Potential of biomedical sensors: state of the art and future perspectives

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The old-time biosensor

The future of monitoring

Sensors are all around us

- Industry
  - Counting, sorting, reading, tactile
- Cars
  - Motor
  - Tire pressure
  - Collision activate air bag
- Office
- Home

Biosensor

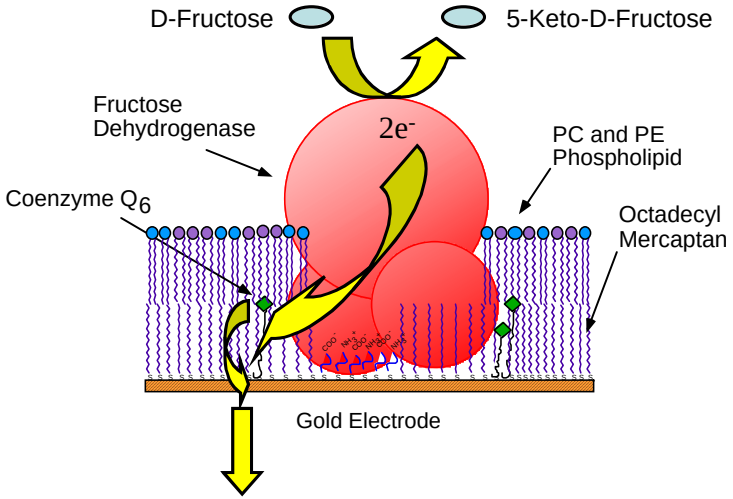
- A sensor used to obtain information about a life process
- Biosensors are devices that can detect and/or quantify molecules of interest. Sensing occurs when there is an interaction between the target molecule and a biological macromolecule (e.g. enzyme, antibody, receptor or DNA strand).

What is a biosensor?

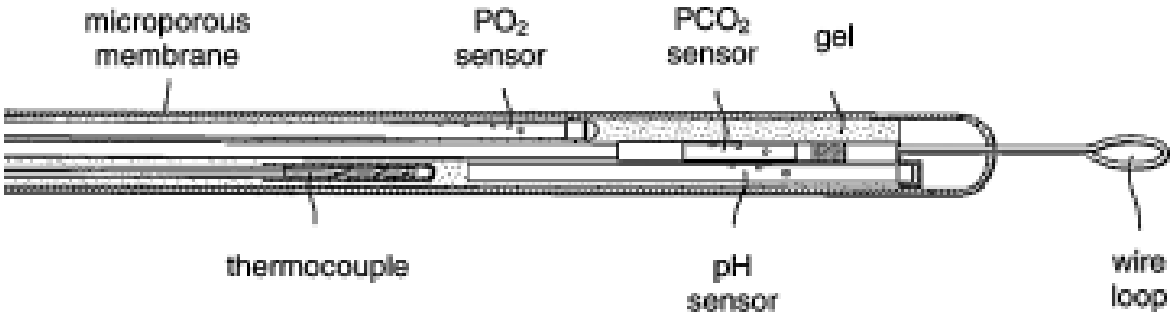
- Broader definition: Sensing (measuring, monitoring) a functional biological parameter in an organ or systemically
- In vitro
  - Point-of-care
- Ex vivo
- In vivo

Many types og tecnnology

- Electrochemical



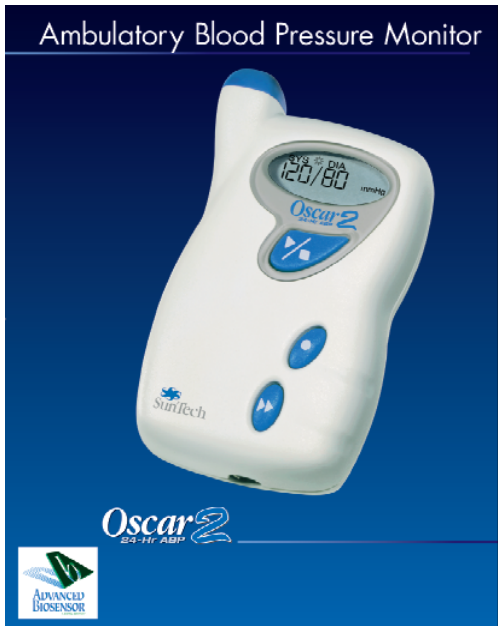
- Fiberoptic

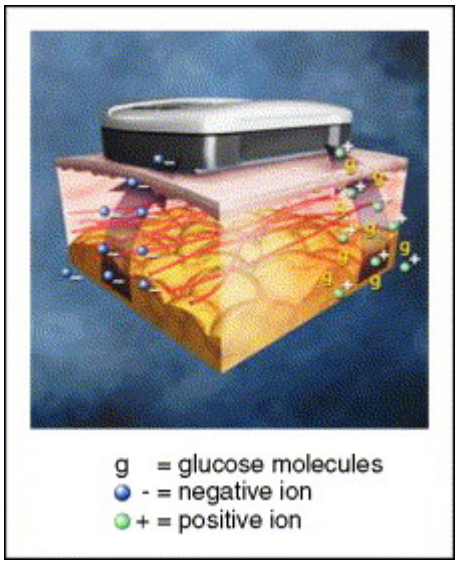


Time resolution

- One time shot
- Repeated measurements
- Continous, real-time

The evolution of glucose sensors





Alpha Series

Beta Series

Some defining events in the history of commercial biosensor development

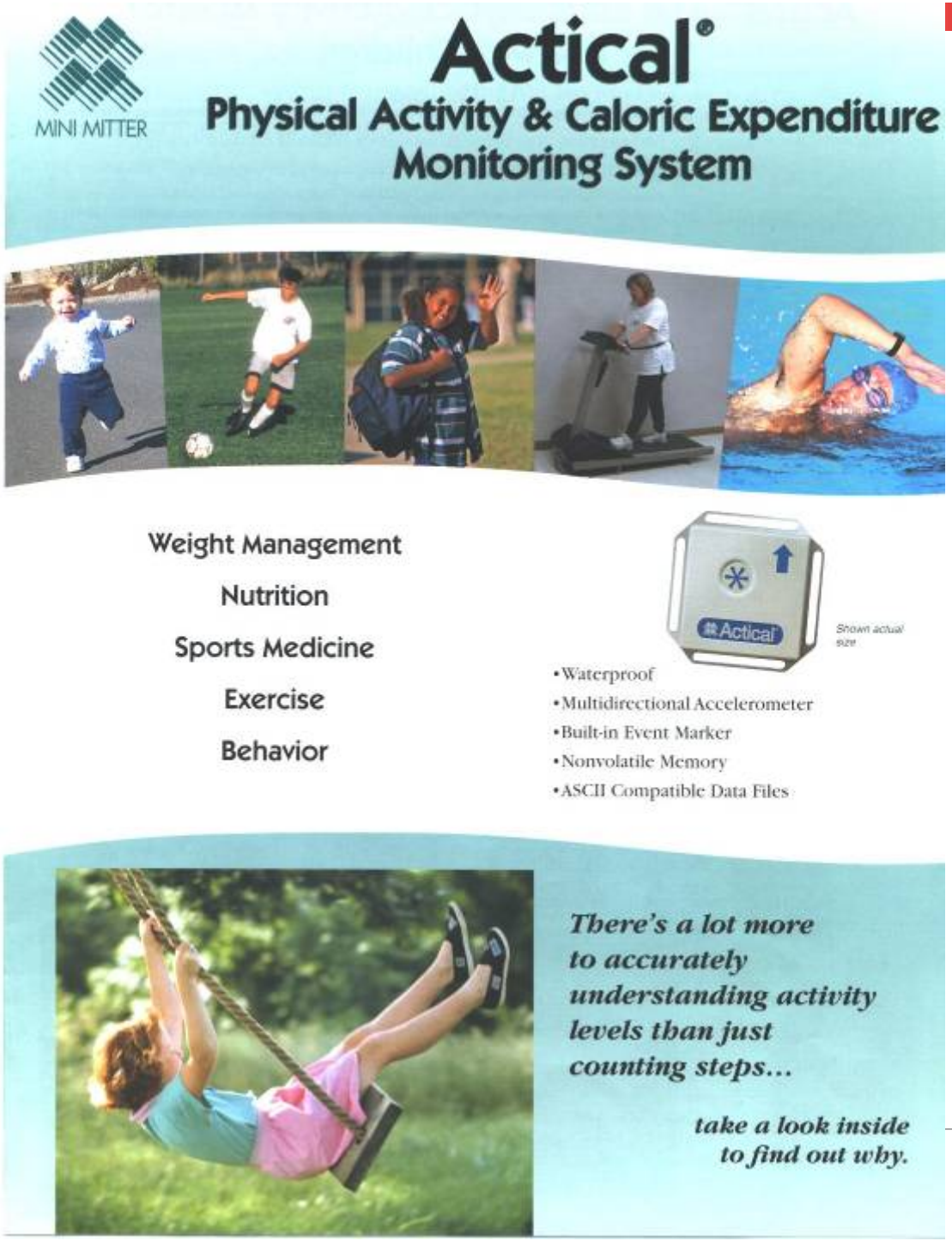
Date	Event
1916	First report on the immobilisation of proteins: adsorption of invertase on activated charcoal
1922	First glass pH electrode
1956	Invention of the oxygen electrode (Clark, 1956)
1962	First description of a biosensor: an amperometric enzyme electrode for glucose (Clark and Lyons, 1962)
1973–1975	First commercial biosensor: Yellow Springs Instruments glucose biosensor
1976	Miles Biostator: first bedside artificial pancreas
1982	First fibre optic-based biosensor for glucose (Schultz, 1982)
1984	First mediated amperometric glucose biosensor: ferrocene used with glucose oxidase for the detection of glucose (Cass et al., 1984)
1987	Launch of the MediSense ExacTech blood glucose biosensor
1992	i-STAT launches hand-held blood analyser
1996	Glucocard launched
1996	Abbott acquires MediSense for $867 million
1998	Launch of LifeScan FastTake blood glucose biosensor
1998	Merger of Roche and Boehringer Mannheim to form Roche Diagnostics
2001	LifeScan purchases Inverness Medical's glucose testing business for $1.3 billion
2003	i-STAT acquired by Abbott for $392 million
2004	Abbott acquires TheraSense for $1.2 billion

