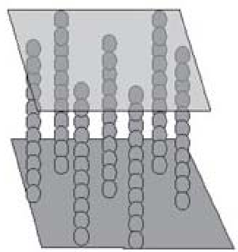
A novel method, based on microfluidics

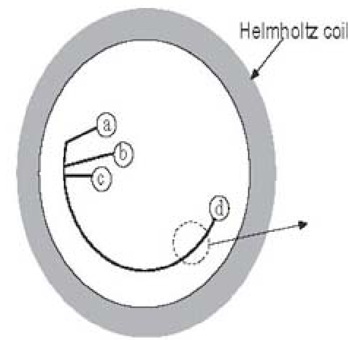


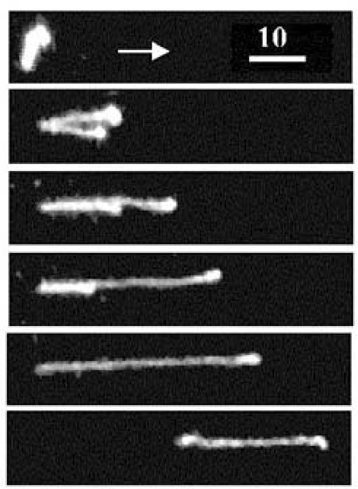
CHEMISTRY

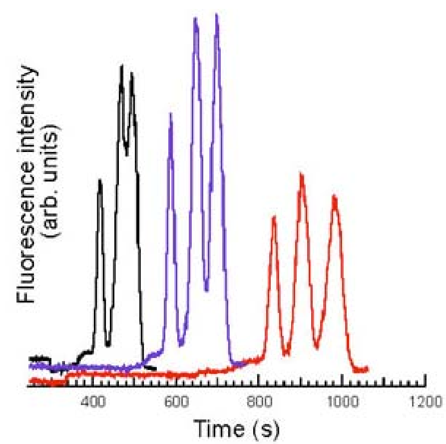
Self-Assembled Magnetic Matrices for DNA Separation Chips

Patrick S. Doyle,[1] Jérôme Bibette,[2] Aurélien Bancaud,[3]
Jean-Louis Viovy[3]*





