



Microdialysis

in Basic Research

The Principle, the System and the Applications

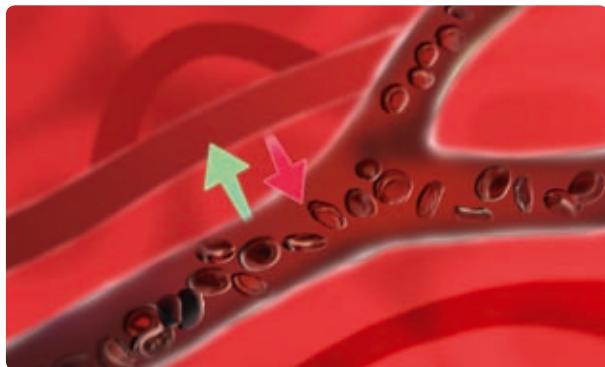


CMA *Microdialysis*

www.microdialysis.com

What is Microdialysis?

Microdialysis is an *in vivo* bioanalytical sampling technique for continuously monitoring events occurring in a living tissue.



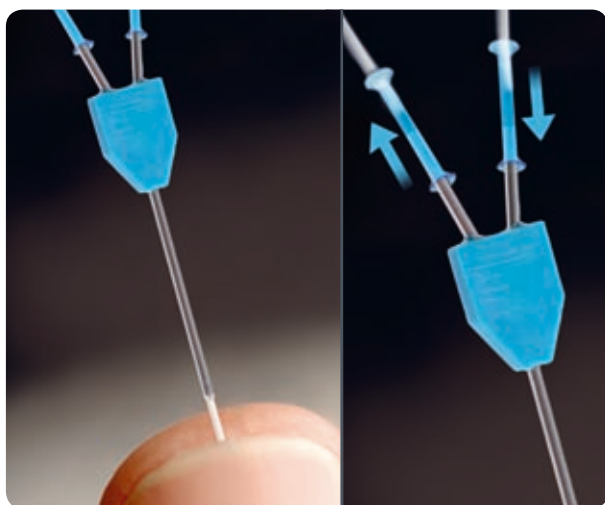
Before a molecule from the blood can enter a cell in an organ, or vice versa, it must first traverse the extracellular space. The extracellular space is filled with a fluid and comprises approximately 20% of the total tissue volume.

However, this crucial compartment for chemical communication between the cells (including neurotransmission) is experimentally inaccessible by conventional methods of bioanalytical chemistry.

Microdialysis is based on sampling endogenous substances from the extracellular space. This process is accomplished using a unique device - The Microdialysis Probe.

The Microdialysis Probe mimics the function of a blood vessel. The probe is constantly perfused with a physiological solution at a low flow-rate (usually less than 2 $\mu\text{l}/\text{min}$). Once the probe is implanted into the tissue, endogenous substances are filtered by diffusion out of the extracellular fluid into the perfusion medium.

By reversing the process the probe can be used to locally infuse exogenous compounds, nutrients and drugs for periods of up to several days. Samples are collected and then analyzed.



The Microdialysis Probe is a specially designed cannula with a semipermeable membrane at its tip. A variety of probe types with more than 20 different membrane and shaft length combinations are available. Corresponding guide cannulae facilitate easy insertion into organs, such as brain, muscles or blood vessels. They may also be used for long-term studies.

The inlet side of the Microdialysis Probe is connected to the CMA 400 or CMA 402 Syringe Pump and the CMA 110 Liquid Switch or the CMA 111 Syringe Selector. The outlet tubing is attached to the CMA 470 Refrigerated Fraction Collector or to the CMA 142 Microfraction Collector. Microdialysis combined with an appropriate analytical technique is the ultimate solution in the search for a universal, real-time biosensor.

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Configurations and Accessories

Complete Microdialysis System with collection of cooled fractions

A full system consists of a set of instruments for multiple probe sampling where the most important feature is the collection of cooled fractions into capped or open vials to prevent chemical degradation and evaporation.



CMA 470 Refrigerated Fraction Collector

The collector is specifically designed to collect microliter volume fractions typical of Microdialysis. Samples can be collected into capped or open vials from up to four probes simultaneously. Cooling prevents evaporation and chemical degradation. Includes four cassettes holding 64 vials.

CMA 150 Temperature Controller

The controller monitors and maintains the constant body temperature of small animals under anaesthesia. A heating pad and a rectal thermometer with accuracy of $\pm 0,2\text{ }^{\circ}\text{C}$ at $37,5\text{ }^{\circ}\text{C}$ regulates the temperature of the animal.