Our vision

- BSD is dedicated to improving human safety and well-being through innovative, fast-working, cost effective and reliable disposable sensors for the medical, food, security, environmental and other diagnostic communities. It is envisioned that BSD sensors will be widely used in slaughterhouses, factories, hospitals, and doctor’s offices worldwide, with some applications extensively employed in homes and on battlefields throughout the world.

Biosensors agains terrorism

- - The Bush White House has endorsed a $3.25 billion Senate bill to beef up the United States' ability to detect and respond to biological and chemical attacks.



Biosensors against obesity

THE CANARY SINGS AGAIN

Early warning

The everyday problem..

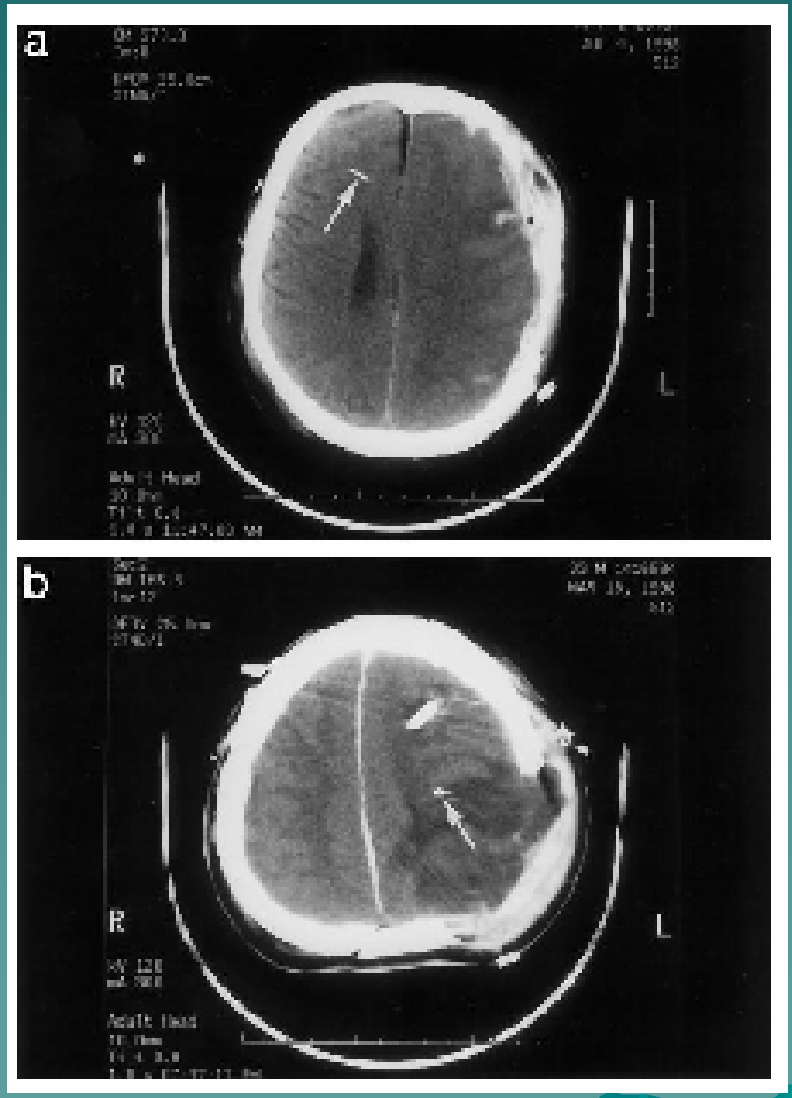
We obtain the global parameters

- but we do not know what happens in the organ

Injury to most organs are detected too late

- Except for EKG, we do not have real-time detection of organ injury
- Most organs reveal symptoms late
- In the anesthetized patient and the ICU patients, symptoms are absent
- Reliable biosensors are badly needed

Placement of a sensor

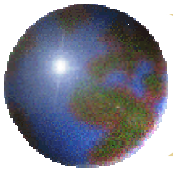


Why use a biosensor?

- Early detection imply better prognosis
- Continuous measurements enable us to titrate treatment according to response
- Diseases may be treated even before symptoms occur

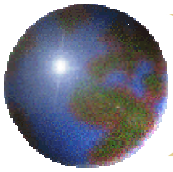
Ischemia

- Most prevalent cause of mortality and morbidity in the Western world (myocardial infarction, stroke, trauma)
- If ischemia is detected early it is most often reversible
- Except from EKG, there is no clinical method available for real-time monitoring of ischemia
- Indirect methods (enzyme analysis etc) are often unspecific and slow



The diagnosis of ischemia is often retrospective

- We diagnose that the injury has occurred-
  but it is too late because the injury has become irreversible

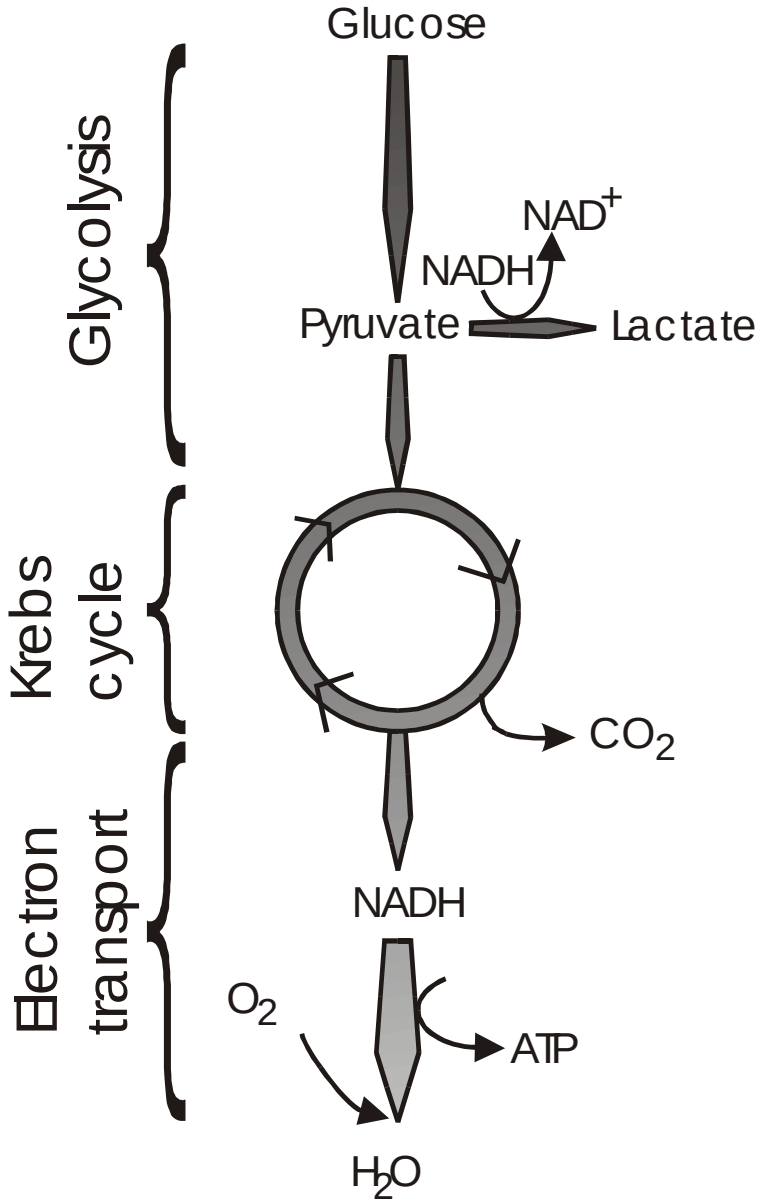


How do the cells try to survive without oxygen?

