METRIS

LABORAS™
Let the computer score!

Innovative equipment
for recording,
automatic identification,
analysis &
reporting of
behavior in rats & mice

MR STC
(주)미래에스티씨

**METRIS B.V.
The Netherlands**

Overview

LABORAS is a powerful system that fully automates the behavioural scoring of small laboratory rodents, like rats and mice. Unlike many other systems, such as photo-beam trackers and video tracking, LABORAS not only provides tracking related data but also provides you a large number of real behaviors. It is this unique functionality, which enables you to perform your behavioral research faster, more consistent and more efficient than, what can be achieved by human observations or other currently available systems.

How does it work?

LABORAS is based on vibration and force analysis to determine both the behavior and the position of the animal. To provide reliable behavioral scores, which have a high correlation with human observations a combination of dedicated mechanics, electronics and software was developed. The basis of the system is the measurement platform, which converts the movements of the animal into electrical signals. The cage with the animal is placed and is held at a fixed position on the measurement platform. The triangular shaped platform consist of:

- a heavy "Corian" baseplate in which the force transducers are mounted
- a very light weight and stiff "Carbon Fibre" measurement plate which is positioned on the top of the transducers
- a construction that holds the upper part of the cage.

The vibrations evoked by the movements of the animal are picked up by the carbon fibre measurement plate and are passed to the force transducers below it.
The transducers are connected to a dual low-noise pre-amplifier and signal-conditioning unit, which is mounted in the measurement platform.
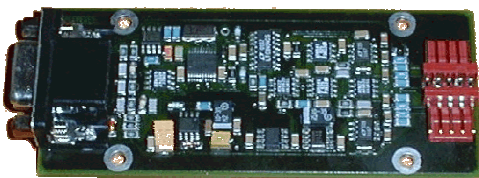
The gain and offset of the pre-amplifier are adjusted based on the weight of the laboratory animal, which is entered by the user of the system. To eliminate difficult and time-consuming manual settings of the amplifiers all gain and offset adjustments are performed by the software, using a simple calibration routine. The pre-amplifier also takes care for the proper filtering of the signals.

The output signals of the amplifiers are send to the LABORAS Control Unit (LCU), which converts the analog signals into a digital format. The LABORAS Control Unit can handle the

signals of up to eight measurement platforms. The LCU sends the data over a serial line to the PC for further processing.
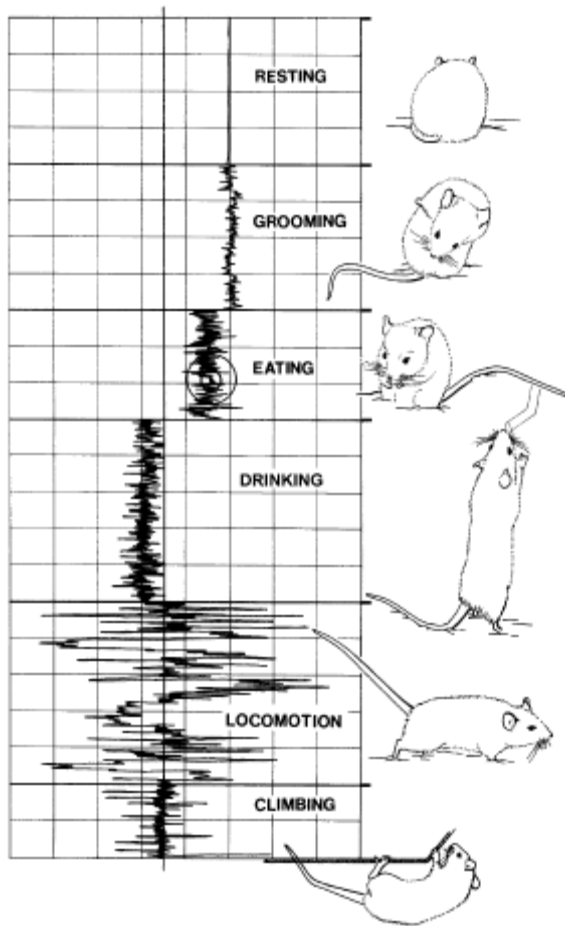
The processing of the vibration signals forms the heart of the software. The LABORAS software uses the latest pattern recognition and signal analysis techniques to reliably recognize a number of behaviors of rats and mice.

Each behavior has its own unique signature of signal characteristics, which can be detected by the LABORAS software to identify a behavior.

This is illustrated for a couple of behaviors in the picture on the left. In addition to the behaviors detected by LABORAS, the software is also able to extract the position of the animal from the transducer signals and various other tracking details like velocity, maximum velocity and travelled distance.

Unique Features

Based on the innovative technology of LABORAS, the system provides the user with a couple of unique features.

