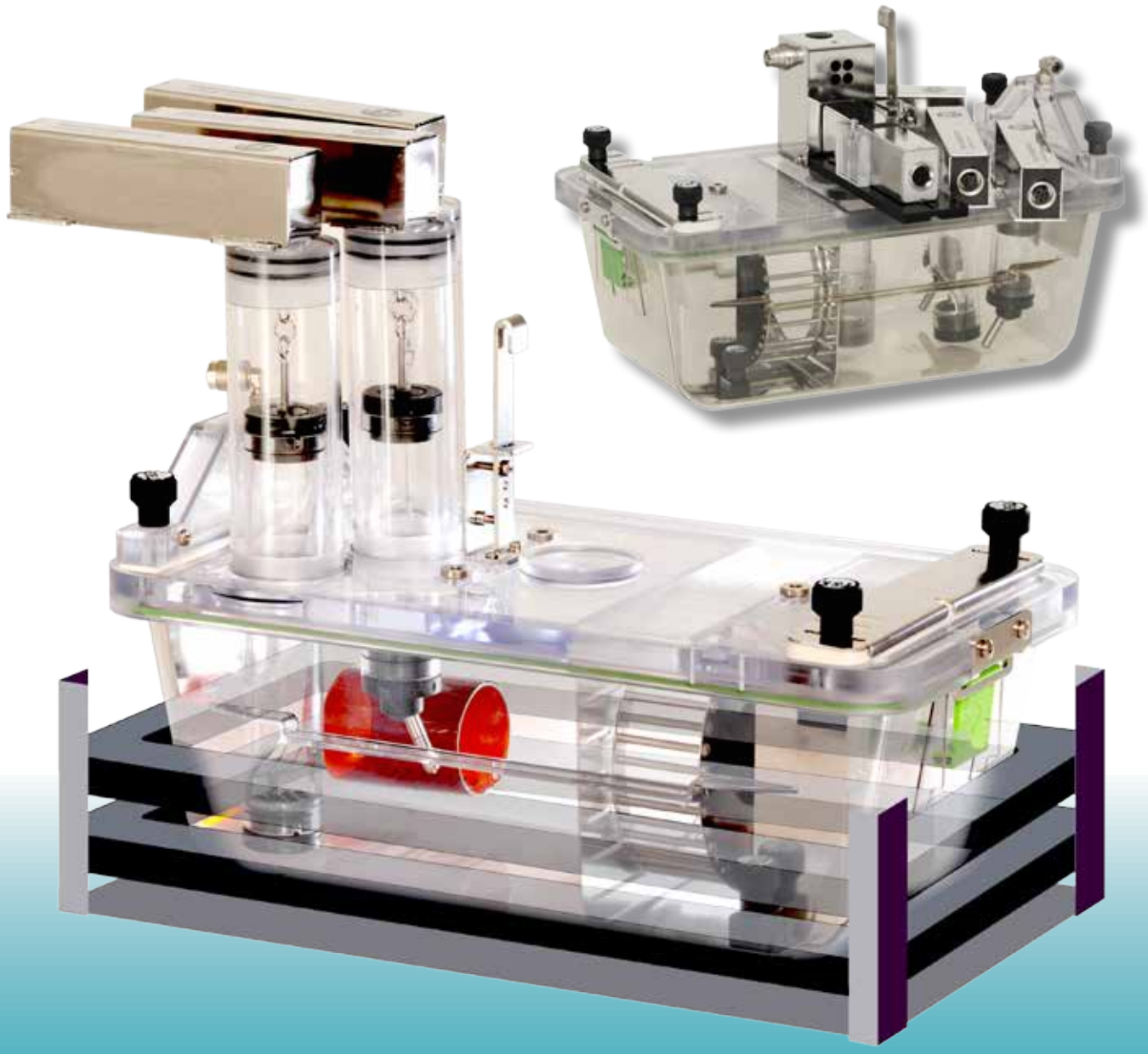
Sophisticated Life Science Research Instrumentation