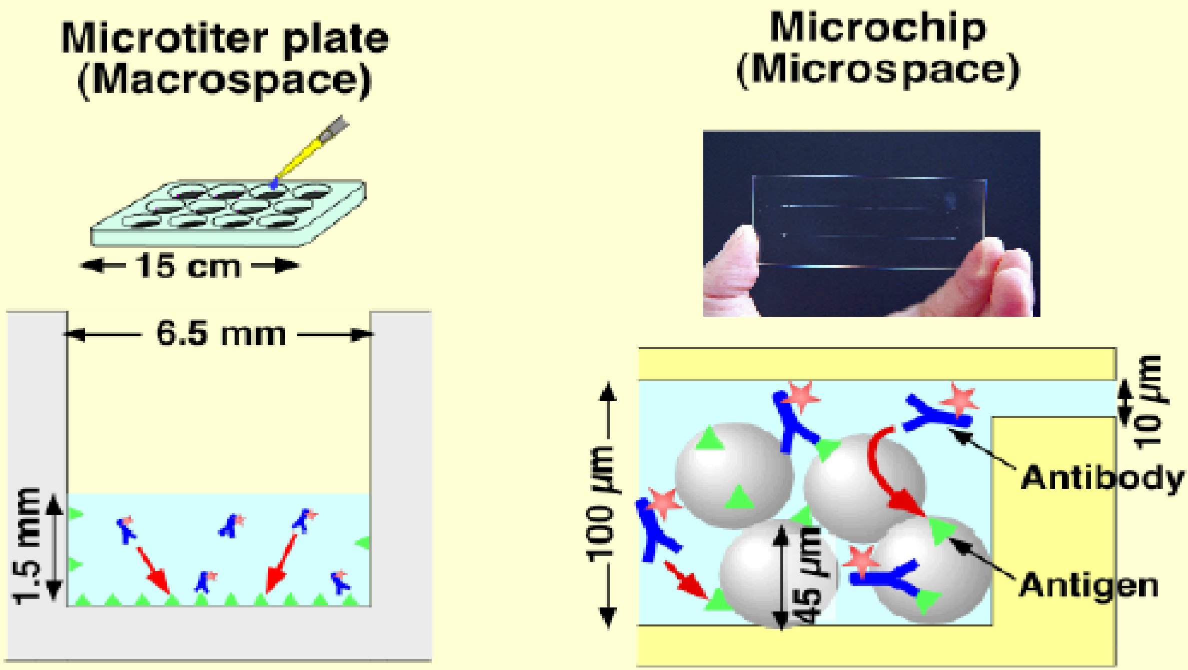




Institut Curie
ESPCI

SAMPLE ANALYSIS IS AN IMPORTANT TOPICS IN MICROFLUIDICS.
ALL SORTS OF SYSTEMS HAVE BEEN MICROFABRICATED

Macro- & Microspace for Immunoassay

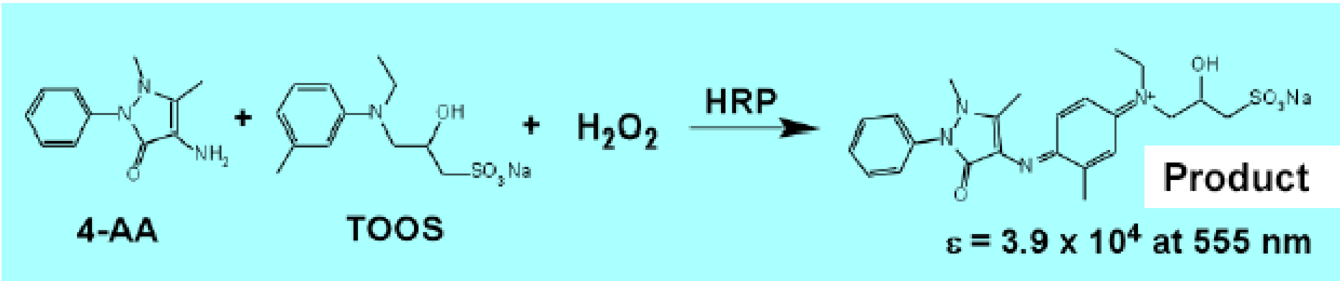


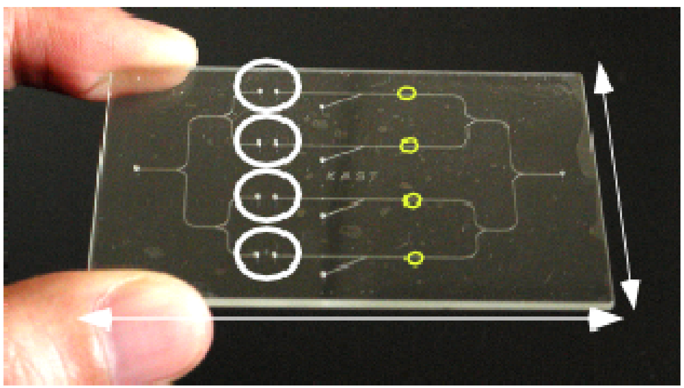
Diffusion distance ～ 1 mm
(Reaction time ～ 15 hour)

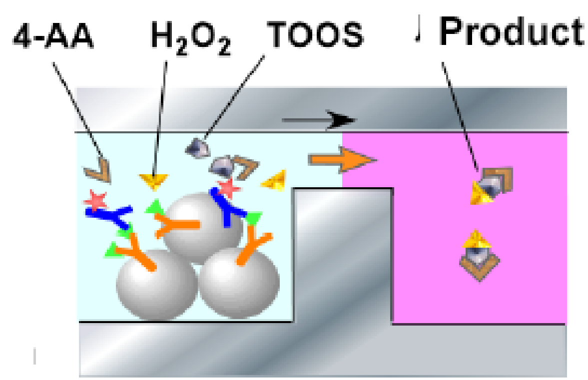
Diffusion distance ～ 10 μm
(Reaction time ～ 10 min)