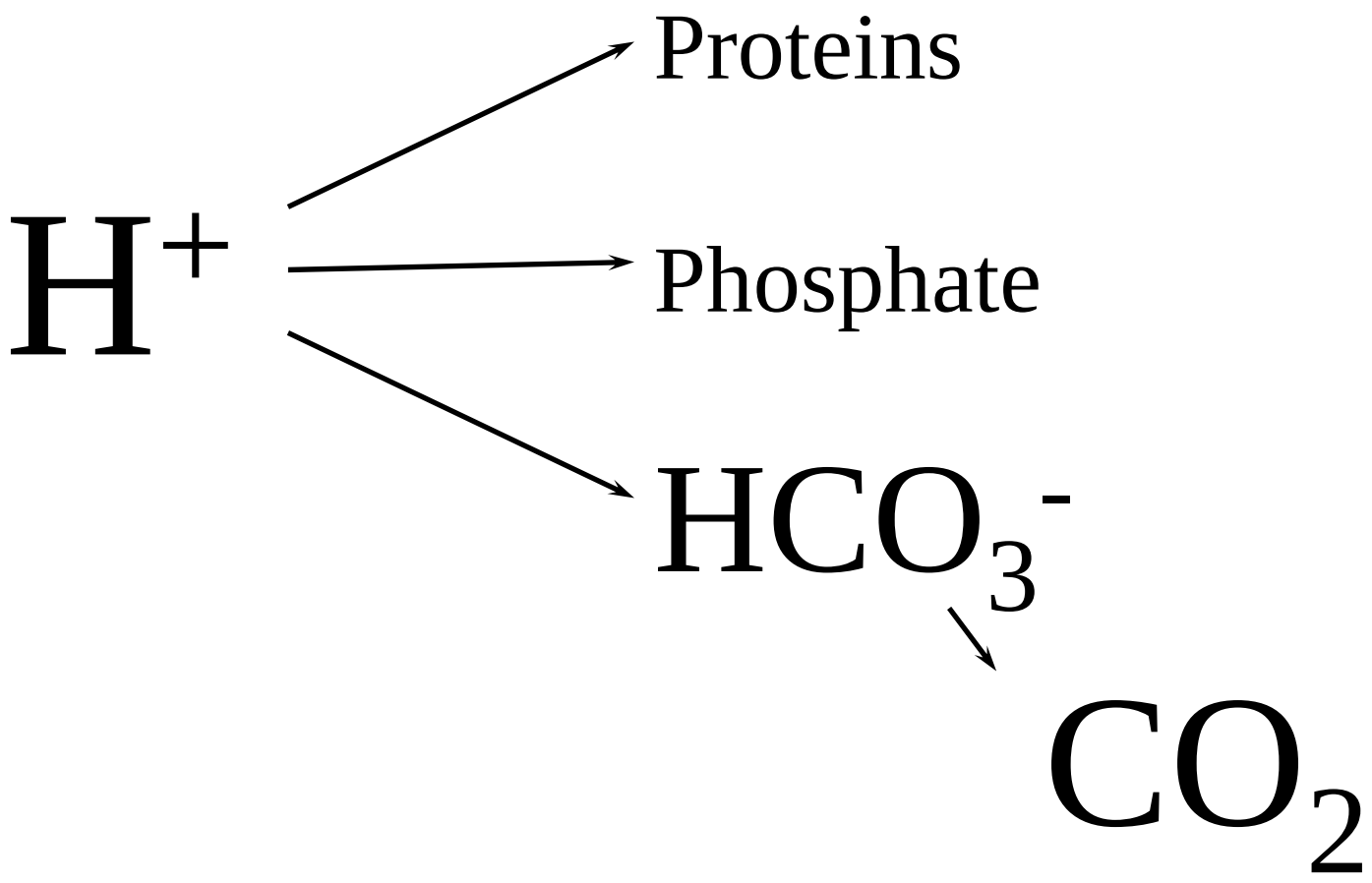
- Reduce ”luxury metabolism” (O_2 conformity)
  - Kidney
  - Heart
- Deplete the storage of energy rich substances
  - Skeletal muscle
  - Liver
- Convert to anaerobic metabolism

Anaerobic metabolism

- Desperate attempt to survive until oxygen reappears
- Secure a small energy production
- Side effect: Acidification of the cells

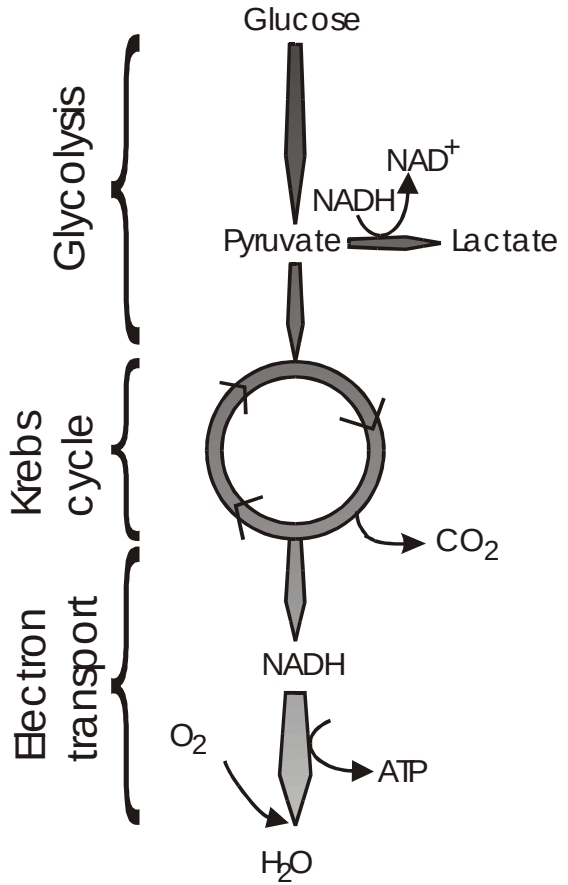


Intracellular acidosis



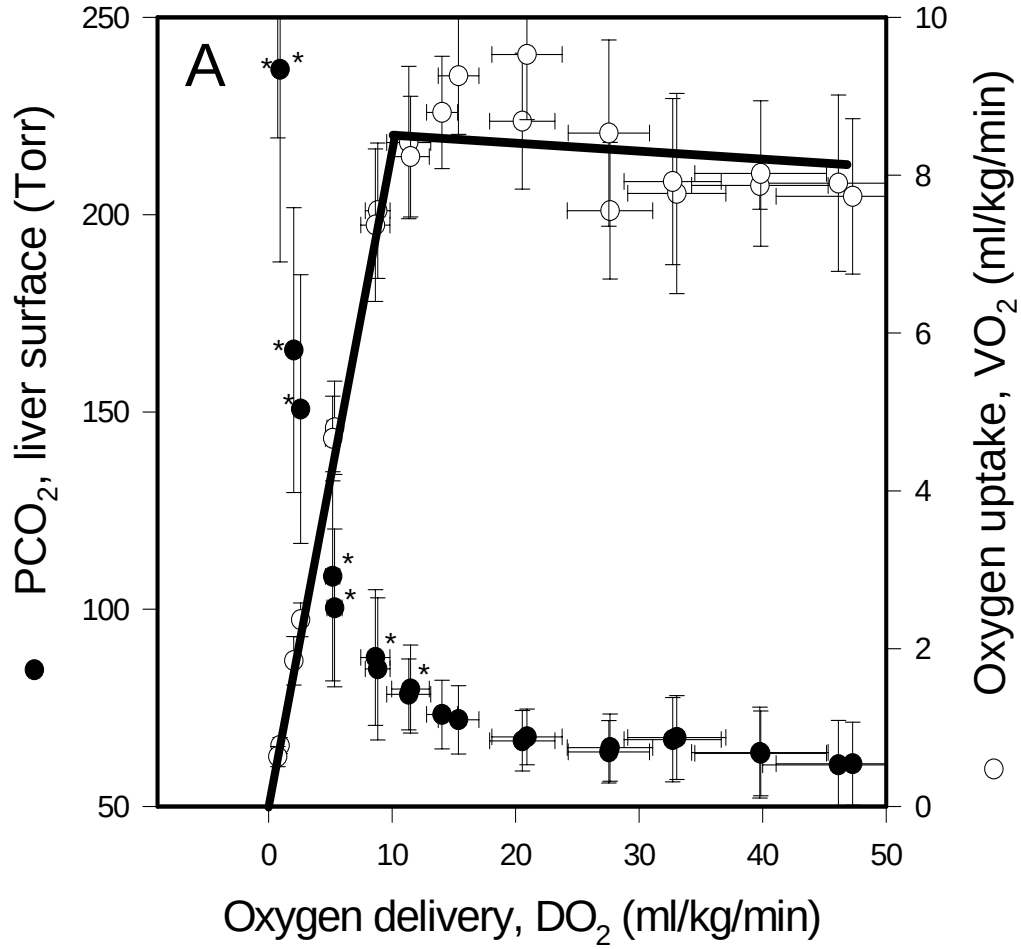
CO_2 production

- Oxidative phosphorylation
  - Large production
  - Rapid elimination by perfusing blood
- Anaerobic metabolism
  - Less CO_2 produced, but it is not transported away due to lack of blood supply, and will accumulate in the organ