- *One-Stop-Shop for rodent tracking and behavior identification*

The LABORAS technique enables simultaneous tracking and determination of behavioural elements in rats or mice. It is no longer necessary to combine several limited or dedicated systems or to perform separate tests with multiple test set-ups to acquire all the behavioural data for your research.
LABORAS provides you with a one- stop-shop for your behavioural experiments. The "raw-data" picked up by the sensors contains much more information than currently used in the LABORAS behavior identification algorithms. Initial feasibility studies revealed that in addition to the detection of the current set of behaviors and tracking parameters, the automatic extraction of several stereo-typical behaviors (startle, tremors, twitches, convulsions etc.) and energy related parameters are feasible.
Metris is fully committed to continuously develop new algorithms keeping up with the highest research demands of our clients.

- *Measurements in total darkness*

A well known problem with techniques based on video is that many experiments with rodents have to be performed in darkness or at least at low illuminations which will degrade the contrast of the camera and lead to low quality, low-resolution video images, making tracking difficult and automated object recognition less reliable.
LABORAS does not use video techniques; as a consequence the rodent can be studied under any light condition necessary for your research, eliminating undesired lighting condition during the experiment.

- *Home cage type environment*

The cages used on the LABORAS system are Polycarbonate type-II and type-IIIh cages, which comply with the requirements (floor area, height and feeder) for respectively housing of mice and housing of rats. The rat cage is specially designed to meet to most stringent height requirement used in the UK and to enable (free) rearing behavior.
The cages can contain a limited amount of bedding material reducing the stress of the animal during the experiments.
The use of these cages enables the possibility to perform long-term automated experiments, exceeding more than 24 hours. LABORAS can measure for a consecutive period of 7 days.
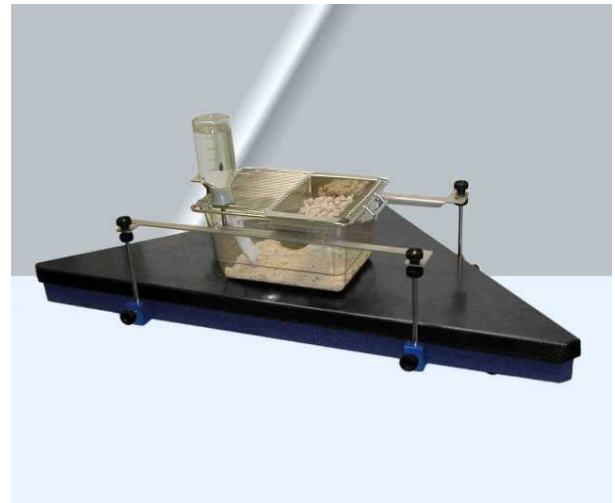
LABORAS vs. other Methods of Behavioral Observation

Methods of behavioral observation /monitoring	Open Field test Human observations of crossings	Treadmill ROTAROD Rotations, Duration	Photocell cage Interruption of infrared light beams	Video tracking Changes in video image	LABORAS Vibration patterns on sensor platforms
Automated system	No	Semi-automatic	Yes	Yes	Yes
Nr. of behaviors automatically Recognized	0	1	2-3	2-3	> 6
Automatic behavior detection capability					
- Locomotion	-	±	+	+	+
- Immobility	-	±	+	+	+
- Climbing	-	-	-	-	+
- Rearing	-	-	±	±	+
- Grooming	-	-	-	-	+
- Drinking	-	-	-	-	+
- Eating	-	-	-	-	+
- Stereotypical behaviors	-	-	-	-	±
Position tracking capability					
- X/Y position plot (track)	-	-	+	+	+
- Speed, average speed, max. speed	-	±	±	+	+
- Distance traveled	-	±	+	+	+
- Position Distribution	-	-	±	±	+
- Circle counting	-	-	-	+	+
Measurement resolution (in time)	Medium	Medium	Low	Medium	High
Measurement Characteristics					
- Independent of lighting conditions	No	Yes	Yes	No	Yes
- Multiple animals in one cage	No	No	No	Yes	No
- Mice and rats	Yes	Yes	Yes	Yes	Yes
- Independent of animal color	Yes	Yes	Yes	No	Yes
- Long term measuring	No	No	Possible	Possible (up to 6 hrs)	Yes (up to 7 days)

'-' = not capable, '±' = potential capability, '+' = capable

Applications

Laboras is used by a variety of users and in several types of research. Some major application areas are CNS, toxicology, pharmacology, safety etc. Among the users are for example contract laboratories, pharmaceutical companies and academic institutes.

The applications of LABORAS can be divided in the following main categories:
- Monitoring of behavior or behavioral changes after:
  - Drug treatment
  - Genetic Modification
  - Surgical Procedures
  - Environmental manipulations / Social experience
- Monitoring of special neurological & anxiety parameters *(system growth potential)*

Effects of drug treatment (e.g. pharmacology, toxicology)

Especially in research where high capacity screening with (transgenic) rats or mice is important LABORAS can be a great tool to reduce lead times and perform experiments, which are virtually impossible with traditional means of behavioural observation. Examples of drug effects, which can be investigated with LABORAS are:
- sedation, stimulation,
- circling behavior (e.g. intensity, duration, speed)
- stereotypical behaviors (Wet Dog Shakes, Head Shakes, Scratching, Purp. Chewing)
- dose respons curve for behaviours (such as for the Formalin Test),
- long term tests (e.g. sleep-wake pattern, eat-drink pattern),
- experimentally induced behaviors (e.g. grooming, eating, drinking, stereotypies, circling).

