TSE systems

Metabolism

LabMaster – Metabolism Research Platform

Drinking & Feeding – Metabolic Performance – Activity

Contents

– Specifications subject to change without notice. –

Sophisticated Life Science Research Instrumentation
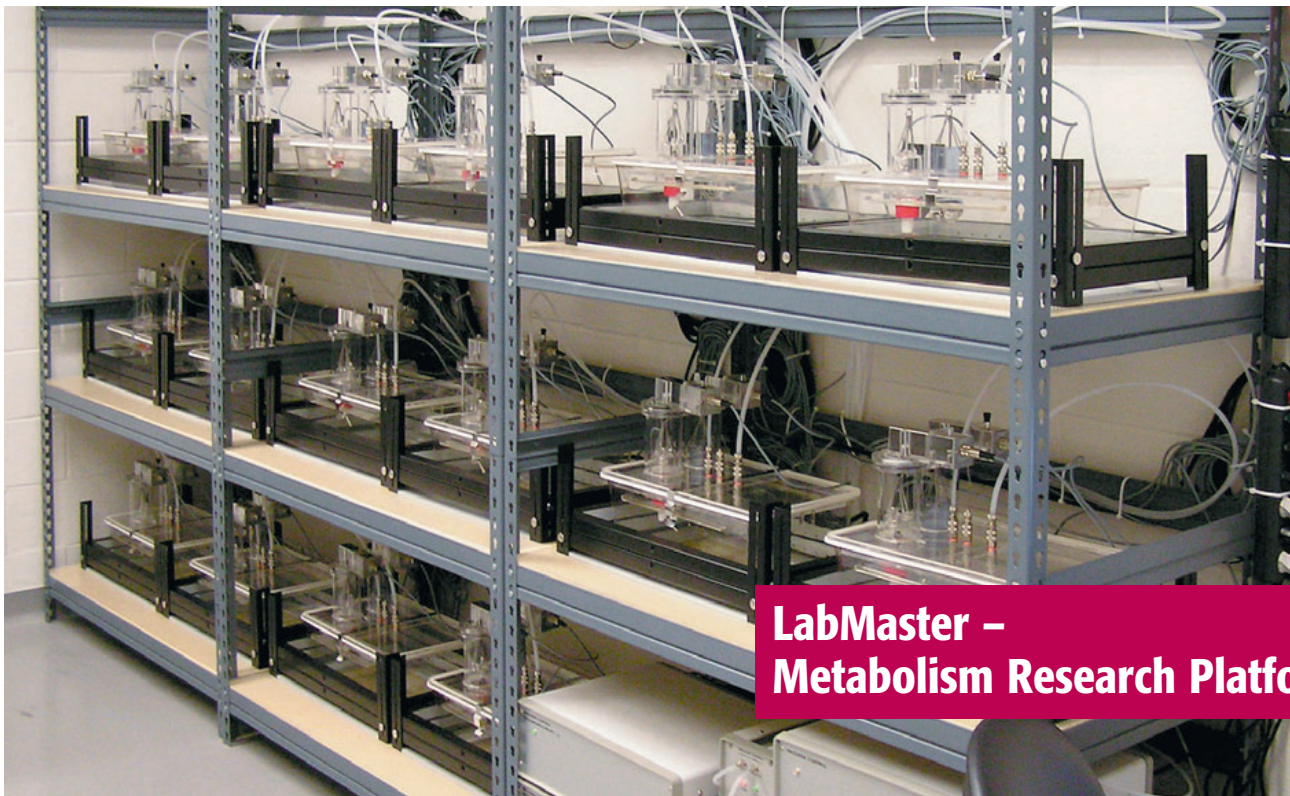
**LabMaster –
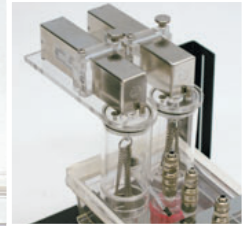Metabolism Research Platform**

■ *LabMaster 16-place: drinking & feeding, activity and metabolic monitoring*

LabMaster Key Features

- ■ Advanced modular metabolic animal research system
- ■ Most flexible system on the market
- ■ User-friendly with easy to use hardware & software
- ■ Standard home cage environment for unbiased stress-free animal behavior
- ■ All standard home cages can be used without any modification
- ■ Combination system for mice & rats:
  - ◆ drinking & feeding
  - ◆ urine & feces
  - ◆ indirect calorimetry
  - ◆ activity
  - ◆ wheel
- ■ Short-term / long-term monitoring for even several days in a row
- ■ Turnkey systems for a large number of animals / cages simultaneously
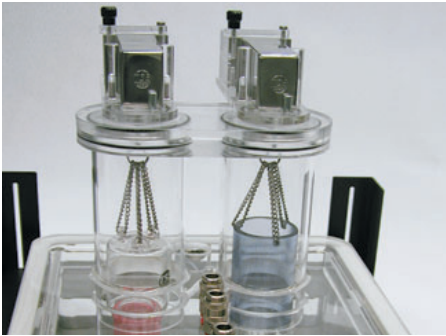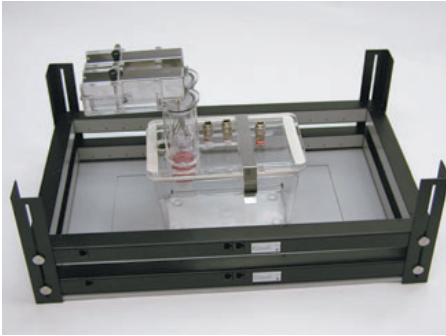
■ *LabMaster details*
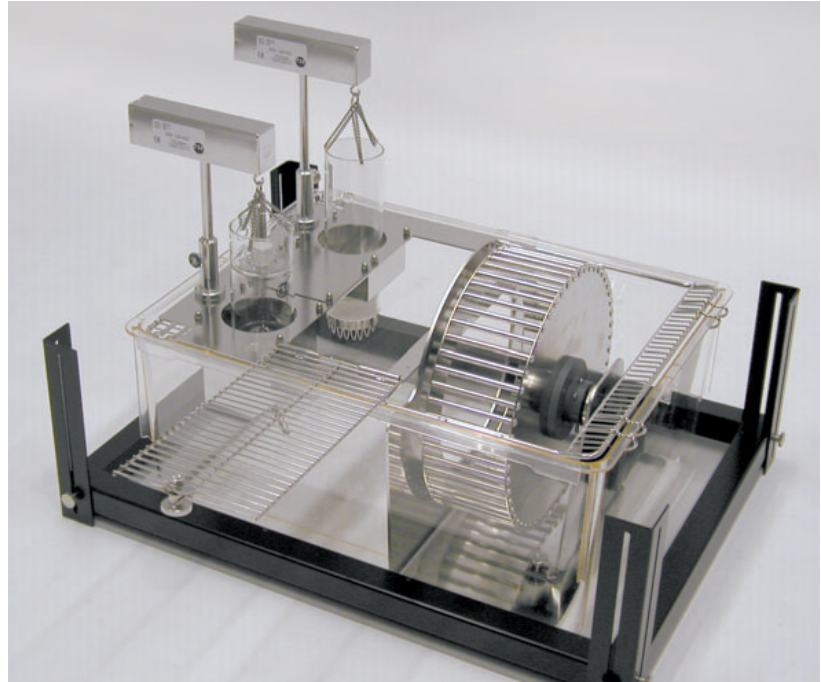
■ *LabMaster with drinking & feeding, activity (X,Y) and running wheel (rat)*

LabMaster Philosophy

The TSE LabMaster System represents a modular animal research platform for top-of-the-art metabolic and behavioral investigations. It combines a range of different sensors and integrates a vast amount of information for each animal. LabMaster allows automated, non-invasive long-term monitoring for a large number of animals (24-hours or even several days in a row). LabMaster simultaneously monitors several physiological and behavioral parameters in the stress-free home cage environment for mice or rats.

These parameters are:
- Drinking & feeding (amounts / patterns)
- Metabolic performance
  (O_2 consumption, CO_2 production, RER)
- Home cage activity
- Running wheel activity (optional)

The LabMaster System forms the basis for an even more extended upcoming solution for automated physiological and behavioral phenotyping of mice and rats: TSE PhenoMaster System.