$$H^+ + HCO_3^- \Rightarrow CO_2$$

PCO_2 during progressive flow reduction



Monitoring of organ metabolism

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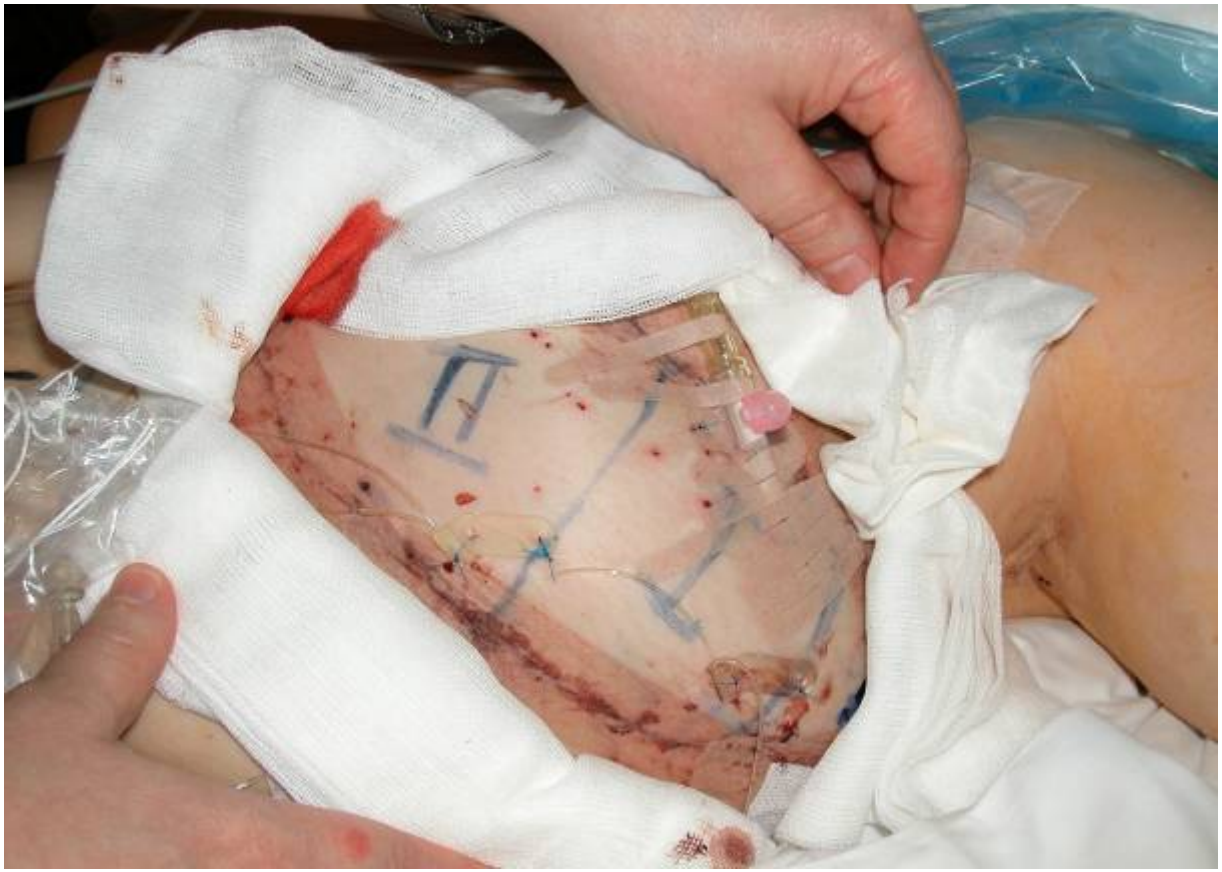
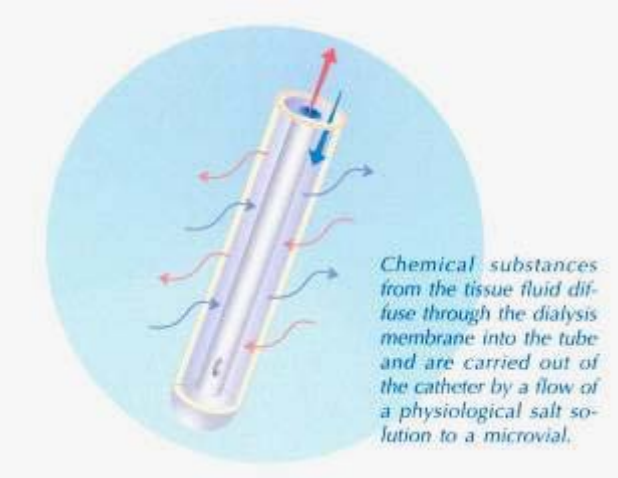
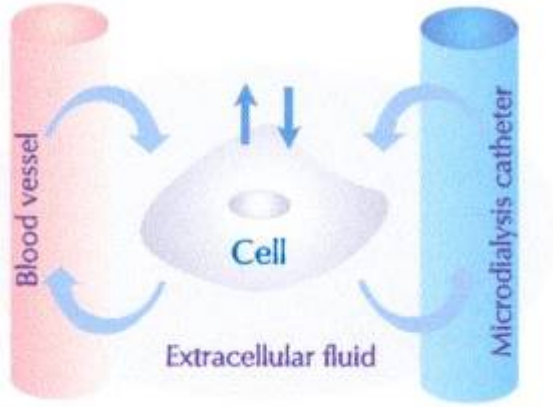


Principle of microdialysis





Mikrodialyse (CMA 600)

D

C

B

A

The perfusion fluid is pumped from the CMA 106 or CMA 107 Microdialysis Pump (A) through the Microdialysis Catheter (B) into the microvial (C). The microvial is tranferred to the CMA 600 Microdialysis Analyser (D) for analysis. The results are shown as trend curves on a screen.

The CMA 600 Microdialysis Analyser

rodialysis Analyser is a point-of-care
nalyzer. Its uniqueness lies in its compact
handle extremely small sample volumes,
s. Four different analytes can be analyzed
data are displayed graphically within a few
three patients can be handled simulta-

available for the most important
sue energy metabolism, lipolysis
ge:

te and pyruvate are markers for ischemia,
ypoglycemia in peripheral and central

narker for lipolysis in peripheral tissue
brane damage in brain tissue

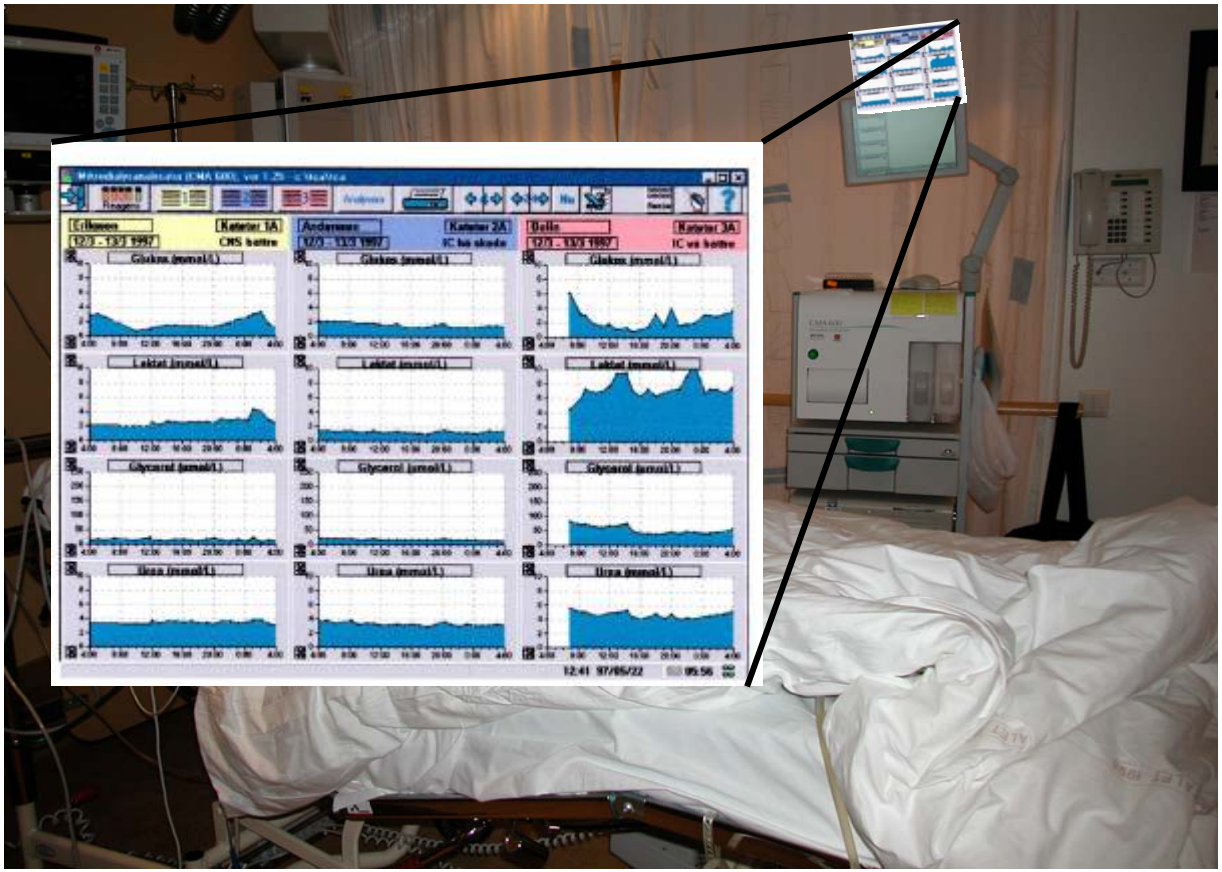
a marker of cytotoxicity in brain tissue