Effects of genetic modification

Today, many laboratories are working with genetically modified mice or rats. Often, the effects on behavior are not known or difficult to predict. To investigate the effect of genetic changes on the behavior of the animals LABORAS can be valuable tool. The observation time and lead-time to obtain reliable results that meet the required statistical significance can be extensive in this type of research, when traditional means of observation are used. To benefit from LABORAS, it can either be used to support or replace the human observations.

Effects of surgical procedures

Many experiments involve animals, which have gone through some kind of surgical procedure preceding the experiment. Examples are: CNS lesions, CNS implants and the implantation of telemetry devices. To reduce the effect of surgical procedures on your experiments it is important to know when the animal behavior has returned to normal by comparing them to groups, which are not operated. In some circumstances, such as experimental paralysis it can of interest to investigate the behavior of the animal directly after the procedure.
In the past LABORAS was amongst others used to investigate the effects on behavioral of mice after the surgical procedure necessary to implant a telemetry device, revealing interesting figures on recovery times.

Effects of environmental manipulations / social experience

Examples of this type of tests, which can be performed using LABORAS are:
- behavioral changes of animal after a social defeat
- learned helplessness
- conditioned fear
- acoustic startle (future option)

For example, LABORAS can determine the animal's favourite spots or places, which are avoided in the cage. It can detect overall or sudden changes in the amount of locomotion, immobility, grooming, eating, drinking, changes in average or maximum speed, travelled distance etc.

Special neurological & anxiety parameters

A feature of LABORAS is the identification of stereotypical behavior. Every years several behaviours are added to the capabilities of the LABORAS system. At this moment LABORAS can detect the following special behaviours:
- Hind limb licking - Rats (Formalin Pain test)
- Scratching – Mice (Dermatology, CNS, Phenotyping)
- Purposeless Chewing – Rats (CNS)
- Wet Dog Shakes – Rats (CNS, Phenotyping)
- Head Shakes – Rats (CNS, Phenotyping)
- Head Twitches – Rats (CNS, Phenotyping)
- Seizures, Barrel Roll – Mice (CNS)
- Seizures, Tonic Clonic – Mice (CNS)
- Seizures - Mice, Racine Scale P4 & P5 (CNS)

Early investigation showed the potential of LABORAS to detect many more neurological & anxiety parameters. Example of such parameters, which will be further investigated by Metris for algorithm development are: startle response, tremors, special type of convulsions, forepaw treading, skin- & head twitches.

The algorithms for the automatic detection of hind limb licking, circling and scratching are available since 2006. For more information on new behaviors visit our website or contact us at info@metris.nl.

LABORAS operation

Running an experiment has never been so easy. LABORAS is designed in such a way that the number of actions is minimized and difficult system settings and adjustments are part of history.
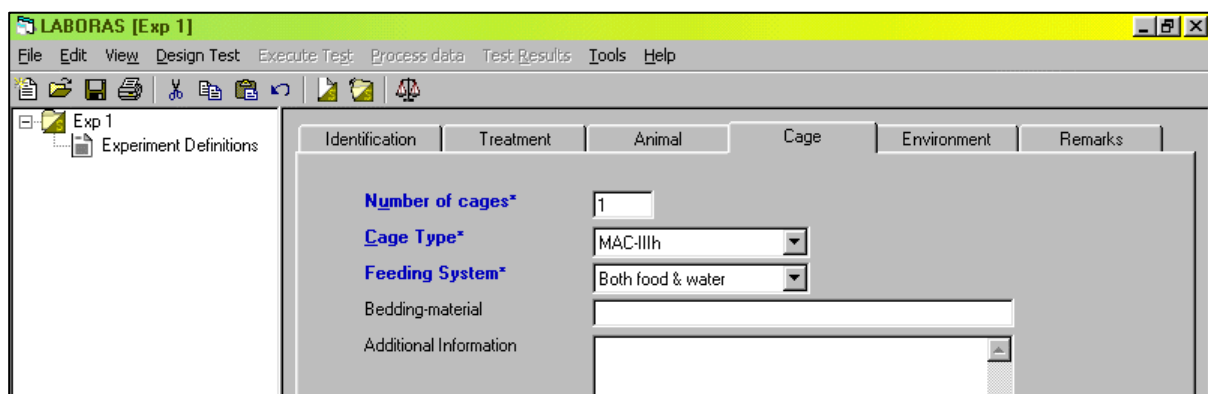Normally an experiment using LABORAS will consist of the following steps:

- Defining the experiment
  - *Step 1: Definition of the overall experiment*
- Preparing a test session
  - *Step 2: Definition of a test session*
  - *Step 3: Preparing the animals and the cages*
  - *Step 4: Calibration of the LABORAS equipment*
- Data collection
  - *Step 5: Starting the delayed or direct data acquisition*
- Data Processing
  - *Step 6: Processing of the acquired data by LABORAS*
- Generating and viewing the test results
  - *Step 7: Generating test result summaries*
  - *Step 8: Quick overview results or export of results to other packages*

Defining the experiment

LABORAS provides the user with an extensive experiment administration. An experiment is defined by filling out a number of data fields. The data fields are grouped by subject on the following pages:
- Experiment identification,
- Treatments,
- Animals,
- Cages
- Environment
- Remarks

It is not necessary to fill out all fields. Depend on the experiment and the level of administration required by the user it can be limited to the required fields (marked blue).