KITAMURI

Multi-Channel Micro ELISA System



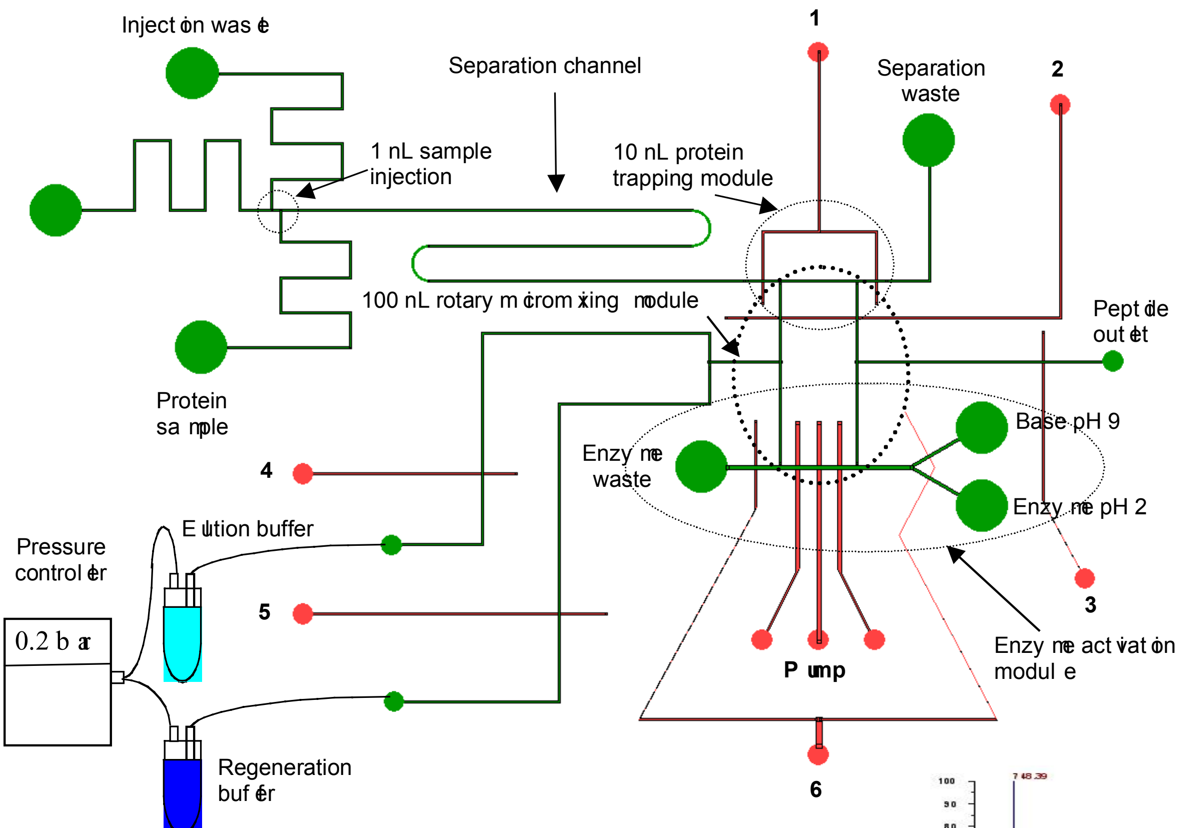




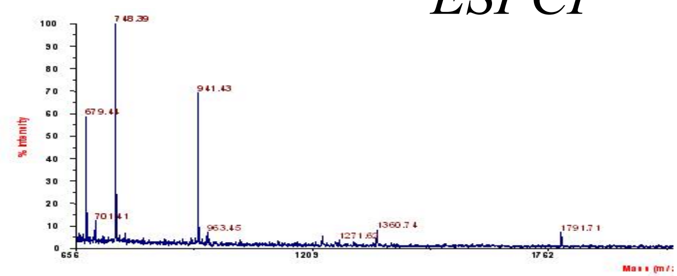
- **TLM detection conditions**
  Excitation : YAG laser (532 nm)
  Probe : He-Ne (633 nm)

KITAMURI

LAB ON A CHIP DEDICATED TO PROTEOMICS



ESPCI



Chip demonstrated with a Sample of FITC, Lysosyme, BSA

THIS WAS THE LAST TRANSPARENCY

THANK YOU FOR YOUR KIND ATTENTION

The end