ser for urea clearance during hemodialysis.

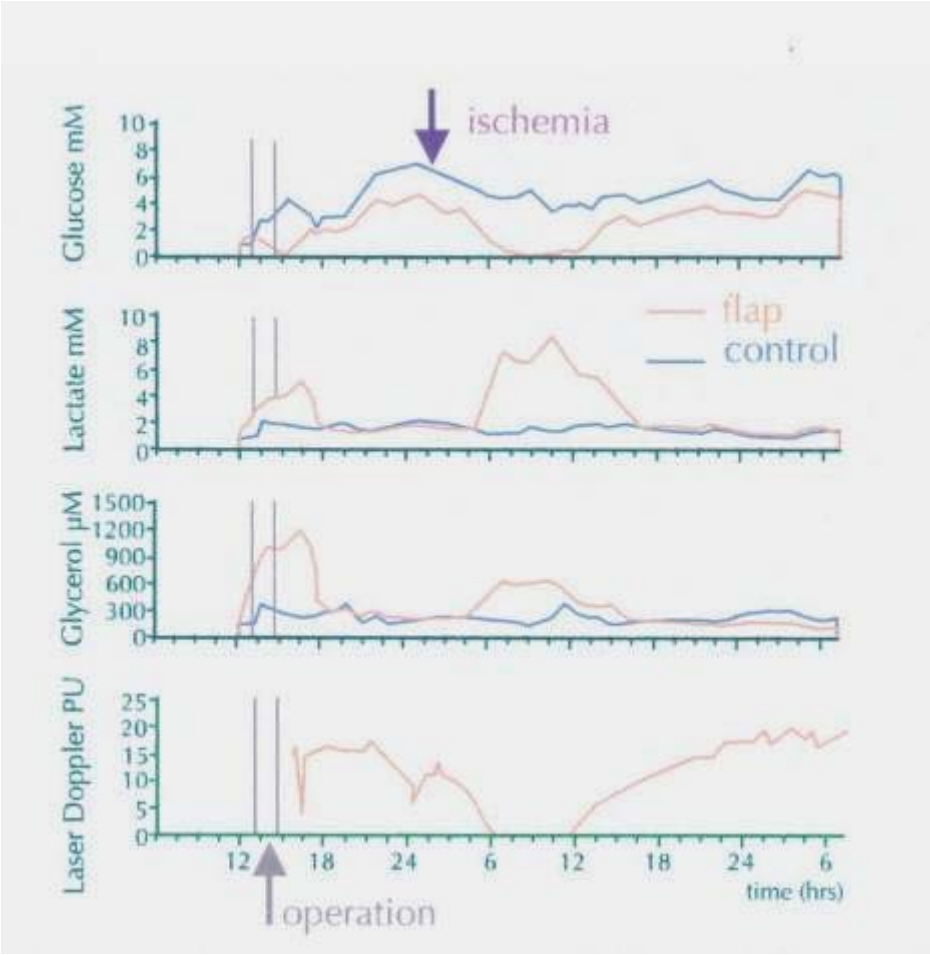
rodialysis Analyser comes with a wheel
uality display, a powerful computer, a
y back up and an isolation transformer,
or use in an ICU or Operating Room.