Standardized components of well-proven classical TSE animal monitoring systems are used. These components are combined and assembled modularly to provide an efficient tool for scientific research according to your particular needs.

Multi-sensor monitoring features

- Drinking & feeding:
  - Most flexible and highly sensitive sensors, mounted on the lid of the cage
  - Various sensor numbers / configurations possible
  - For mice or rats

- Metabolic performance:
  determined by open circuit calorimetry

- Home cage activity measured by means of:
  - Infrared light-beam frame surrounding the cage
    or
  - Infrared heat sensor on top of cage lid

- Running wheel to be added
  - Passive running wheel activity within home cage
    or
 - Active CaloWheel performance with controlled speed profiles / work loads

Sub-System Features

Drinking & Feeding

Drinking & feeding behavior of the animals is recorded by means of special sensors with the appropriate drinking bottle or food container mounted.

Various configurations from one up to four sensors per cage are possible according to the required number of drinking and / or feeding stations.
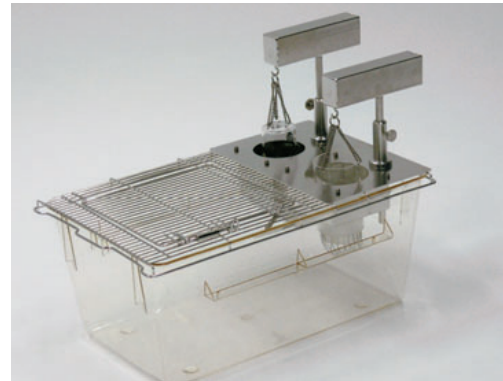
■ *Drinking & feeding standard monitoring*

Activity

… via light-beam sensor frames

Activity measurements via classical infrared light-beams can be performed by means of a sensor frame surrounding the home cage. The frames are equipped with light-beams in the basic plane (X or X, Y). Rearing indicators with an adjustable height (Z) are available.

Various parameters can be determined such as total activity, ambulatory & fine movements, rearing. If needed, full tracking and further quantification is possible.

■ *Infrared light-beam frame (X, Z)*

… via InfraMot sensors

Total activity can be measured for given time intervals with an infrared heat sensor attached to the cage lid.

This sensor registers the activity of one or more subjects by sensing the body heat image, i.e. infrared radiation, and its spatial displacement as a function of time. In this way total movement within the home cage can be quantified.
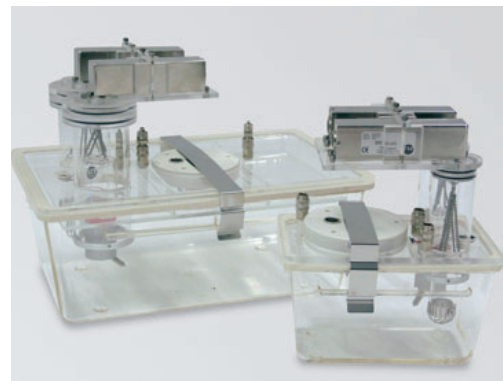
■ *LabMaster cages with InfraMot sensors attached*

Wheels

… via passive running wheel

A passive running wheel can be put into the cage in order to obtain the number of rotations performed voluntarily by the animal as an additional activity parameter.

… via CaloWheel

An active, motor-driven wheel is available, surrounded by a sealed housing for performing calorimetric measurements during exercise (CaloWheel).
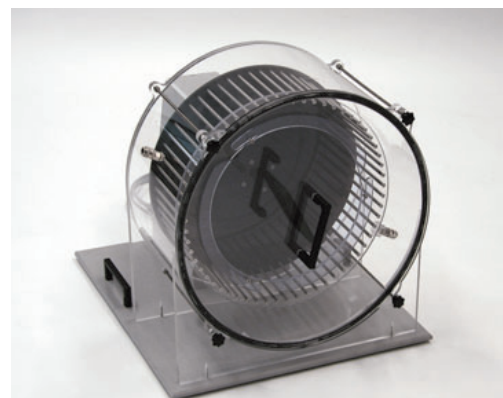
■ *CaloWheel*

■ *Calorimetry cage: basic model*
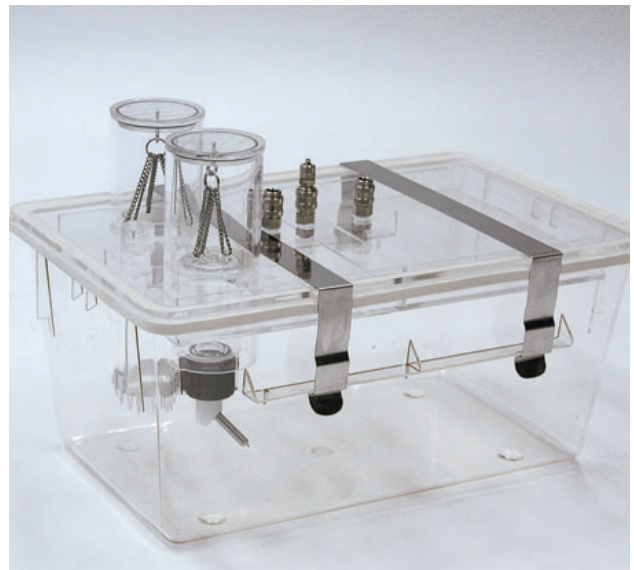
■ *Adaptation for subsequent extension with drinking & feeding sensors*
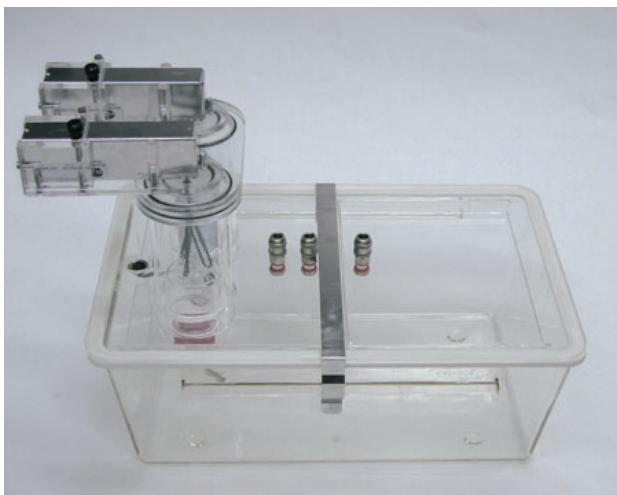
■ *Calorimetry cage for rats with drinking & feeding stations*

Calorimetry

The calorimeter components are used for automatically recording and analyzing metabolic parameters of the animals in the calorimetry cages with the sandwich structured lids.

The calorimetry system is operated as an open circuit measuring system for determination of O_2 consumption, CO_2 production, respiratory exchange rate (RER), heat, as well as the difference in O_2 consumption and difference in CO_2 production during an experiment.

The parameters may be calculated and displayed both online and offline by the TSE LabMaster software. The display mode and the parameters shown can be arranged as required by the user.
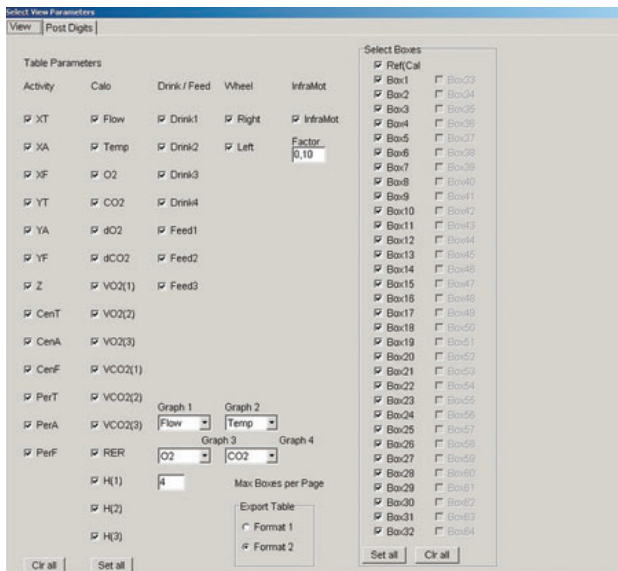
■ *View menu – selection of view parameters*
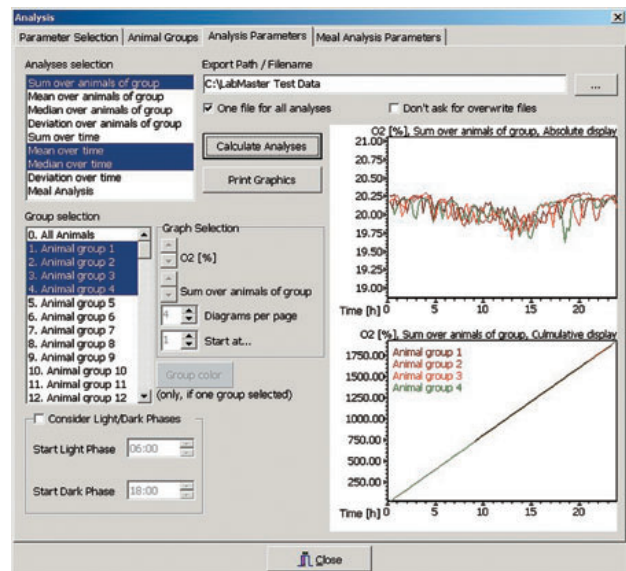
■ *Analysis menu – evaluation parameters*