CMA 130 In Vitro Stand

The *in vitro* stand stores Microdialysis probes in solutions between experiments and facilitates *in vitro* calibration and recovery tests. Includes Connecting Rod for Clip and Stereotaxic Adapter.

CMA 111 Syringe Selector

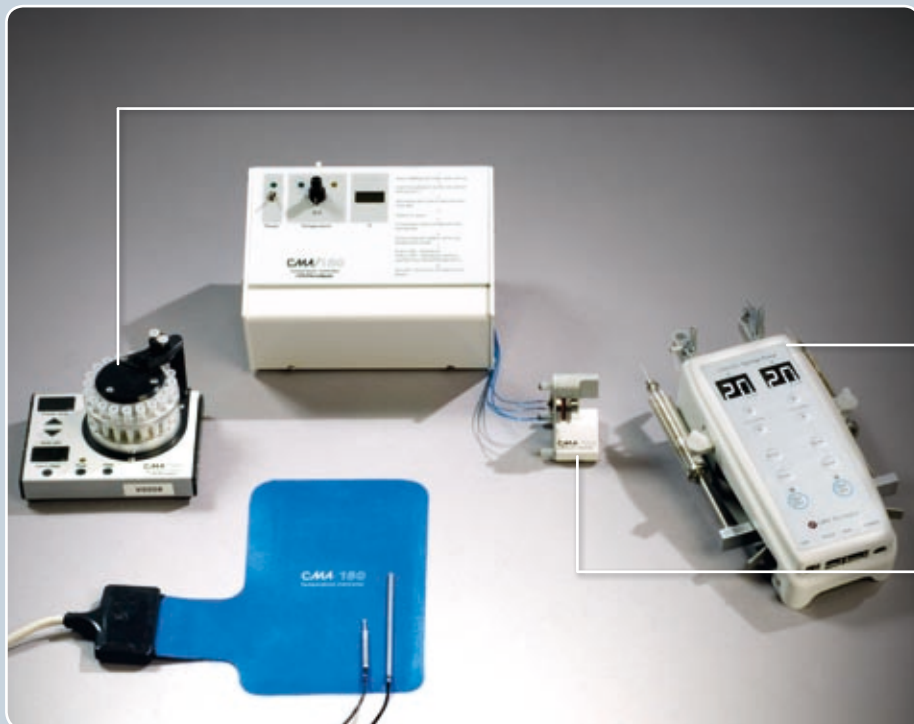
The syringe selector connects the Microdialysis probe to one of three syringes placed in the CMA 400 Syringe Pump. Switching between different perfusion fluids is achieved without any risk of introducing air bubbles or interrupting the flow.

CMA 400 Syringe Pump

This multifunctional syringe pump satisfies the requirements of Microdialysis for a continuous pulse-free delivery of a perfusion fluid at a microlitre per minute flow rate. Preset flow and total perfusion volume and time are displayed on a front panel for easy reference.

Basic Microdialysis System

The typical application for this setup is for microdialysis sampling and analysis of pharmaceuticals, cell nutrients, metabolites and inorganic ions. These compounds are usually stable and do not need immediate refrigeration.



CMA 142 Microfraction Collector

For collections from one or two Microdialysis probes (1 x 20 or 2 x 10 samples respectively). Simple operation and a convenient size makes it very useful for all *in vitro* tests and short duration experiments.