Microdialysis

Looking closer…



Ischemia in microsurgical free flap



Neurotrend

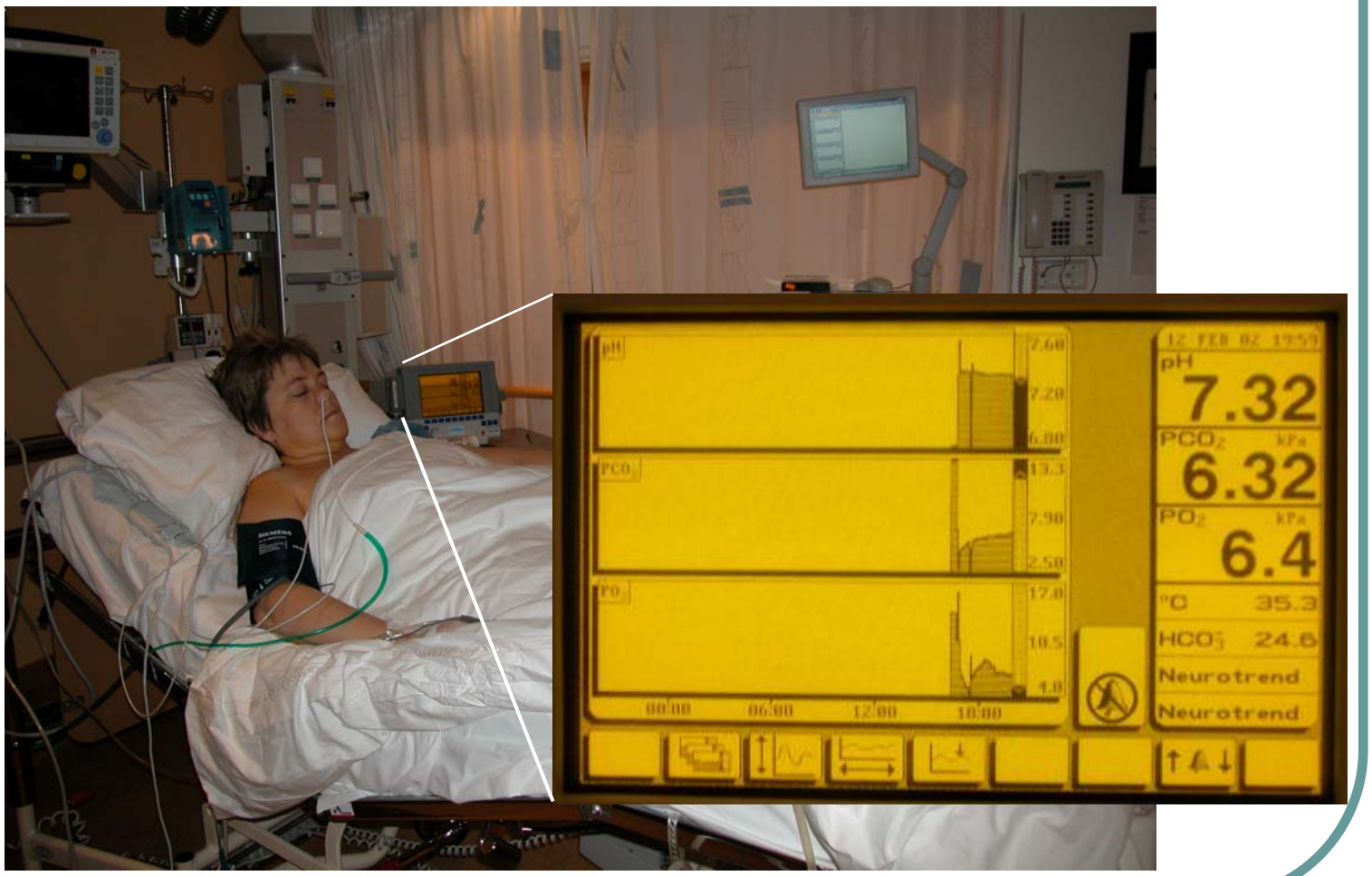
- pH
- PCO_2
- PO_2
- Temperatur

Neurotrendkateter

- Diameter 0,5 mm
- Membranlengde < 2,5 cm
- Må beskyttes mot lys
- Trykkfølsomt

Monitoring of organ metabolism

Monitoring of organ metabolism



DIEP-lapp

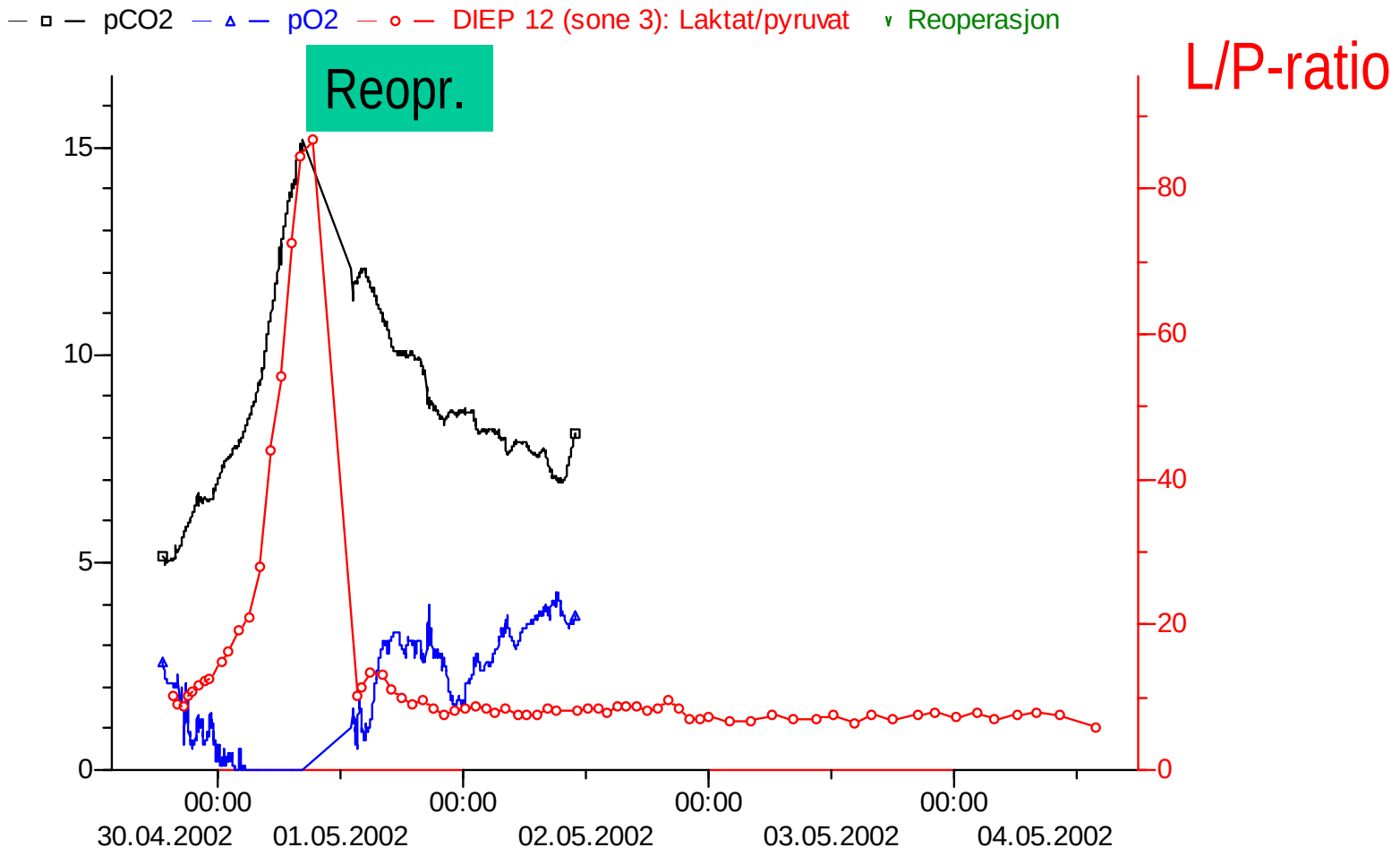
(Deep inferior epigastric perforans)

- Fri lapp.
- Hud og fettvev med tilhørende blodkar hentes fra nedre del av abdomen.
- Små kar anastomoseres.
- Den hyppigste komplikasjonen er svikt i blodforsyningen.
- Klinisk vurdering kan være vanskelig og sviktende blodforsyning kan oppdages sent.

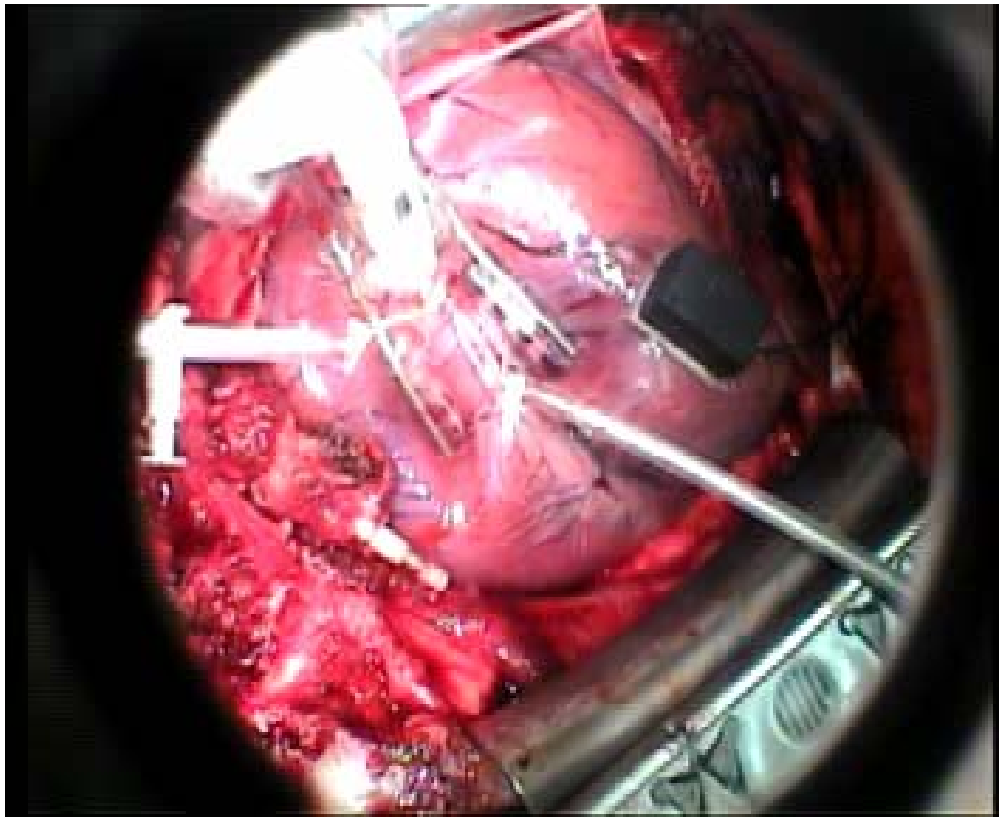
Venøs insuff.