LabMaster Software Concept

LabMaster software is designed as the general integration platform to handle information from all the different sensors installed. LabMaster software is structured within modules. Depending on the system configuration only the corresponding software functions are activated. A convenient data table and a graphic display are used for management of the measuring parameters.

The whole experimental procedure as well as data collection is automatically controlled by the software. The individual experimental parameters are defined within the Setup menu.

The graphic display of available measuring parameters when running the experiment and of results after finishing the experiment is defined within the View menu. Individual measuring values may be inspected during the experiment using the Status display.

Measurement analysis is enabled using different evaluation tools, for example:

■ Mean values
■ Median values
■ Sum values

… with respect to time or to all animals within the experiment.

Additional special analyses are available such as meal analysis for drinking & feeding data, etc.

User-specified group definition and analysis is also possible.

Drinking & Feeding

■ *Standard drinking & feeding monitoring system – 24-place system*

Key Features

- ■ Most flexible drinking & feeding monitoring technology on the market
- ■ All standard home cages usable without any modification
- ■ Mountable to any type of cage lid
- ■ High-precision sensors of 0.01 g / 0.01 ml resolution
- ■ Supply of liquid & food from the top of the cage – similar to standard home cages – for unbiased stress-free animal behavior
- ■ Sensors may be used either in a drinking or feeding station with a drinking bottle or food container attached
- ■ Variable number of sensor stations (liquid or food), maximum 4 per home cage
- ■ Choice preference measurements for liquid or food easily possible by inter-changeable use of the same sensors
- ■ No space restrictions for liquid & food access for normal or obese mice / rats as well as for young or old animals
- ■ Automated food access option – pre-programmable for time and / or amount (yoked and paired feeding)
- ■ FeedTime training for defined feeding rhythms in home cages

Sophisticated Life Science Research Instrumentation

■ *Drinking bottle with special nipple & food container*
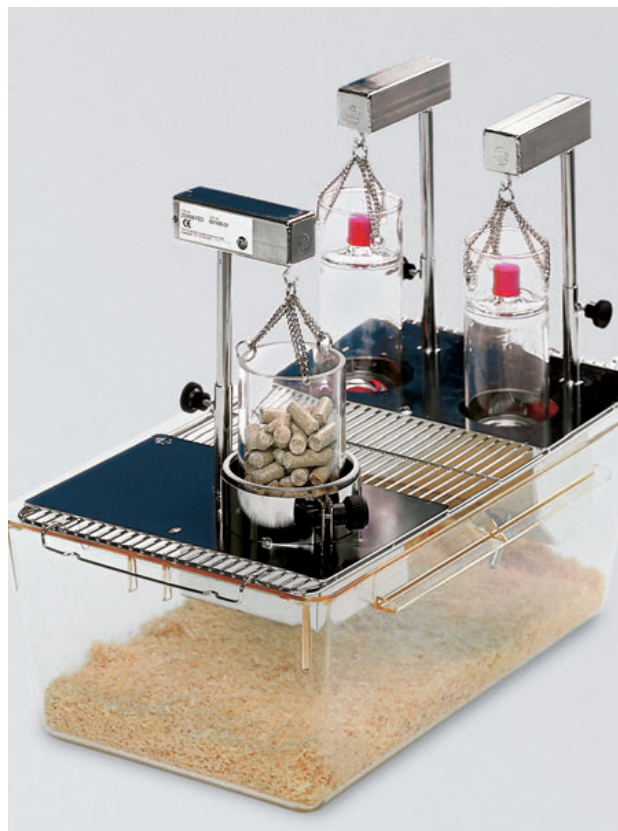
■ *Three-sensor configuration*

Hardware Design

The drinking & feeding behavior of the test animals is measured by means of high-precision sensors attached to the top of the cage lids. The removal of liquid or food from the drinking bottle or the food container is monitored continuously by amount and time, the software records the data.

A drinking station consists of a sensor with a liquid filled glass bottle, which projects into the cage, connected to a sensor. The animal drinks via a special nipple ensuring no liquid loss.

A feeding station consists of a sensor with a food container projecting into the cage. It contains standard or special food pellets for mice or rats.

Access to the food is given via a round stainless steel wire basket. The animals can gnaw off pieces of food through the steel bars in the same way as they do with the ordinary food cribs.
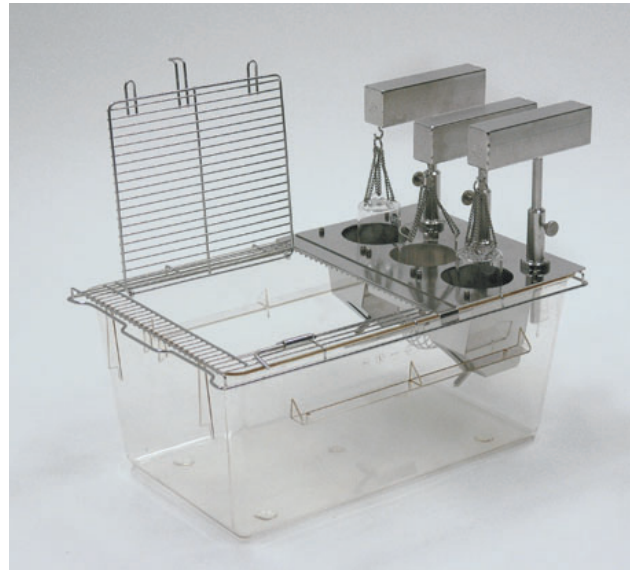

■ *Drinking & feeding sensors*

Sensors for drinking & feeding monitoring are available for mice (filling amounts of 50 g or ml or 100 g or ml) and for rats (filling amounts up to 250 g or ml). Sensors are universal and may be used for liquid or food.

■ *Standard dual-sensor configuration*

■ *Three-sensor configuration for choice preference*
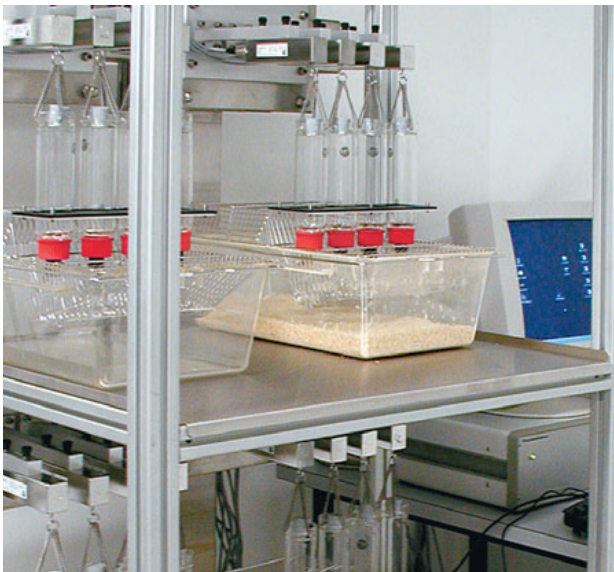
■ *Alcohol research system (four bottles)*

Sensor configurations

The standard configuration is the dual-sensor home cage system with one drinking and one feeding station. This is also the configuration with the standard LabMaster system, where the sensors are attached in a special way to the sandwich lid of the calorimetry cage (see page 17).

