

High-quality Measurements of Rodent Behaviour, Tracking and Ultrasounds Using LABORAS™ and SONOTRACK

a report by

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LABORAS Automates Behavioural Scoring and Tracking

LABORAS is a validated, automatic system measuring the behaviour of rats and mice. In addition, it provides complete position tracking of animals. This single system generates the most extensive behavioural data with the highest quality available today. The system can be used for behavioural phenotyping of transgenic mice or for high-throughput behavioural screening and profiling in drug discovery processes. The major advantages of LABORAS automated behaviour recordings include:

- objectivity and standardisation of data collection;
- reduction of inter- and intra-observer variation;
- reduction of experimental variation;
- saving time, animals and costs
- GLP-compliance; and
- a reduction of lead-time.

LABORAS enables the researcher to do more and better experiments in less time with less animals and equipment.

LABORAS in Drug Discovery

Target Discovery

Behavioural phenotyping of transgenic animals is a pivotal element in chasing promising targets for future drug development. To screen huge amounts of genetic modifications, endless tests have to be done. In this new area of research, people look for quick and easy behavioural methods that have a high capacity and produce high-quality data.

(Safety) Pharmacology and Toxicology

When studying the efficacy and safety of a future drug, animal behaviour is a very important and sensitive end-point. A reliable, automated high-throughput behavioural screening method as a 'primary observation test', would greatly enhance efficiency and reduce lead-times. In the phase of drug profiling, safety pharmacology and toxicology,

an objective and high-quality method for behaviour registration is required.

The Use of LABORAS

For all research areas studying rodent behaviour, LABORAS is the solution. LABORAS accurately measures the most common rodent behaviours, such as locomotion, immobility, grooming, eating, drinking, rearing, climbing and hind-limb licking. At the same time, it provides complete position tracking parameters, like XY-position, (maximum, average) speed, distance moved and position distribution.

LABORAS can be used for behavioural phenotyping of transgenic mice or for high-throughput behavioural screening and profiling in drug discovery processes (see *Table 1*).

LABORAS data are reliable and free of inter- and intra-observer bias or anticipated scoring, thereby providing a standard behavioural measurement around the world. The system is GLP-compatible.

How Does LABORAS Work?

LABORAS uses a unique (non invasive) technology based on vibration measurement and pattern recognition developed by skilled engineers of Metris b.v. A triangular sensor platform picks up every tiny movement (even breathing) that the animal evokes. Each behavioural element produces a characteristic vibration pattern (see *Figure 1*)^{1,2} that can be recognised by the software. The system automatically determines the onset and end of the recognised behaviours with a great accuracy. Studies have shown a 90% to 95% correlation with human observers for most of the behaviours detected by LABORAS.³

LABORAS for Quality and Efficiency

With LABORAS, the researcher obtains the widest spectrum of behaviours including complete position tracking with the highest accuracy using just a single system.



Table 1: Examples of Applications of LABORAS in Drug Discovery

Test	Result
Behavioural phenotyping transgenic mice ⁵	Target discovery for future drug development
Primary observation test ⁴	Adverse drug effects
Homecage 'open field' test	e.g. sedative, stimulant, anxiolytic, anxiogenic properties
Formalin test (hind limb licking)	Analgesic properties
Telemetry and Behaviour ⁶	Integrated data
Antagonism of pharmacologically induced effects, such as M-CPP hypolocomotion and hypophagia ⁷	Pharmacological antagonist efficacy
8-OH-DPAT hyperlocomotion ⁷	
d-Amphetamine hyperactivity ⁷	
Angiotensin II polydipsia ⁷	
Orexin-A induced grooming ³	
Excessive climbing	
Near Future Applications	
Antagonism of pharmacologically induced effects, such as Tremours	Pharmacological antagonist efficacy
Seizures	
Turning/circling behaviour	
'Wet dog' shakes	
Startle response	
Future Applications	
Respiration	Adverse effects
Heart beat	Efficacy and safety issues
Sniffing	Exploration/anxiety measure
Digging	
Jumping	
Energy spent	Metabolic effects

The system is ready-to-use (turn-key), user-orientated (as it was developed together with researchers), has a good laboratory practice (GLP)-compatible user interface and data management with pull-down menus and an experiment navigation tree.

The software allows for extensive experiment data administration and produces time-tagged behaviour and position files. The test result summaries, including behaviour durations and frequencies and tracking parameters, can be calculated over user-definable windows. The test results can be exported in several commonly used formats, such as MS-Excel, SPSS, SAS, SAS/JMP, etc.

One LABORAS unit can handle up to eight sensor platforms simultaneously and can acquire data for up to seven days continuously (in light and absolute dark). This single system generates the most extensive behavioural data with the highest quality available today.

Advantages of LABORAS

The major advantages of LABORAS automated behaviour recordings include objectivity and standardisation of data collection, reduction of inter- and intra-observer variation, reduction of experimental variation, saving of time, animals and costs, GLP-compliance (21CFR/Part 11) and reduction of lead-time.

Because LABORAS measures vibrations it does not rely on (infrared) light or multiple (special) cameras and does not have the problems of reflections, poor resolution or large datafiles of videosystems. The identification of behavioural elements with LABORAS is far more sophisticated and extensive.