pCO_2

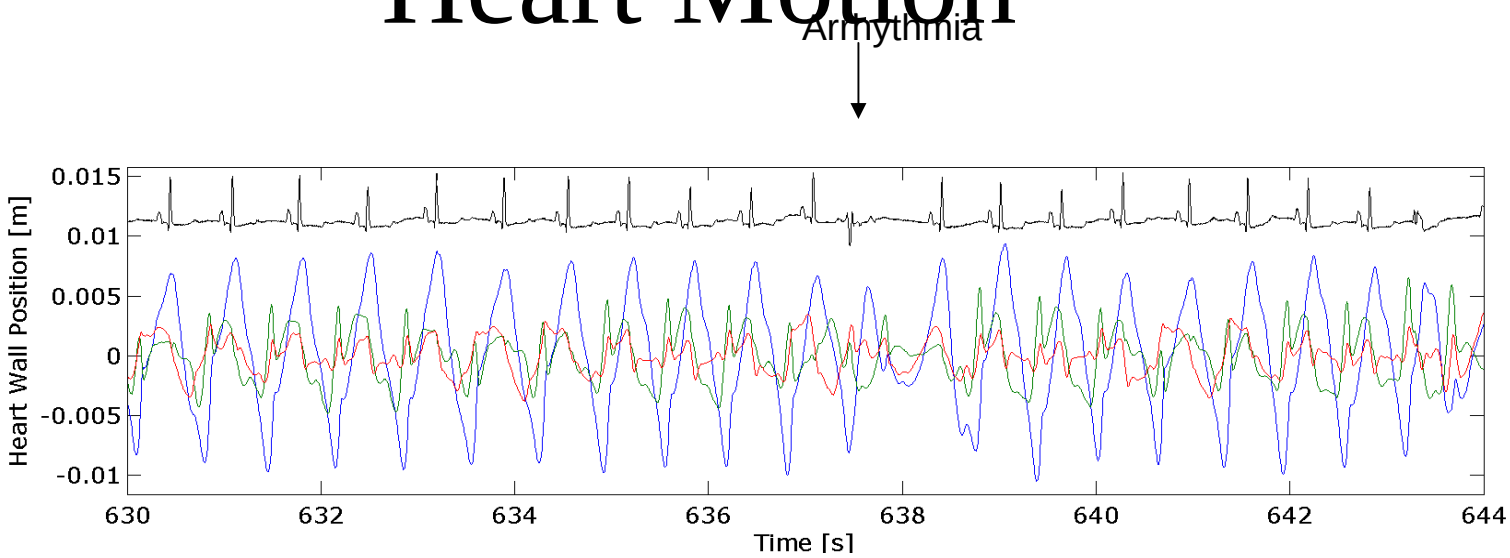
pO_2



First prototype 3-axis accelerometer sensor



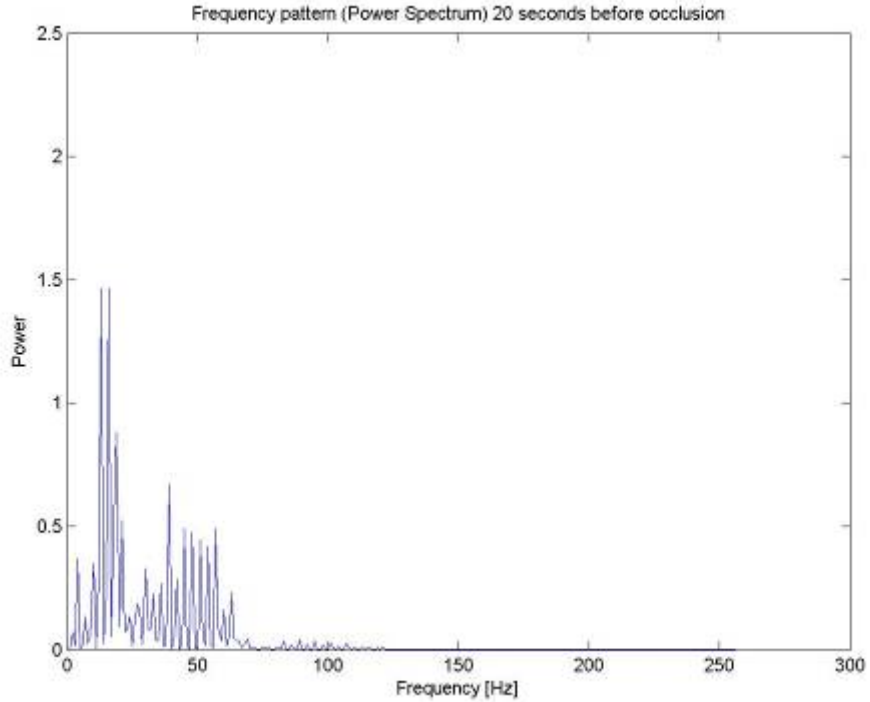
Heart Motion



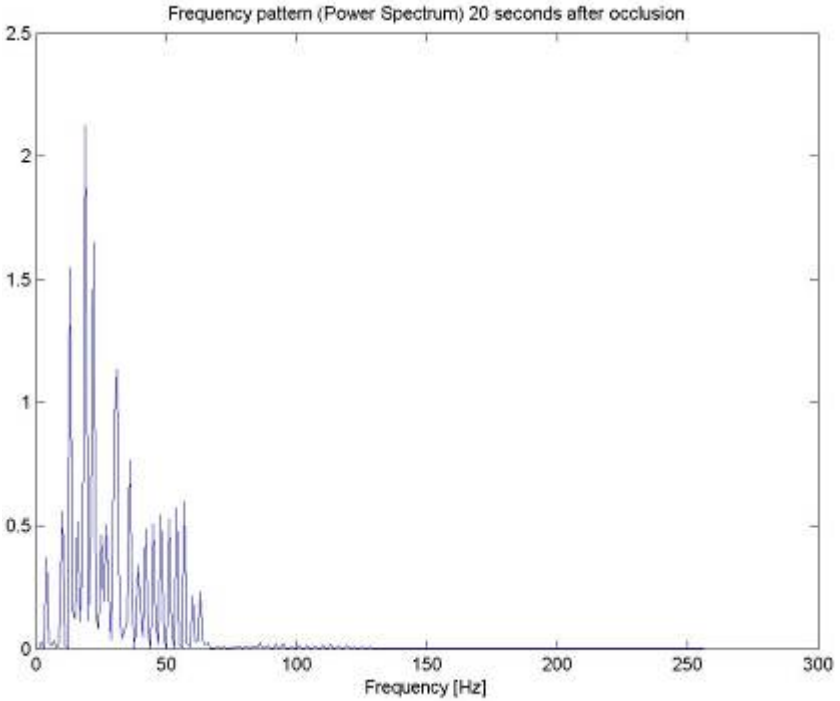
- Heart motion measurements
  - Good precision
  - 3 axes: Full 3D motion pattern
- Motion abnormalities seen
  - Arrhythmias, fibrillation, influence
- More subtle changes: More sophisticated signal analysis needed
  - Ischemia seen as changes in frequency plots