For choice preference investigations a three-sensor (side by side) configuration is most attractive: It can be used as

■ 2 x drinking   1 x feeding (middle)
■ 2 x feeding   1 x drinking (middle)

by simple remounting.

Up to 4 sensor stations can be mounted on the lid of a home cage (type 3), for example, in alcohol research 4 bottles side-by-side are possible.

There are several ways of combining drinking & feeding with simultaneous activity monitoring (see chapter "Activity").

Practically an unlimited number of sensor stations can be connected to the monitoring system for screening purposes.

Sophisticated Life Science Research Instrumentation
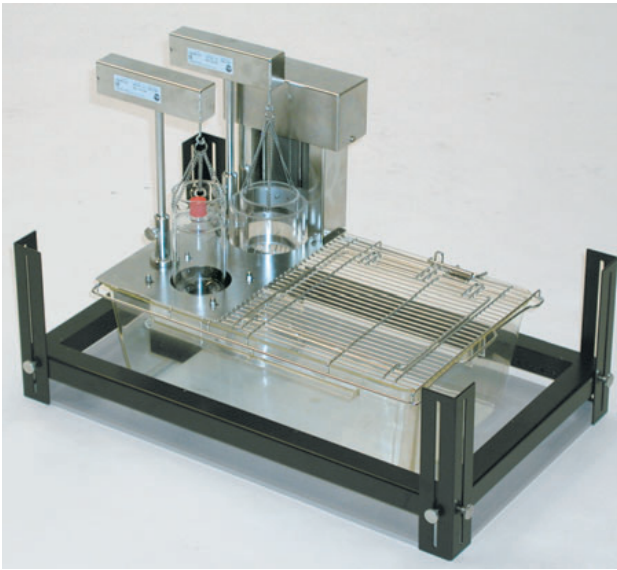
■ *Feeding station with automated food access*
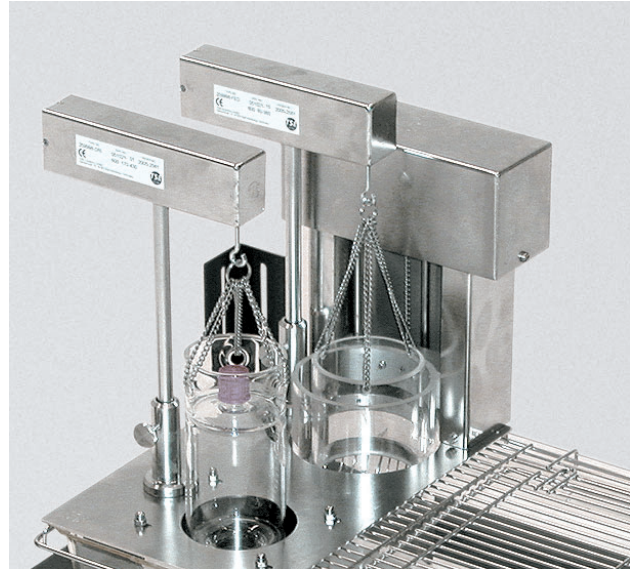
■ *Time and/or amount restricted food access*

Automated liquid / food access

There is an automated liquid / food access option available for the sensor stations which is pre-programmable

■ for time (time-controlled liquid / food access)
  or
■ for amount (yoked and paired feeding).

FeedTime

Additionally, a special home cage time-controlled food access system (FeedTime) allows training through its defined feeding rhythms.

■ *FeedTime – time-controlled food access*

■ A feeding roller in the food crib can be turned time-controlled via the software enabling or disabling the animal's access to the food
■ Individual feeding times and durations are programmable according to a user-defined time schedule

■ *Setup menu for drinking & feeding module*

■ *Trial Monitor – at trial start and after removal of substance*

Software Features

The drinking & feeding software module controls the experiment, records the amount of liquid & food removed and stores, analyzes and documents all the measured data.

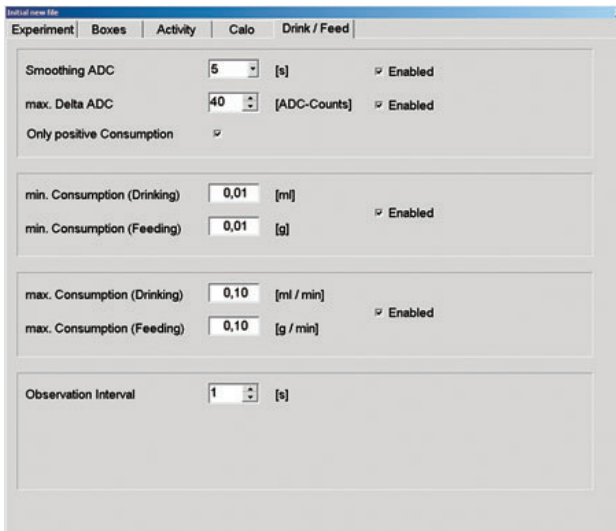Drinking & feeding monitoring can be achieved with the following steps:

- Preparing the setup for an experiment
- Running the experiment, and
- Analyzing the collected data.

In addition to the observation time interval the experimenter can set the upper limit for one single liquid or food removal. Within these limits the amounts of liquid and food removed will be recorded. Values outside these limits, e.g. those possibly caused by knocking the container against the sensor or by the animal lifting the container, will not be taken into account.

During the experiment the trial monitor directly displays the amounts of liquid & food consumed by the animal so far.

The monitor displays the status of the drinking and feeding containers by colored bars – blue = drinking, green = feeding. Red areas show the amounts removed by the animal since the start of the experiment or since the last refill. The remaining gray area on the bars indicates that the container had not been completely filled.

The figure below the sensor bars quantitatively displays the current consumption (in g or ml) during a running experiment.

Automated food access

Using timed-controlled access to drinking bottle or feeding container the exact times for access may be pre-programmed.

The program tests all the entries in the corresponding programming table in sequence to check whether the given time has been reached and then carries out the command.

This procedure is repeated each day in a long-term experiment.

Sophisticated Life Science Research Instrumentation
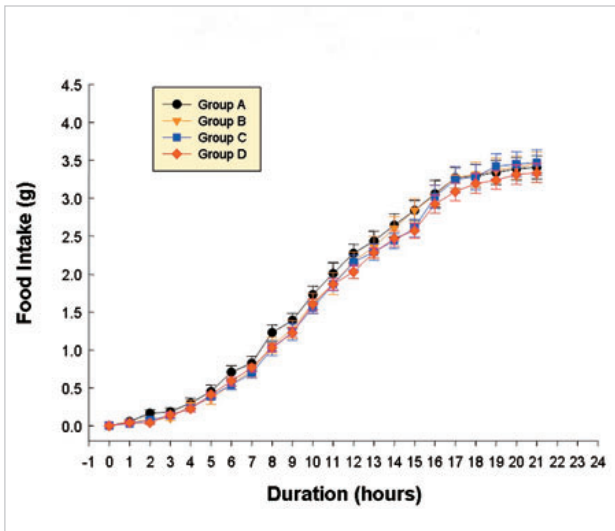
■ *Food intake for 21 hours – 40 mice, 4 groups each of 10 mice, untreated*
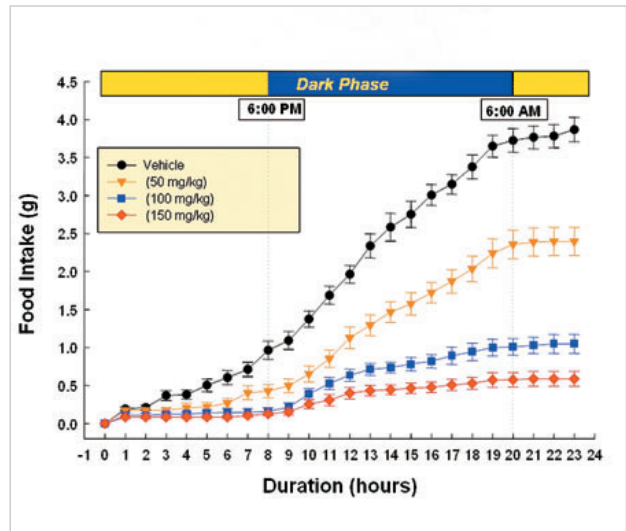
■ *Food intake for 23 hours – 40 mice, 4 groups each of 10 mice, different dosages*