A newly created experiment will automatically appear in the experiment navigation tree, enabling easy switching between different experiments.

Preparing a test session

LABORAS uses a hierarchical architecture for the experiment administration. Each experiment defined can contain multiple test sessions.
The preparation of a test session consists of three steps:

First the user has to fill out the test session fields, which further define the specifics of the test session such as test duration, id's of animals used for this session, their corresponding treatments and the weight of the animal. The weights of the animals are used by LABORAS to perform the internal calibration of its electronics.

After this the cages are prepared by putting the desired bedding material in the cages. Next the animals are given the desired treatment and weighted.

Finally, LABORAS is calibrated. This is done without no animals in the cages and by following an easy procedure in which the user has to put a calibration weight on the LABORAS measurement platforms. The calibration procedure takes about 10 seconds for a single platform set-up. After this the animals are put in the LABORAS cages.
If it is important to measure the direct effect of a treatment, it is also possible to give the treatment after the calibration of the LABORAS system.

Data collection

The data collection can be started after a user-defined wait cycle or instantly. In case of a delayed start the user has to enter the desired start time during the preparation of a test session.

During data collection LABORAS will show the raw data from the sensors. The user can switch between the connected measurement platforms to check if all systems are collecting data and if the signals are within the normal boundaries.

LABORAS will automatically end the data collection when the end of the test period has been reached.
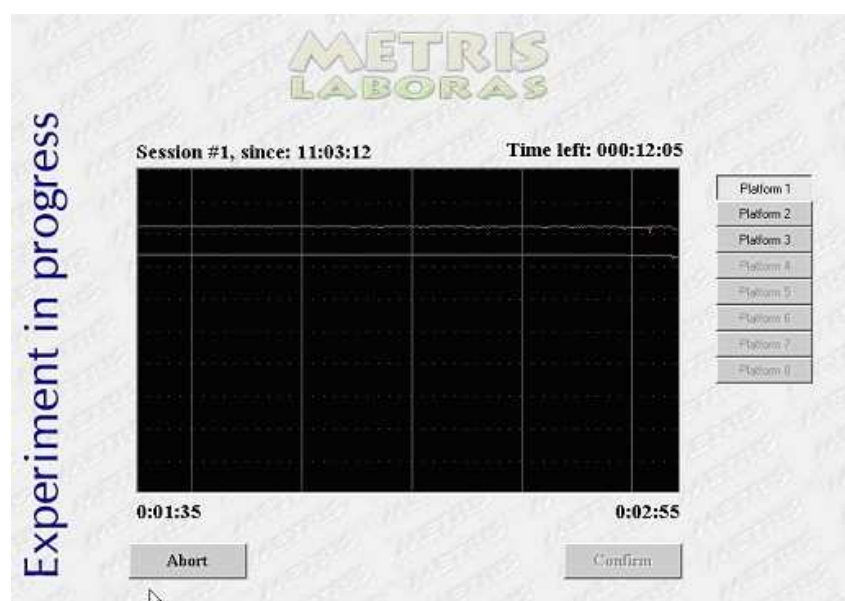
Data processing

During data processing the LABORAS software uses the collected raw sensor data to calculate the tracking parameters and the behavior data. The data processing can be done for multiple test sessions and at a time convenient to the user. The software will show a progress indicator on the screen indicating the remaining data processing time.