LABORAS in the Future

As yet, LABORAS detects at least 14 behaviours (total for mice and rats), but the LABORAS technology still has more possibilities. Detection of tremours, seizures, circling, startle response or 'wet dog' shakes, for example, is possible, but no algorithms have been developed for this as yet. Adding other user-defined behaviours, e.g. stereotypies, is possible depending on the evoked signals.

Conclusions

LABORAS enables the researcher to do more behavioural experiments in less time with less animals and equipment, while obtaining higher quality data. The LABORAS system can be a valuable tool to standardise behavioural measurements, especially for disciplines falling under GLP regulations.

Recording and Analysis of Ultrasounds Using SONOTRACK

SONOTRACK is a new, non-invasive method to detect and analyse ultrasounds. Rats and mice produce ultrasonic vocalisations in a variety of situations, e.g. in response to stress, anxiety or pain, or during sexual behaviour. Animal models in drug discovery may use ultrasound production as an informative experimental end-point. SONOTRACK is the best choice for measuring ultrasounds as it records the full frequency spectrum (15–100kHz), not involving tuning of bat detectors. The graphical presentations of the signals by the SONOTRACK software enable the user to analyse this 'animal language' in much more detail than ever before. SONOTRACK out-performs other systems available on the market with a favourable performance-to-price ratio.

Ultrasounds in Drug Discovery

Ultrasonic vocalisations are sounds with a frequency of 20–100kHz, which is well beyond the human hearing range. In the animal kingdom, communication via ultrasounds is well-known, for instance in bats, dolphins, rodents or insects. Rats and mice produce ultrasounds in stressful situations, e.g. when a predator is present,⁸ when a pup is separated from its mother,^{9,10} or when a rat is conditioned to an aversive stimulus,¹¹ or in relation to sexual behaviour.¹² These ultrasounds fall into several categories with different frequencies according to the specific situation, suggesting they may be used as an indicator of emotional and motivational status. In animal models of stress, anxiety, pain or sexual behaviour, but also in studies of well-being of animals, ultrasound production is an accepted and sensitive parameter.^{9–11}

SONOTRACK in Drug Discovery

Measuring and analysing ultrasounds over the full spectrum (15–100kHz) is the job of SONOTRACK (see Figure 3). It is a new non-invasive method (not involving bat detectors) with special microphones and hardware to allow a clean record of animal ultrasounds. The very time-consuming and labour-intensive method with a bat detector and a tape recorder is no longer an option for versatile measurements.

The ultrasounds are transformed to digital format, can be played back and can be converted to audible (for humans) sounds. The graphic presentations of the signals by the SONOTRACK software enable the user to analyse this ‘animal language’ in much more detail than ever before. Sonograms, which are plots of frequency against time, can be displayed as two-dimensional (2-D) and 3-D graphs. The unique advantages of SONOTRACK are:

- a full spectrum analysis of all ultrasounds produced (not only peak counts in a limited frequency band);
- multichannel continuous recording (up to four channels, easy playback and export to .wav files);
- high performance microphones (cover every frequency, record low intensity calls); and
- graphical presentations of ultrasonic vocalisations (sonograms, spectrograms). ■

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Figure 1: LABORAS System



Figure 2: Artist Impression of Vibration Patterns Evoked by Different Behaviours

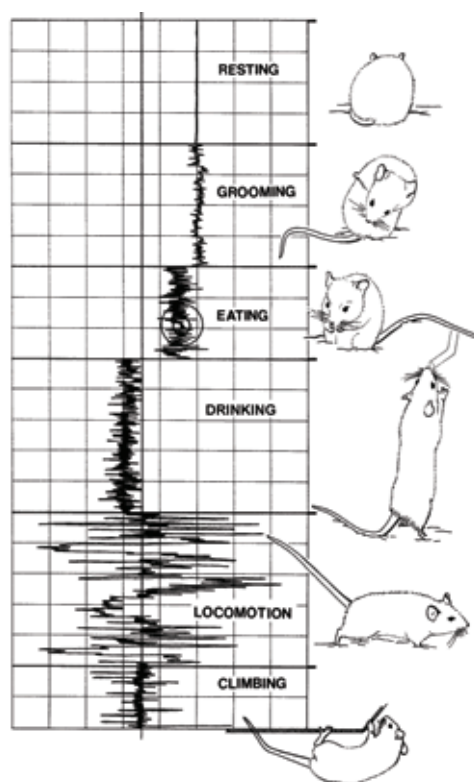
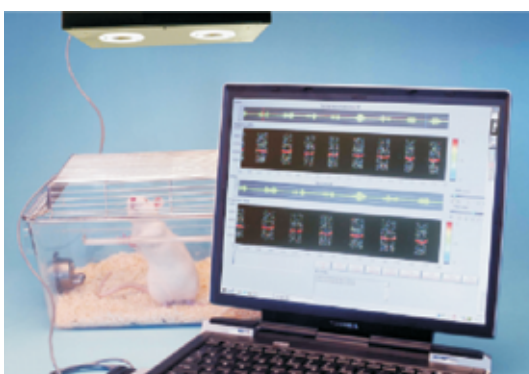


Figure 3: SONOTRACK system



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- (see also list of publications on www.metris.nl)

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