Graphical display

In the run graph the liquid and food consumption is documented graphically for each animal. Data is displayed in a coordinate system with the time as the X-axis and the amount as the Y-axis. All sensors allocated to each cage are displayed simultaneously. The units on the X-axis can be selected (min, h, days).
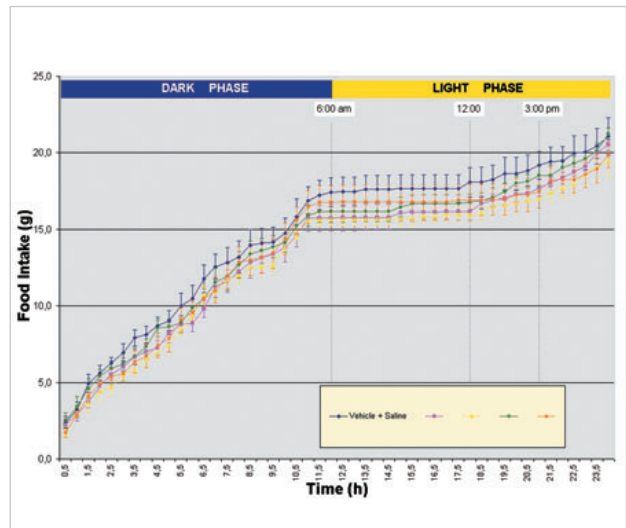
■ *Food intake for 24 hours – 40 Wistar rats, 5 groups each of 8 rats, untreated*

■ *Light-beam frame (X, Y, Z) for rats and mice*
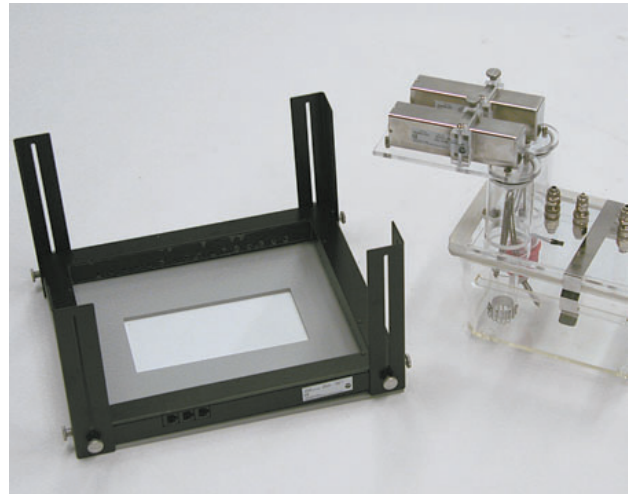
■ *Light-beam frame (X, Y) for mice*

Activity

- In the three dimensions X, Y, Z, separate infrared light-beam frames surround the home cage
  or
- Total activity monitoring by infrared heat sensor on the top of cage lid (InfraMot)

Light-beam Frames

Components design

For activity measurements the animal cage is put inside the infrared light-beam frame. Light-beams may be installed in both axes of the basic plane X, Y, and complemented by a rearing indicator at an adjustable height Z (parallel to X-axis).

In combination systems for mice and rats templates are used to position the smaller mouse cage inside the larger frame for rats.

Two distances between two neighboring infrared light-beams are available allowing the necessary spatial resolution.

No calibration is needed when using the light-beam frames. They are ready for use after installation.

The status of interruption of the light-beams is changed by the movement of the animal. Each such change is registered as a count. This means that permanently interrupted light beams will not be taken into account.

Sophisticated Life Science Research Instrumentation
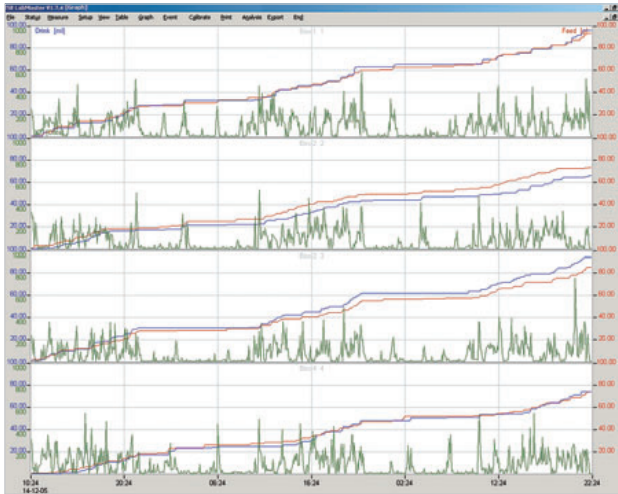
■ *Long-term simultaneous drinking & feeding and activity monitoring*

■ *Spatial distribution in home cage*

■ *Histogram of distances moved and number of rearings*

Software module

The software records the number of light-beam interruptions caused by the animal's movement – in contrast to the residence time in front of the light barriers.

Light-beam breaks are divided into ambulatory (breaks of any two different beams of light at the X or Y level) and fine movements (two consecutive breaks of a single beam of light at the X or Y level) whose sum provides the total number of light-beam breaks. Rearing of the animal is indicated by the frame at the Z level.
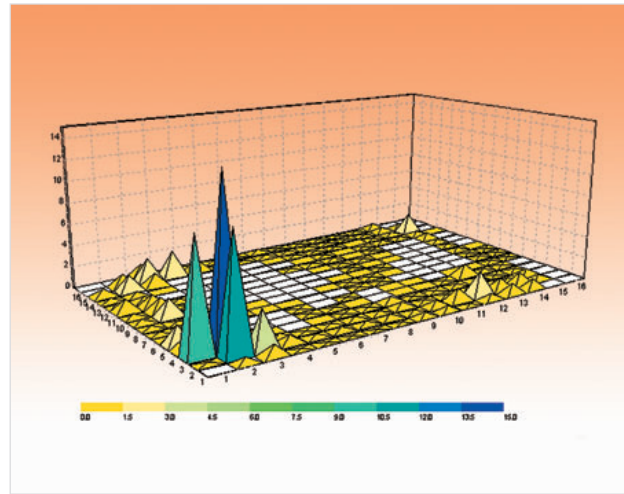
Movements that are repeated at short intervals, e.g. tail flicking, can be ignored by defining a refractory period, i.e. if short-term movements are detected within this defined period then no count will be registered.

The user can define a part of the light-beams as the "Center". This allows the measurement area to be adapted to suit animal cages with different sizes as well as the definition of 2 different measuring ranges (central and peripheral).

■ *InfraMot activity sensor mounted on home cage lid*
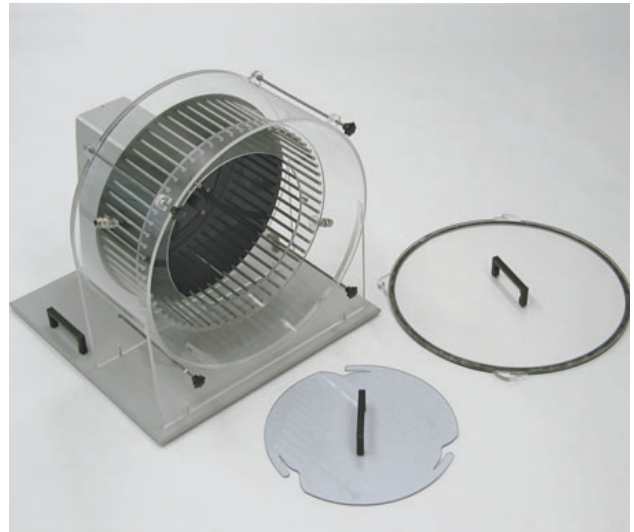
■ *CaloWheel for exercise calorimetry*

InfraMot Sensors

Total activity measurements of mice, rats and other small laboratory animals in the home cage can easily be done via an infrared heat sensor attached to the cage lid.

Activity can thus be measured under any lighting conditions. Measurements can even be made in complete darkness.

The sensor registers the activity of one or more subjects by sensing the body-heat image, i.e. by infrared radiation, and its spatial displacement as a function of time. In this way movement within the cage can be reliably determined and quantified. This even includes movements which have a duration of only a few milliseconds.