Generating and viewing test results

After data processing the results are available as large text tables providing the behaviors, position and velocity against the time. The user can use this data to generate its own test result summaries or graphs or use the LABORAS build in features to summarize or display the test results.
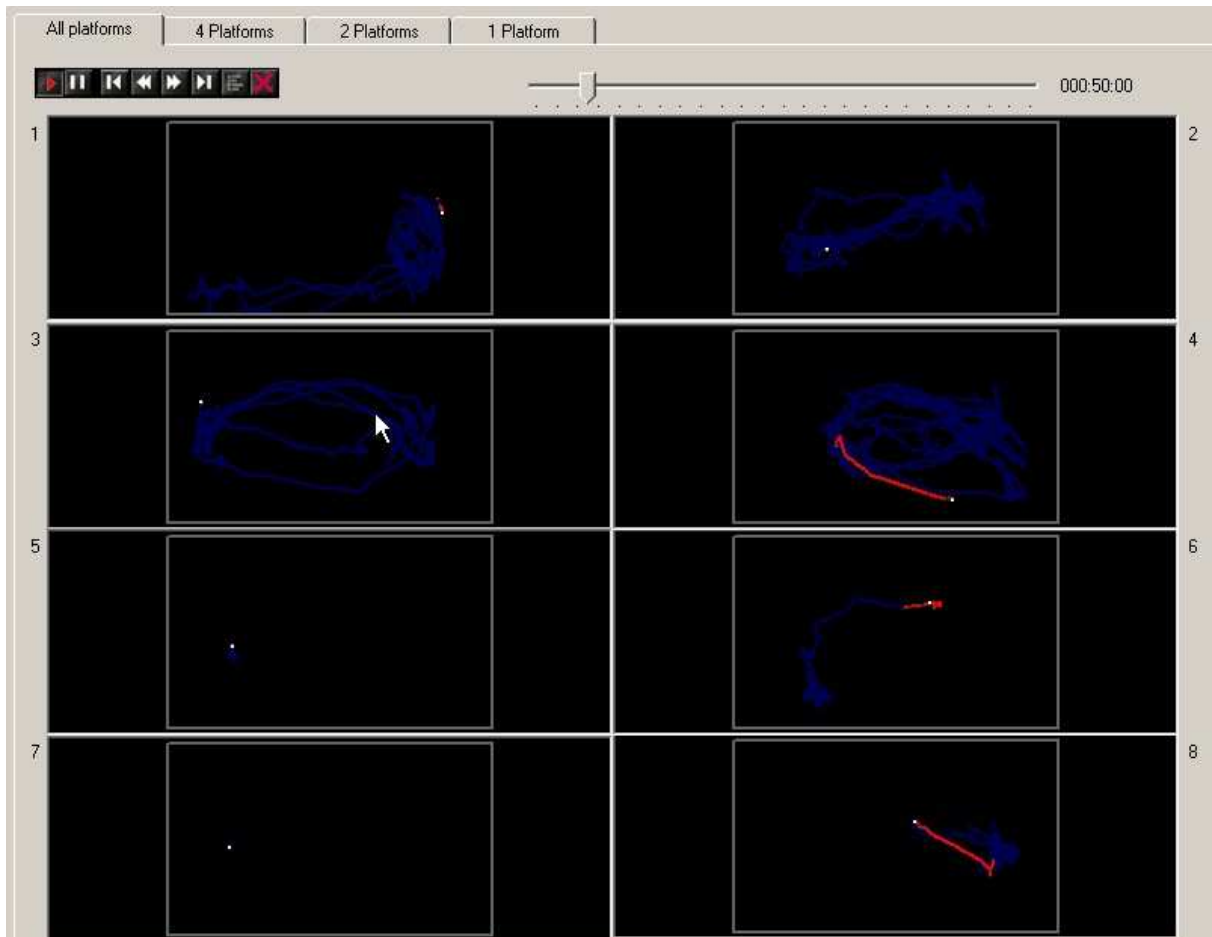
Test results: position tracks of eight animals
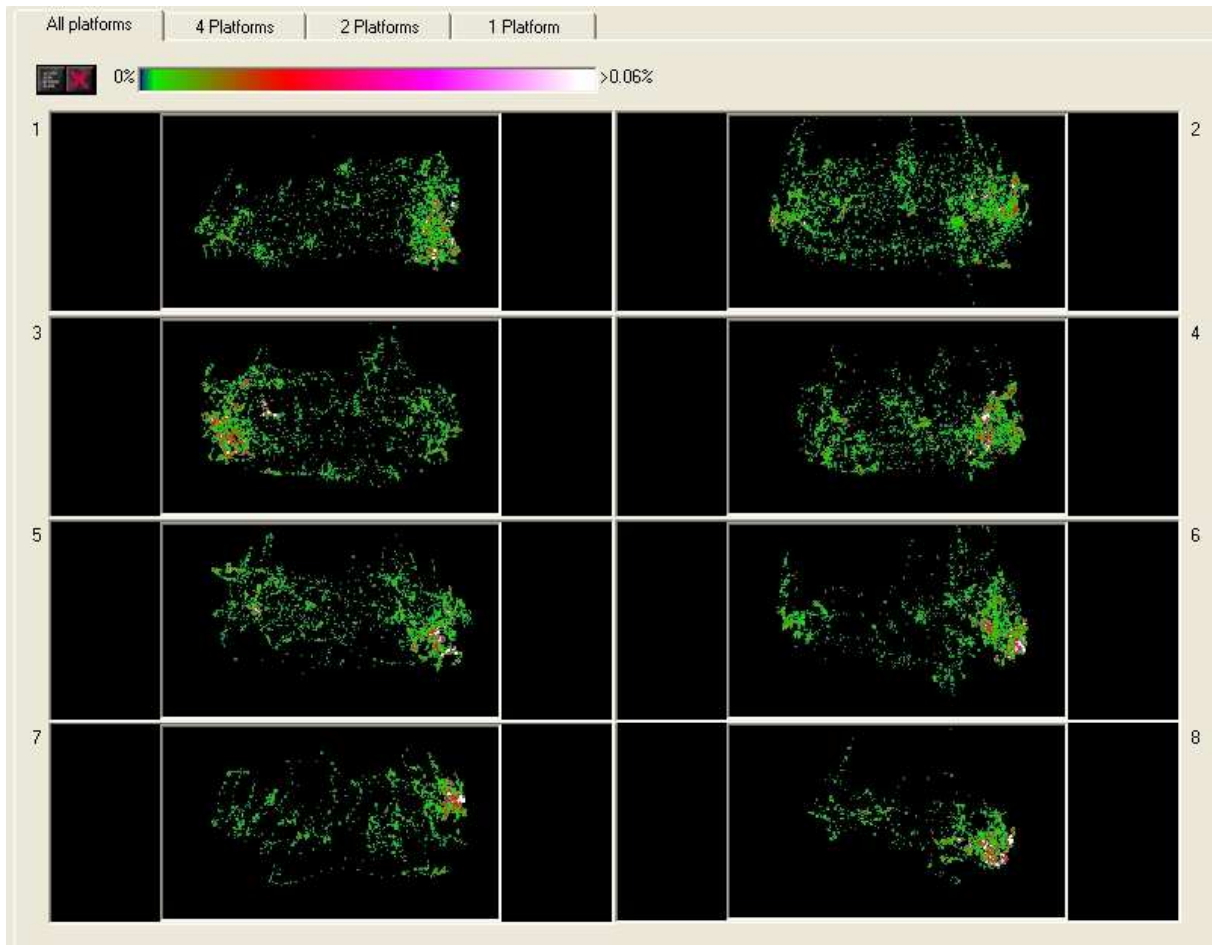
Test results: place preference of eight animals (option position distribution)
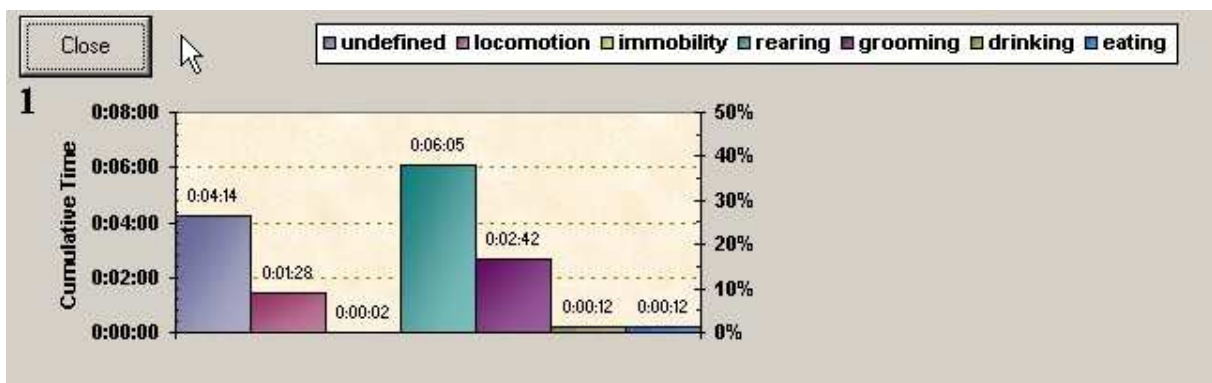
Test results: behavior bar chart for one animal