CMA 402 Syringe Pump

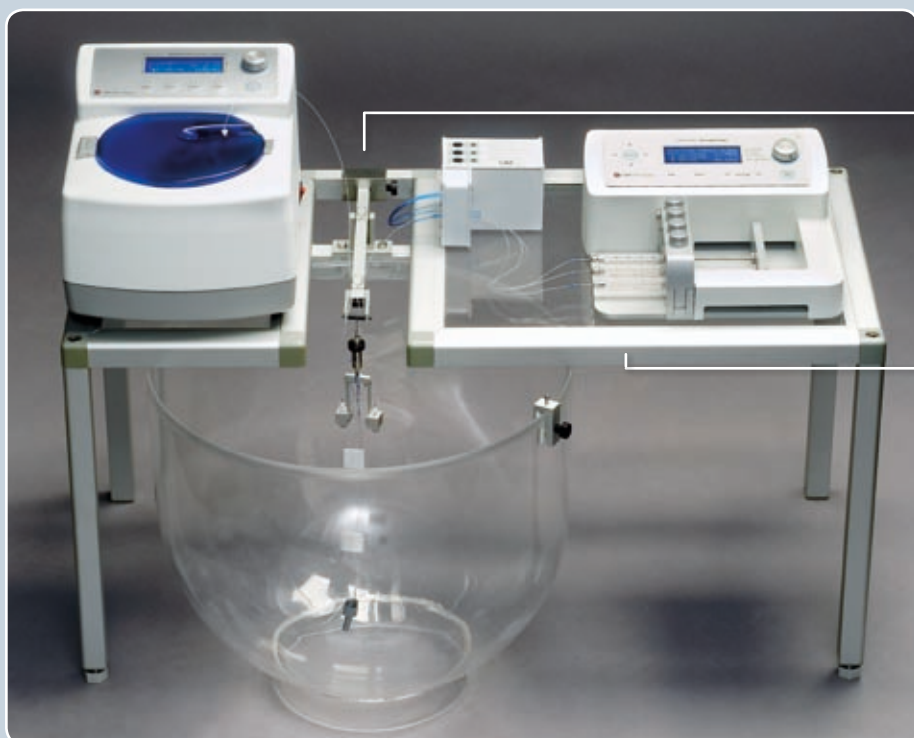
A dual syringe pump designed with low pulse-free flow suitable for Microdialysis experiments. Start/stop and flow rate can be set individually for each syringe.

CMA 110 Liquid Switch

Permits manual switching between up to three perfusion lines to a Microdialysis probe without any risk of introducing air bubbles or interrupting the flow.

System for Freely Moving Animals

Research in behavioral pharmacology, cognitive sciences, toxicology and many other fields requires experiments on conscious animals. The CMA 120 system can be combined with any Microdialysis configurations described above, providing the most sophisticated and versatile *in vivo* research technology available today.



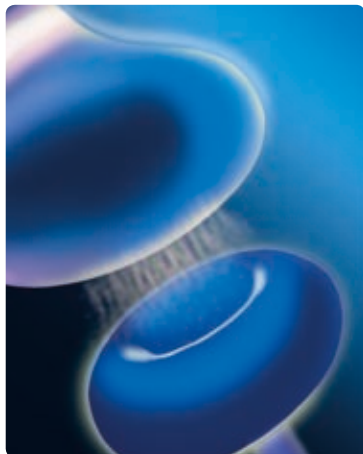
CMA 120 System for Freely Moving Animals

Permits Microdialysis studies on conscious, small animals over long periods of time. The probe tubing is attached to the instruments via a dual channel swivel and a balancing arm, allowing free movement of the animal.

CMA 120 Instrument Table

Where can Microdialysis be applied?

Psychopharmacology



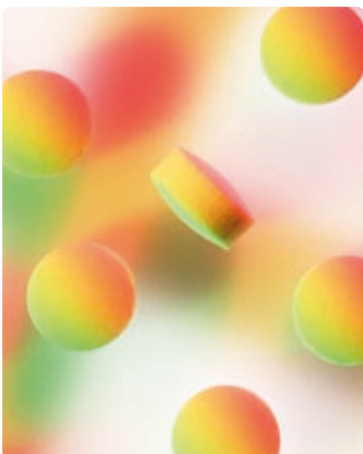
Mechanisms of drug action on release, uptake and interactions among neurotransmitters and neuromodulators represent the classical application field for Microdialysis. Neurochemical correlates to different models of mental disorder, behavioral and cognitive functions can be studied in chronically implanted freely moving animals.

Neuropathology and cancer research



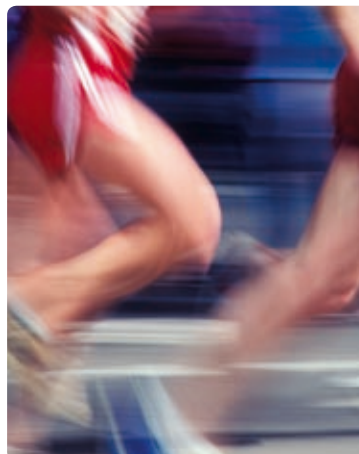
Microdialysis is an excellent tool for monitoring the compounds proposed as markers of brain injury. Neurodegenerative diseases, such as ischaemia, hypoglycaemia and epilepsy, as well as, processes related to neuronal plasticity, regeneration, neurotransplantation or tumor growth have been elucidated by Microdialysis.