The wide-angle infrared detector also allows rearing events to be included in the activity data.

The standard sensor assembly includes a stainless steel sensor housing and is designed to be mounted on top of a home cage lid. The sensor unit is available as a stand-alone version or mounted on the lid of the cage together with the drinking & feeding sensors.

The software records the total counts (changes of the heat image) during a measuring time interval. This measuring data – during each consecutive time interval (to be set) – provides a relative measure of the duration and intensity of the animal's activity.

Running Wheels

■ Passive running wheel integrated into home cage
or
■ Active CaloWheel for speed-controlled exercise calorimetry with surrounding sealed housing.

Passive running wheel

A passive running wheel can be integrated into the home cage in order to provide an additional parameter for motor activity. The number of revolutions in a time period as well as the direction of rotations performed by the animal can then be monitored.

CaloWheel

Active calorimetric wheels are available for performing speed-controlled exercise tests. These CaloWheels are motor-driven and are enclosed in a sealed housing which is connected to the calorimetric system. This provides calorimetric compartments with a special geometry. PC controlled speed profiles can be run automatically. The animals' metabolic performance under different workload conditions thus can be investigated.

Sophisticated Life Science Research Instrumentation
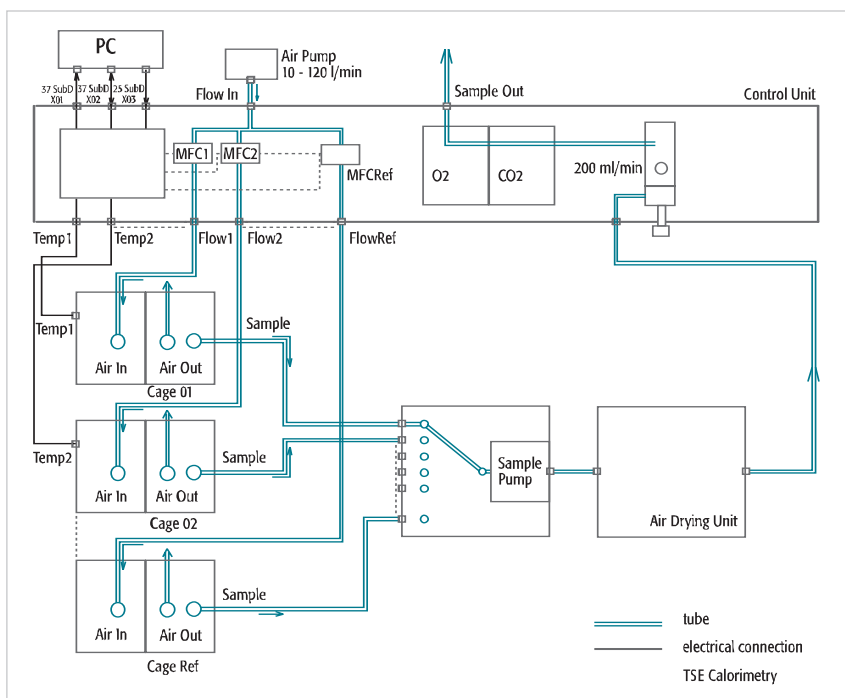
■ *Calorimetry: components and working principle*

■ *Calorimetry cage for mice with D & F stations*

Calorimetry

■ Easy-to-use straight forward design
■ High accuracy, using individual mass flow controller for each cage
■ No daily calibration necessary

Hardware design

The calorimetry module is an open circuit measuring system for determining the parameters O_2 consumption, CO_2 production, respiratory exchange rate (RER), heat production and temperature as well as O_2 and CO_2 difference (animal cage O_2/ CO_2 minus reference air O_2/ CO_2).

A special cage lid design ensures spatial separation of air inlet, air outlet and a separate sampling connection.

Each animal calorimetry cage can be adapted to simultaneous drinking & feeding monitoring by means of special gas-tight weighing sensor kit. The calorimetry measuring module can be configured to run with a certain number of special animal cages. Each cage is continuously provided with fresh air from an air pump.

The control unit contains the connections for data transmission with the computer and in addition the special sensors for O_2 and CO_2 concentration measurements. With the help of a multiplex sample switch unit air samples are taken at defined intervals from each animal cage.

The air samples from the cages are transferred to the control unit, where O_2 as well as CO_2 gas concentrations are measured. The sample concentrations are compared to a fresh air reference.

With the help of temperature sensors the temperature in the test cages can be measured and recorded for the whole experiment.

Moisture that could be deposited on the O_2 and CO_2 sensors is removed from the air samples by an air drying unit.

Each individual calorimetric cage has its own high-precision mass flow controller ensuring precise and uniform flow throughout the whole experiment.
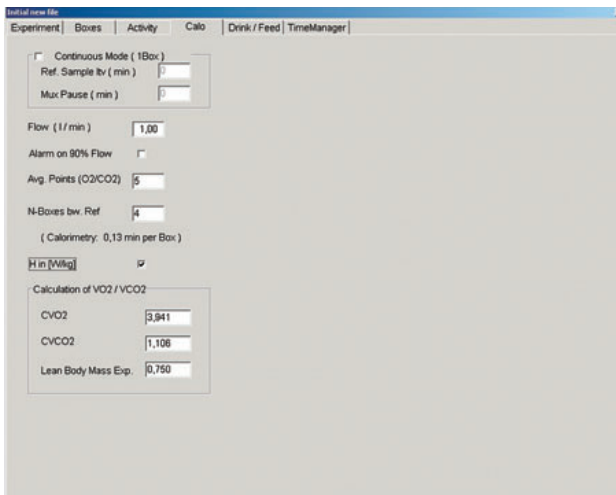
■ *Setup menu for calorimetry module*

■ *Graphical display of calorimetric parameters*

Software features

The calorimetry software module enables you to:

■ Specify measurement parameters
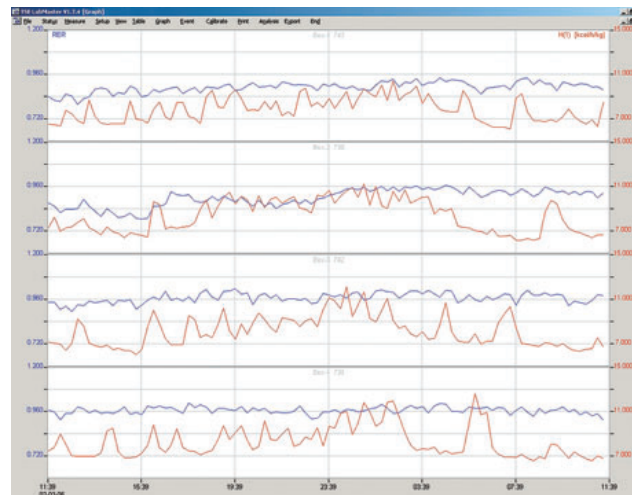■ Control all hardware components
■ Display recorded values
■ Record and store the measured values
■ Calculate calorimetric data

As a special function the lean body mass index can be taken into account. It is possible to specify standard or user-defined values as well as to neglect the body mass.

A tabular display shows the numerical listing of the calorimetric values together with the set flows. User-defined concealment of individual parameters or animals on the monitor and in the export table is possible.

Additionally, a four-channel graphical display is available with individual setting of X and Y scales, parameter choice, etc.

The particular system configuration is displayed in a separate window – assignment of the hardware channels, channel identification, etc.

Event markers may be set at specific times during a running experiment in order to provide a more detailed description of this test.

Individual results tables or curves can be generated by using the analysis menu – free grouping of the individual parameters and test animals is provided.