LABORAS can generate test result overviews, which summarize the data over user definable time windows. In the summary LABORAS will provide total time that each behavior was detected and the number of times that each behavior occurred. In addition LABORAS can present various graphical presentations of the results to get a quick impression of the results of your experiment.

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	WINDOW	START	END	CAGE	ANIMAL	TREATM	UNDEF_D	LOCOM_D	IMMOB_D	REAR_D	GROOM_[	DRINK_D	EAT_D
2		TIME	TIME				[s]	[s]	[s]	[s]	[s]	[s]	[s]
3													
4	1	0:00:00	0:10:00	1	2	1	165.57	23.27	23.65	49.78	323.17	13.78	0.78
5	2	0:10:00	0:20:00	1	2	1	103.83	5.74	231.36	18.06	241.01	0	0
6	3	0:20:00	0:30:00	1	2	1	252.72	5.14	105.65	2.42	234.07	0	0
7	4	0:30:00	0:40:00	1	2	1	0	0	600	0	0	0	0
8	5	0:40:00	0:50:00	1	2	1	13.53	0	586.47	0	0	0	0
9	6	0:50:00	1:00:00	1	2	1	148.76	9.05	226.05	31.67	184.47	0	0
10	7	1:00:00	1:10:00	1	2	1	168.57	0	188	0	243.43	0	0
11	8	1:10:00	1:20:00	1	2	1	110.88	0	218.71	0	270.41	0	0
12	9	1:20:00	1:30:00	1	2	1	140.19	2.48	429.9	0	27.43	0	0
13	10	1:30:00	1:40:00	1	2	1	150.66	1.17	393.76	0	54.41	0	0
14	11	1:40:00	1:50:00	1	2	1	203.78	8.55	203.1	21.68	162.89	0	0
15	12	1:50:00	2:00:00	1	2	1	147.56	0	384.73	0	67.71	0	0

Part of LABORAS result summary showing results in user definable time windows

All test result summaries can be exported to other software packages. Some examples of file formats supported by LABORAS are: ASCII files (for important in MS-Excel), SPSS input files (including header) and SAS-JMP input files (including header).