Frequency distribution in 2 sec time windows before and after occlusion

Frequency footprint
Before occlusion



Frequency footprint
After occlusion

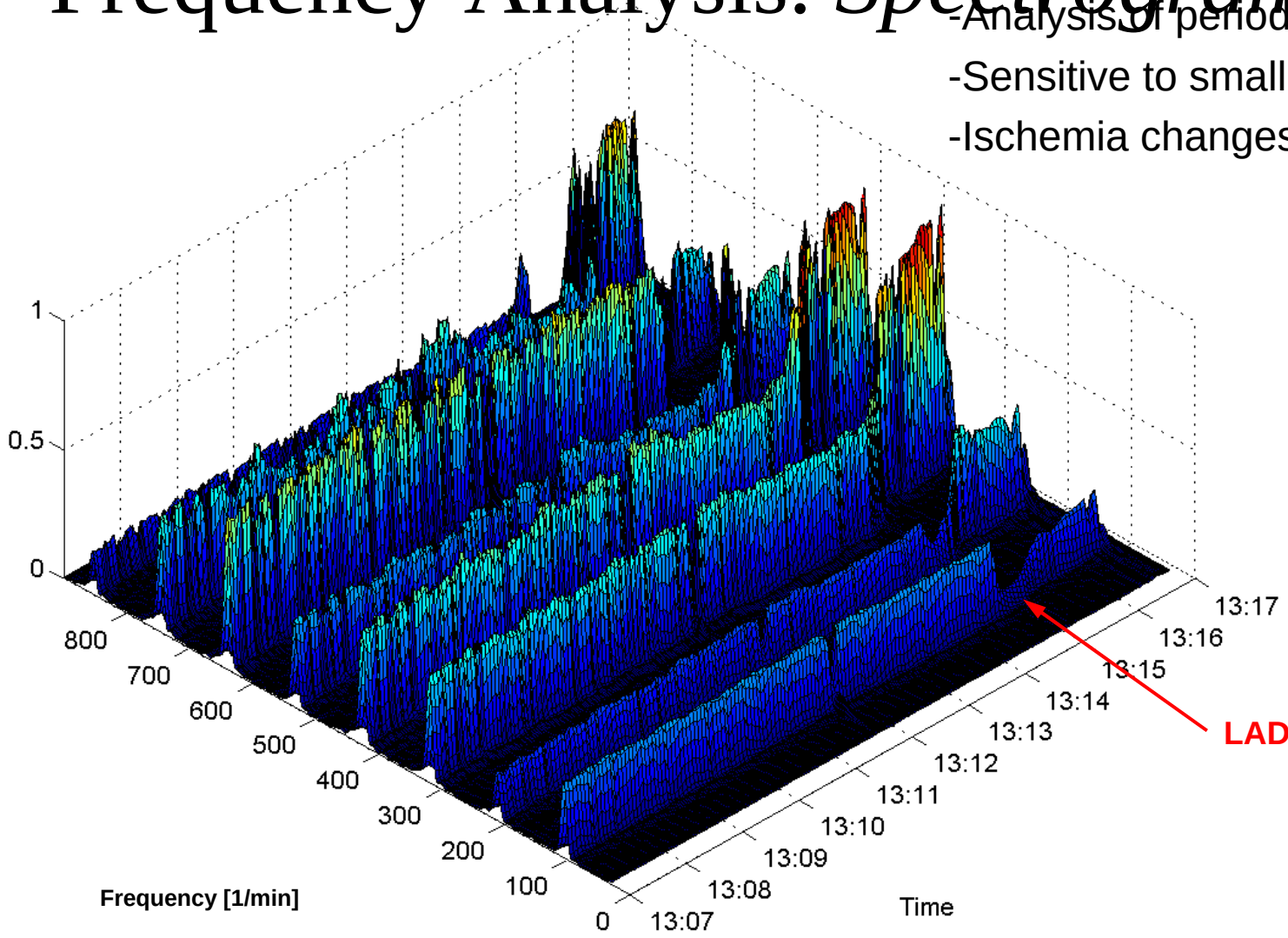


Frequency Analysis. *Spectrogram*

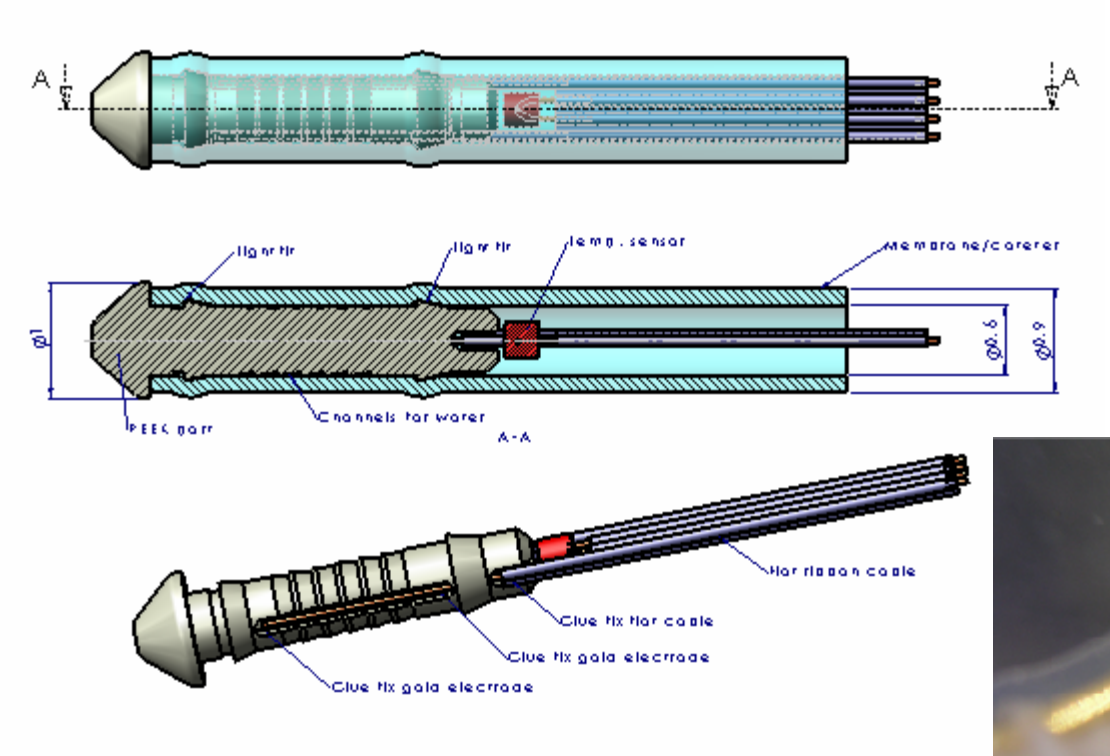
-Analysis of periodic signals

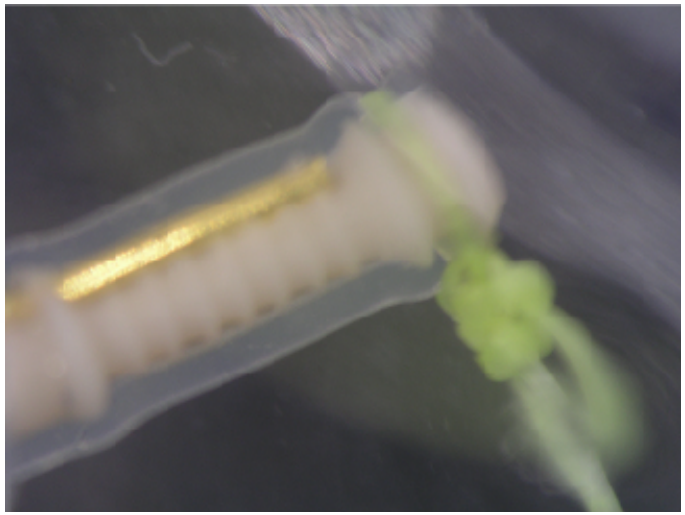
-Sensitive to small changes

-Ischemia changes pattern



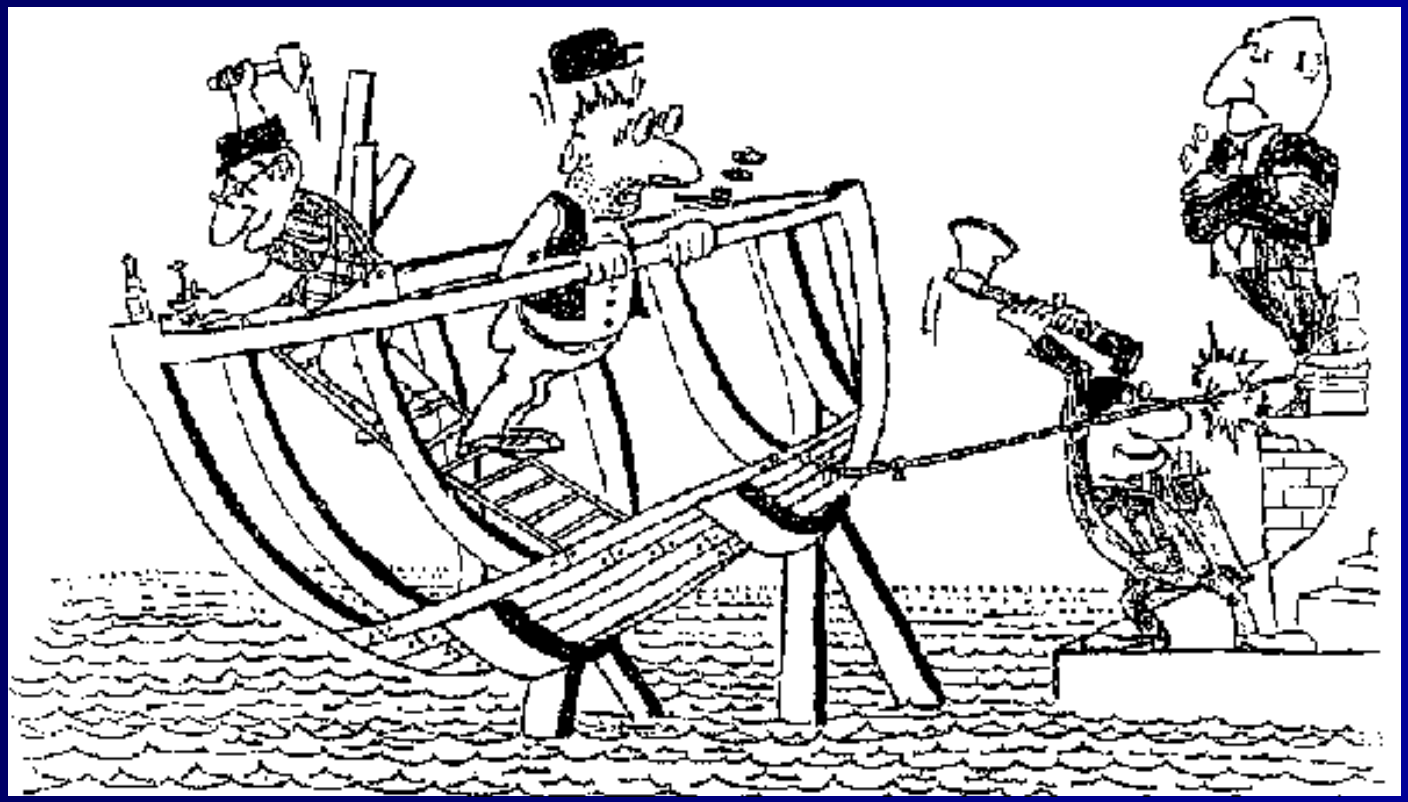
Cooperation with WL Gore



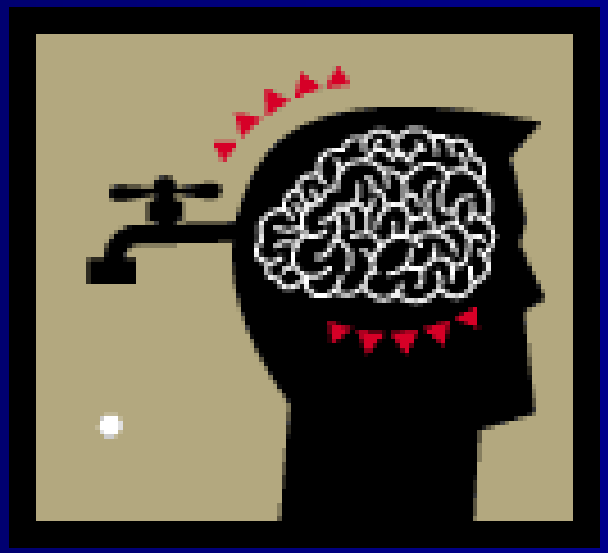


IscAlert

Why did so few succed?



Brain drain



Are we sleeping in an era of new inventions?

Trying again and again

Not every presentation is successful