Pharmacokinetics and toxicology



Microdialysis probes can be implanted simultaneously in several organs (including blood) of the same animal. Distribution and time course of free drug (toxin) concentrations are measured *in vivo*. Pharmacokinetic data can be calculated using theoretical compartment models.

Physiology



Physiological stimuli such as physical exercise, nutrition or stress alter anabolic and catabolic phases of cell biochemistry in peripheral tissues (e.g. muscle, fat). Microdialysis data can serve as a cumulative index of treatment-induced metabolic changes over long time periods in man, animals or even plants.

What is unique about Microdialysis?

Microdialysis is the most flexible *in vivo* technique and possesses some extraordinary features:

- Spatial resolution, allowing local sampling from very small tissue regions e.g. brain nuclei.
- Time resolution, achieved by sampling minute fractions at high frequency over several days.
- Adaptable for monitoring almost any endo- or exogenous substance or related metabolites.

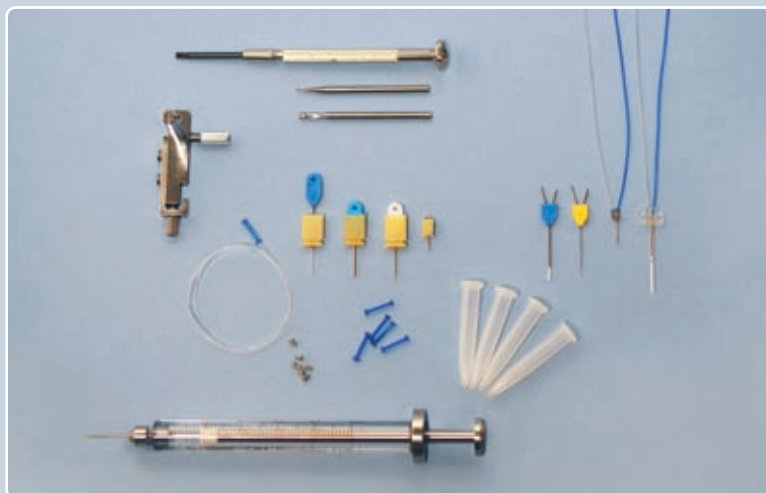


Microdialysis is the most physiological way of *in vivo* sampling, eliminating adverse tissue reactions, because:

- No macroscopic matter is removed or introduced into the tissue.
- The driving force for sampling is only passive diffusion.
- The semi-permeable membrane of the probe protects the tissue from infection and, on the other hand, does not remove large molecules, such as proteins and enzymes, from the extracellular matrix.
- Only the highest quality biocompatible materials are used for probe construction.

No purification of samples is required prior to analysis and there is no risk of enzymatic breakdown of recovered substances.

Calibration of the probes and estimation of absolute concentrations in the extracellular fluid are possible.



Microdialysis technology demands a watchmaker's precision and patience. Even the smallest details concerning the anchor screws or tubing connectors can be crucial for obtaining reproducible data.

ORDERING INFORMATION

	Ref No
CMA 400 Syringe Pump	8002020
CMA 402 Syringe Pump with Accessory Kit	8003100
CMA 402 Syringe Pump	8003110
CMA 470 Refrigerated Fraction Collector	8002770
CMA 142 Microfraction Collector, 230V	8381142
CMA 142 Microfraction Collector, 115V	8381143
CMA 110 Liquid Switch	8308200
CMA 111 Syringe Selector, (powered by the CMA 400 Pump with the use of a CMA 400 Adapter)	8308210
CMA 400 Adapter, for CMA 111	8002030
CMA 130 In Vitro Stand, supplied with four combinations of clips	8309101-04
CMA 150 Temperature Controller for Rat	8315000
CMA 150 Temperature Controller for Mice	8315010
CMA 120 System for Freely Moving Animals	8309049
CMA 120 Instrument Table	8309046

CMA Microdialysis AB

CMA Microdialysis is the pioneer and leading company devoted to the development, manufacturing and marketing of the Microdialysis technique. The company was founded in 1984 as the first company in the world to market Microdialysis products and know-how. Consumables, instruments and computer software are developed and manufactured in Sweden with ISO 13485 certification.

CMA offers an extensive line of basic research products and a complete portfolio of CE approved and 510(k) cleared clinical products. The core technology and the essential peripherals are protected by US and International patents.

CMA Microdialysis AB

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