A sensor calibration routine by means of linear regression is available – automatic storage of calibration data.
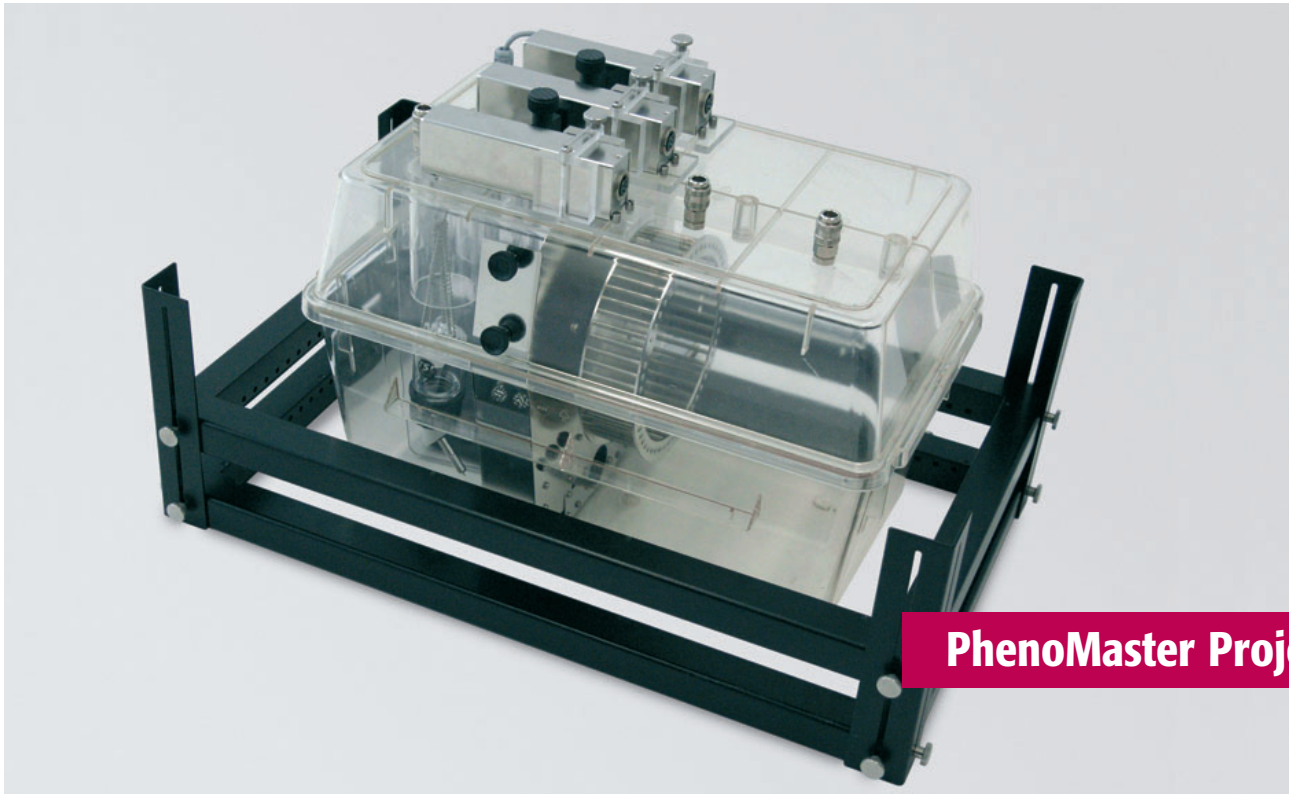
■ *PhenoMaster design study*

PhenoMaster Project

Automated High Throughput Behavioral and Physiological Phenotyping of Small Laboratory Animals (Mice, Rats, etc.)

Key Features

- ■ Based on LabMaster research platform
- ■ Simultaneous and automated operation of multiple PhenoCages for long-term monitoring
- ■ Activity monitoring by infrared light-beam frame (X, Y, Z)
- ■ Drinking & feeding monitoring by high-precision sensors
- ■ Add-ons to be mounted at the special PhenoCage lid:
  - ◆ Passive running wheel
  - ◆ Operant wall for learning & memory tasks
  - ◆ etc.
- ■ Metabolic performance by indirect calorimetry (O_2, CO_2, RER, Heat)
- ■ Physiological parameters by telemetry, transponders

Envisaged cage family:
- ■ PhenoCage
- ■ ObesityCage
- ■ CogniCage
- ■ AddictionCage
- ■ PhysioCage
- ■ CircadianCage
- ■ AnxietyCage
- ■ ChronoCage
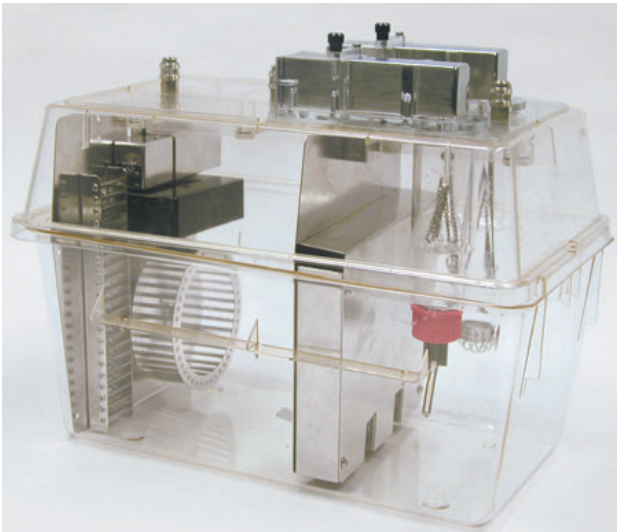
■ *Details: design study view I*

■ *Details: design study view II*

Envisaged Cage Family

PhenoCage System

■ Spontaneous home cage activity (infrared light-beam frame X, Y ,Z)
■ Drinking & feeding monitoring (sensors stations or dispensers)
■ Add-ons:
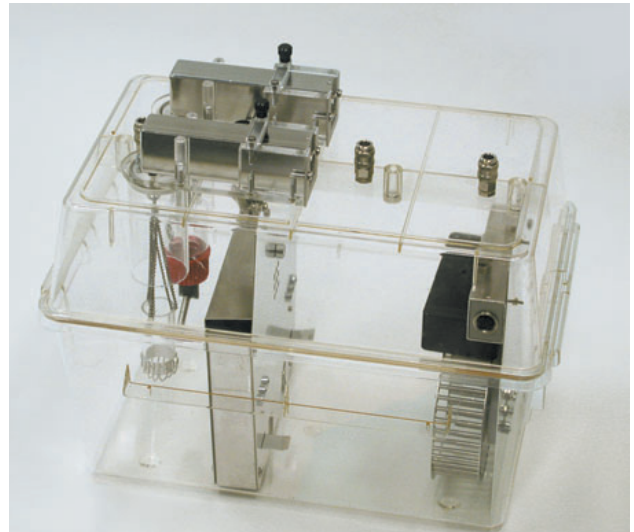 ◆ Running wheel (enabled / disabled, duration, distance, time pattern)
  ◆ Basic operant wall with automatic door, stimulus elements, response elements (nose pokes / levers)
  ◆ Illumination (light-dark cycles, selective / aversive light stimuli)
  ◆ Automatic body weight monitoring
 ◆ Enriched environment (e.g. animal house, etc.)

CogniCage System

■ Additional testing of learning and memory
■ Variety of operant behavioral tasks
■ Completion of PhenoCages with fully equipped operant wall with:
  ◆ Automatic doors
  ◆ Stimulus elements (light, audio, etc.)
  ◆ Response elements (nose pokes for mice, levers for rats)
  ◆ Reinforcer elements: Reward by liquid and / or food access, punishment by aversive air-puff option or electrical shock option

MultiCage Insert Modules

■ Testing of reaction to novel environment, emotional reactivity, anxiety, learning & memory using specific insert modules within light-beam frame
  ◆ Open field test
  ◆ Hole-board test
  ◆ Light / dark box test
  ◆ Place preference experiment
  ◆ Passive avoidance experiment

PhysioCage System

■ Activity (locomotion, ambulatory & fine movements, rearing)
■ Drinking & feeding monitoring (amounts & time patterns)
■ Running wheel (duration, distance, time pattern)
■ Metabolic performance (gas calorimetry O_2, CO_2, RER, heat)
■ Automatic body weight monitoring
■ Telemetry for monitoring of heart rate, animal body temperature, bio-potentials (ECG, EEG, evoked potentials, EMG), blood pressure
■ Transponder technologies for animal identification, monitoring of body surface temperature, upcoming features (heart rate)