Configurations and Accessories

LABORAS is available in several configurations. The LABORAS configuration can be tailored to your requirements by selecting:
- the number of sensor platforms,
- species supported,
- behavior recognition capability,
- tracking capability.

Configurations	No. of platforms	Behavior recognition	Tracking
Track	1,4,8	-	Position, Traveled Distance Speed, Highest Speed Position Distribution
Track	1, 4, 8		Circling / turning counts (CCW, CW, circling speed, circling size, circling time
Behavior Mouse, Basic Behavior Rat, Basic Behavior Mouse & Rat, Basic	1, 4 or 8	Locomotion, Immobility Climbing*, Rearing*	
Behavior Mouse, Advanced Behavior Rats, Advanced Behavior Mouse & Rat, Advanced	1, 4 or 8	Grooming/Scratching Eating, Drinking	
Special Behaviors Mouse	1, 4, 8	Scratching, Seizures (Barrel Roll, Tonic Clonic, Racine P4, Racine P5)	
Special Behaviors Rat	1, 4 ,8	Purposeless Chewing, Wet Dog Shakes, Head Shakes, Head Twitches, Hind Limb Licking (Formalin test)	

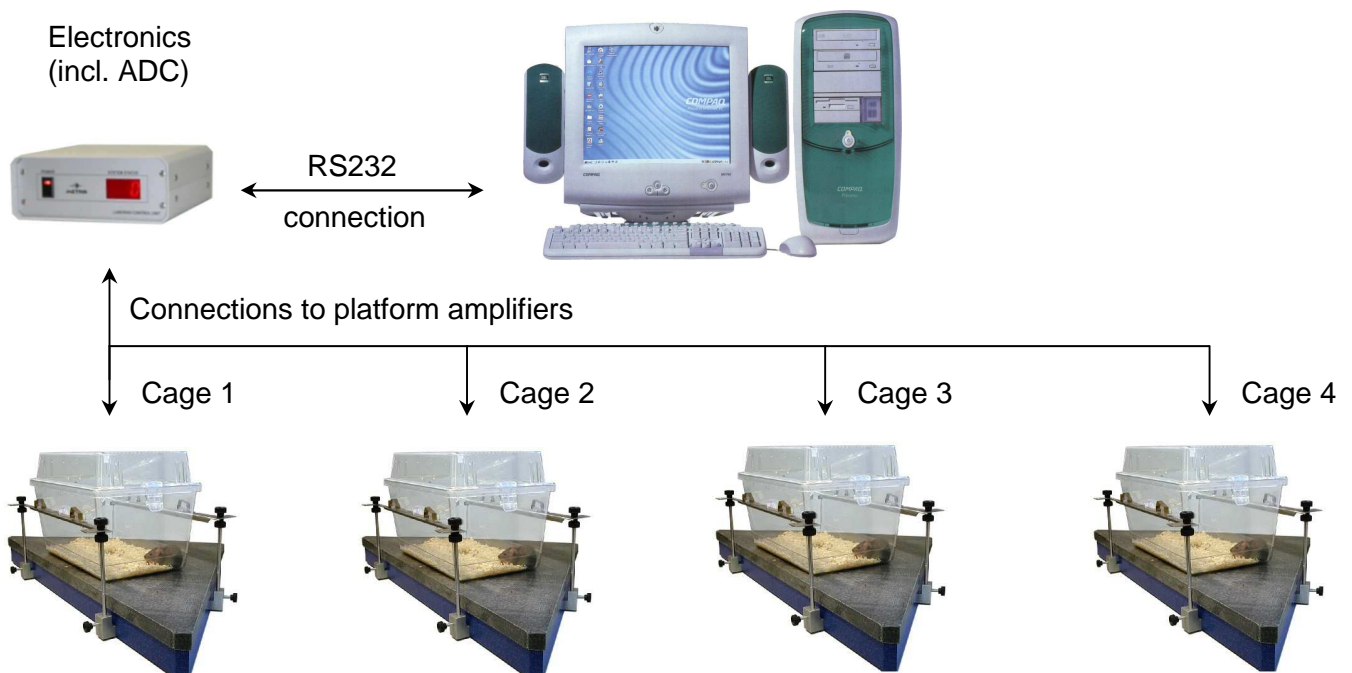*** Climbing for mouse only; Rearing for rat only**

All LABORAS configurations consist of a system unit, one or more sensor platforms and the LABORAS software.
- The *system unit* is modular and contains one or more signal amplifier modules. Each module contains two amplifiers, one for each transducer of a transducer platform. Dependent on the LABORAS configuration, one, four or eight amplifier modules will be installed in the system unit. In- and output cables are included.
- Each *sensor platform* is provided with a Polycarbonate Type II or Type IIIh LABORAS cage.
- The *LABORAS software* will be delivered on CD-ROM. The LABORAS software is designed for use on a Windows-2000 or Windows-XP Professional platforms. The computer and operating system are not included.

Accessories

The LABORAS equipment comes with several optional accessories. An overview is provided in the table below.

Options	Description
LABORAS configuration upgrades, software	Software modules to upgrade an existing LABORAS configuration to another configuration
LABORAS configuration upgrades, hardware	Upgrade to expand the number of measurement platforms of your LABORAS configuration (includes additional platforms and additional amplifiers in the LABORAS platforms)
LABORAS cables	Additional cable (3.0 or 5.0 meter) to connect a LABORAS platform to the LABORAS Control Unit (electronics)
LABORAS power adapter	Additional power adapter (available for various net voltages and frequencies)
Calibration weight	Additional or spare calibration weight
USB External Hard disk backup system (incl. software)	Optional USB Hard disk backup system for data back-ups. LABORAS generates approx. 1.5 MB per platform per hour on the hard disk. This data can be stored in several ways. USB external Hard disks proves to be a reliable and fast back-up system.
Additional LABORAS cages and cage accessories	Additional cages that are prepared for use with LABORAS (incl. special food-hopper and drinking-bottle). There are two types of cages: Polycarbonate Type-II and Type IIIh. Cages, food-hopper and drinking-bottle can also be supplied separately.
Optional behaviors (on customer request)	Development of software for the recognition of other behaviors or behavioral parameters or other laboratory rodents

Electronics
(incl. ADC)

RS232
connection

Connections to platform amplifiers

Cage 1   Cage 2   Cage 3   Cage 4

Service contracts

The LABORAS system is an advanced system that requires proper maintenance procedures to ensure optimal performance. Metris offers various service contracts covering for example system maintenance, repair, components, software updates etc.
Contracts can be offered for one year or three years. Pricing is dependent on the customer's location (country) and the type of contract. For more information contact are customer support desk.

General Specifications

Behavior detection functionality

- *resting (immobility):*
  movements are absent while the animal is in a sitting or lying position.
  Very short movements (e.g. turning over while sleeping) are not considered as an interruption.
- *locomotion:*
  activities such as walking, running, jumping.
- *rearing:*
  the animal is standing upright on its hind legs or moving into this position (mostly against a side wall of the cage).
- *eating:*
  the animal eats food pellets while standing upright, gripping the bars of the food hopper or the climbing grid or eats parts of food pellets from the floor.
- *drinking:*
  the animal stands upright gripping the water bottle and licking water.
- *grooming:*
  the animal is scratching, wiping or licking its fur, snout, ears, tail or genitals.
- *climbing:*
  climbing and hanging on the bars of the wire cage lid or food hopper or on the climbing grid in the enriched cages. While the animal is climbing or hanging, the tail may touch the floor or side wall of the cage.
- *undefined:*
  all behaviours not classified in one of the previous categories.

- *Special behaviours*
  WDS, Head Shakes, Head Twitches, Purposeless. Chewing, Seizures (Barrel Roll, Tonic Clonic, Racine P4/P5), Scratching, Hind Limb licking (formalin test).

- Species: rat or mouse
- Time resolution: < 0.25s
- Validated accuracy (around 90% with a time resolution of 0.05s).

Min. Computer requirements

- Computer: PC compatible
- Processor: Pentium-IV 2 GHz or better
- RAM: 1024 MB or more
- HD: 80GB or more
- Microsoft Windows 2000 or Windows-XP
- Microsoft Office2000 or Office2003

Tracking functionality

- *position:*
  the position of the animal relative to the centre of the cage; resolution = 1 mm
- *distance travelled:*
  the total distance travelled by the animal during the test; resolution = 1 mm;
- *maximum speed:*
  the highest velocity of the animal during the test; resolution = 1 mm/s;
- *position distribution:*
  graphical presentation showing the preference of the animal for certain spots.

- Species: rat , mouse or other rodents < 700gr.
- Time resolution: 0.25s

Output definitions

- *time tagged behaviour files & position files*
- *test result summaries over user definable windows:*
  including Behavior Durations and Behavior Frequencies
- *export of test results in several commonly used formats:* MS-Excel, SPSS, SAS/JMP

User Interface

- *GLP compatible user interface and data management* The software complies to the GLP requirements for software used in laboratory instruments
- *Easy to use interface:*
  straight forward Windows user interface with pull-down menus & experiment navigation tree
- *Extensive and complete experiment data administration*
  all experiment data can be entered in the administration software module of LABORAS. The experiment data is added to the test results. Test sessions and related data being part of one experiment can be kept together in one experimental design.

Certification

CE mark (all electronics)

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Investigator(s), Bibliography
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Quinn L, Stean T, Trail B, Duxon M, Stratton S, Billinton A, Upton N LABORAS: Initial pharmacological validation of a system allowing continuous monitoring of laboratory rodent behaviour *Elsevier Journal of Neuroscience Methods, 130 (Oct. 2003) 83-92, (accepted 9 July 2003)*

Ordering Information

Prices

For details on prices, product part numbers and ordering requirements refer to the most recent pricelist or contact the Metris marketing and sales department or your local distributor for a recent pricelist or a quotation.

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