Sophisticated Life Science Research Instrumentation
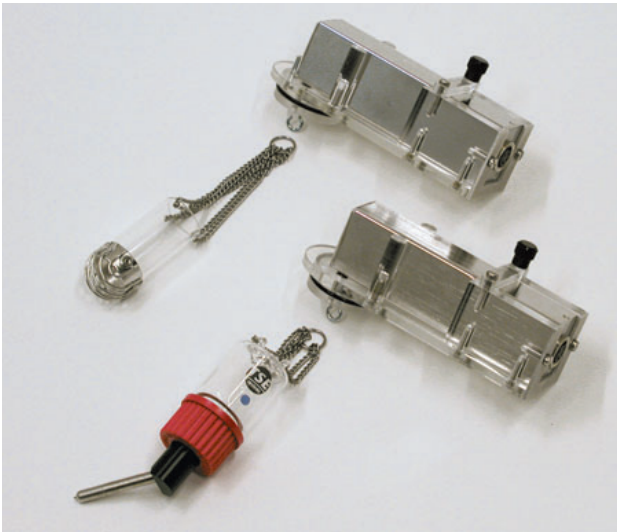
■ *Drinking & feeding sensor stations*

■ *Operant wall with two automatic doors, two levers, stimulus lights and loud-speaker*

AnxietyCage System

■ PhenoCages with operant lid for aversive spot lights, loud speaker, with additional open field and light / dark box test modules, running wheel with electrical shock option, "Vogel test" paradigm (drinking bottle with electric shokking), air-puff option

ObesityCage System

■ PhenoCages or PhysioCages with several feeding / drinking stations with different diets / liquids, operant wall(s) for controlled access, running wheel

■ *Running wheel*

AddictionCage System

■ PhenoCages with up to 4 drinking stations with different liquids (alcohol concentrations)
■ Determination of preference or avoidance of presented liquids as a measure of neophobia

ChronoCage System

■ For chrono pharmacology: PhenoCages with time-controlled access by automatic door(s) to drinking and / or feeding stations, useful also for time-controlled drug administration

CircadianCage System

■ PhenoCages with light intensity and light-dark cycles programmable for all cages (all identical or to be controlled individually per cage), running wheel

General Philosophy

The TSE PhenoMaster System is conceived as an auto-mated **modular high throughput screening system** for the assessment of specific gene-associated functions on the behavioral and physiological phenoty-pes of small laboratory animals (mice, rats, and others). It will allow for the behavioral and physiological phenoty-ping of individual mutant strains using hierarchically organized batteries of automated physiological monitoring and integrated behavioral assays. The PhenoMaster System will be a highly appreciated tool in basic research, in **modern drug screening, experimental pharmacology and toxicology**, as well as in tumor research and animal welfare studies.

- Based on well-established single analysis tools and paradigms in behavioral studies
- Automated modular cage batteries of standard home cage size for mice or rats
- Stress-preventing home cage test environment
- All instrumentation for the screening of basic as well as of complex animal behavior and physiology is included.

The **general phenotyping paradigms** of the new system are primarily based on the simultaneous and automated acquisi-tion of the animals' detailed home cage activities and on moni-toring of drinking & feeding behavior. Furthermore, optional modular add-ons are included, which cover running wheel activity as well as **learning and memory testing** by exposing the animal to selected operant behavioral tasks.

In addition, reaction to **novel environment, emotionality** and **anxiety** can be investigated in an effective manner by exten-ding the functionality of the cage system using special dedica-ted test insert modules.

Also, **sophisticated physiological monitoring of metabolic performance** may be added by integrating the set-up into a metabolic super system. This modular system also will be combined with direct no-touch measures derived from implantable devices such as **transponders** and / or multi-
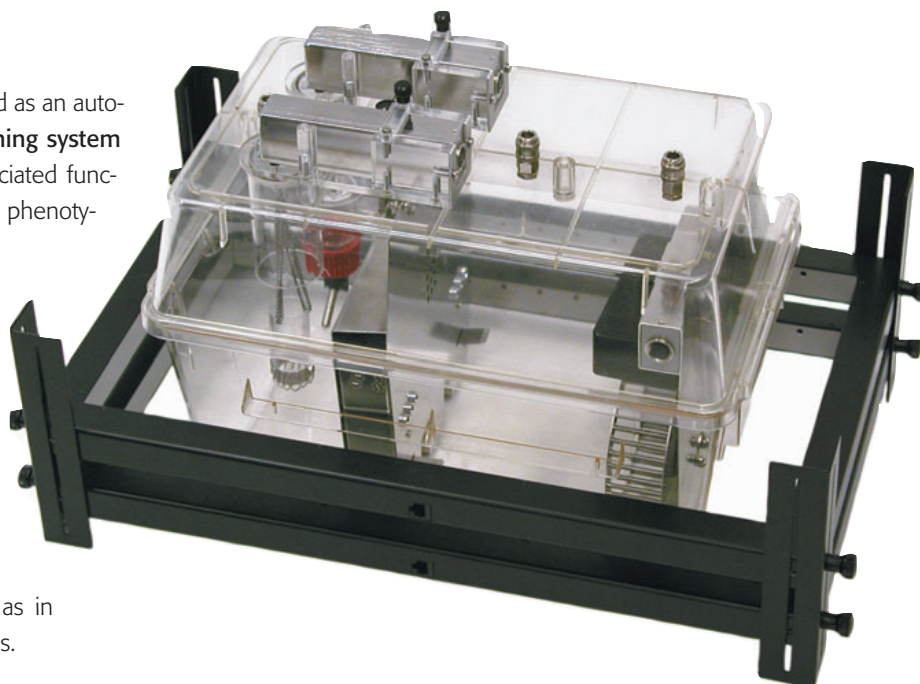
- *PhenoMaster design study*

channel **telemetry transmitters**, allowing the monitoring of basic and higher physiological functions [temperature, heart rate, blood pressure, bio-potentials (ECG, EMG, EEG, evoked potentials), etc.].

System control, data acquisition, storage and data analysis tools are provided by a general new software platform, which covers all the necessary elements for automatic running of the system in a user-friendly manner and gathering all data gene-rated by the hardware effectively and continuously. Data out-put fulfills further requirements for export into Excel and data-base software and even professional data mining solutions. These data mining capabilities will allow the integration of the derived large data sets into general phenomic approaches.

The TSE PhenoMaster System will offer automated behavioral and physiological phenotyping of mice or rats in a high throughput mode using cage instrumentations which cover complementary areas of overall phenotyping.

Product overview

This overview illustrates additional products which are supplied by TSE Systems, detailed information concerning each of the items listed below can be found on our website, for any additional information please do not hesitate to contact us:

- **Behavior**
  Conditioning, Activity & Exploration, Video Tracking, Mazes, Anxiety & Depression, Motor Function & Performance, Rotameter

- **Startle Response**

- **Analgesia**
  Hot Plate, Tail Flick, Randall Selitto, Power Meter (Incapacitance Tester)

- **Physiology**
  Blood Pressure Monitoring – invasive & non-invasive, Hemodynamic, Telemetry, Volume Meter, Bronchospasm Measuring

- **Respiration & Anesthesia**
  Animal Respirators, O_2 / CO_2 Measuring, Respiration Pumps, Vaporizers, Gas Mixing Stations, Anesthesia Units

- **Inhalation**
  Head Nose Only / Whole Body Exposure Units, Aerosol Generation & Conditioning, Aerosol Analysis, Inhalation Software, TracheoLung

- **Stereotaxic Instruments**

- **Microdialysis**

- **Isolated Organs**
  Organ Bath Systems, Langendorff / Working Heart Systems

- **Microtomes**
  Vibrotome, Krumdieck Tissue Slicer

- **Pumps & Infusion**
  Syringe Pumps, Animal Infusion Systems

- **Surgery & Handling**
  Operating Tables, Homeothermic Blankets, Temperature & ECG Pads etc.

Sophisticated Life Science Research Instrumentation

TSE Systems – your Partner!

As your partner TSE Systems offers you solutions that are fully integrated with state-of-the-art technology and powerful software, customized to your specific needs, dependably consistent and easier to use for meeting even the most challenging research work.

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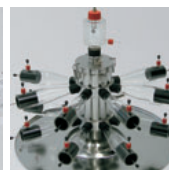
■ *Metabolism*

■ *Behavior*   ■ *Motor Function*   ■ *Physiology*   ■ *Inhalation*

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