PhenoMaster

Highlights in Metabolic, Behavioral & Physiological Phenotyping of Mice & Rats



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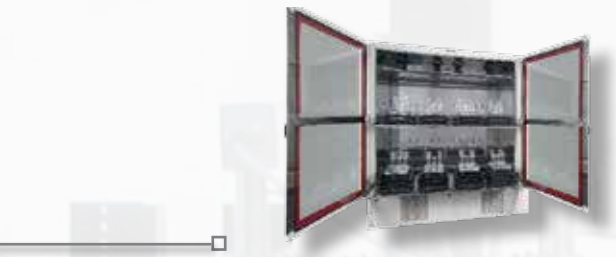
PhenoMaster: The System

We bring the experiment to the animal – into the home cage!

The TSE PhenoMaster System is a unique modular phenotyping platform for mice and rats. It allows fully automated and perfectly synchronized assessment of metabolic, behavioral, and physiological parameters with highest precision in a stress-free home cage environment. Numerous integrative modules and compatible test arenas endow the system with exceptional flexibility. A virtually unlimited number of PhenoMaster cages can be operated in parallel providing ideal conditions for high throughput screening and group comparisons.

PhenoMaster: Modular Design



METABOLISM

Indirect Gas Calorimetry Module (CaloSys)

Using innovative working principles and advanced technology solutions, CaloSys combines the best possibilities for PULL (standard) or PUSH mode indirect calorimetry within the home cage or flexibly in other standard systems, e.g., CaloTreadmill or CaloWheel.

Climate Chamber

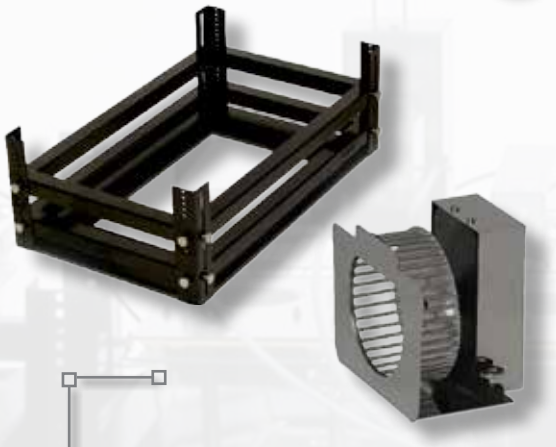
TSE System's climate chambers create tightly controlled temperature, humidity and lighting conditions offering space to multiple cages of various types - ideal for high throughput experiments under thermoneutral or temperature challenge conditions.

Feeding & Drinking

High precision weighing stations in combination with leak- and spill-proof containers provide most accurate analyses of feeding and drinking behavior. Modular access control units restrict feeding and/or drinking by time, duration, or amount according to customized schedules.

Body Weight Monitoring

A red sit-in tube housing connected to a weighing station enriches the home cage and reports the body weight as the animal visits.



BEHAVIOR & COGNITION

Activity Module

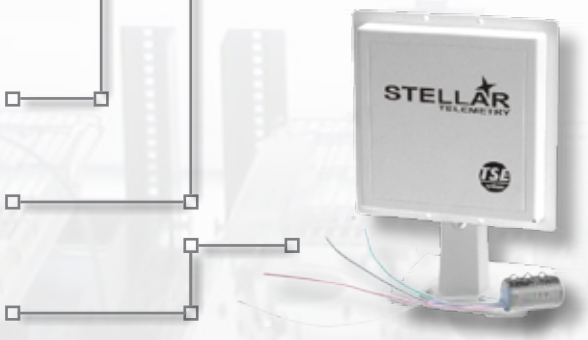
An infrared light beam frame (ActiMot) evaluates spontaneous locomotor activity and stores precise records of the animal's exploration pattern in the X,Y, and Z plane with highest spatial and temporal resolution.

Exercise Module

A variety of specialized in-cage voluntary running wheels allow you to generate running profiles, evaluate motor skills, restrict running in time and/or distance (workload control) and can be an instrumental component of a learning task on the Operant Wall (see below).

Learning & Memory

PhenoMaster is the only home cage testing system featuring a modular integrated operant wall for faster, stress-free, fully automated conditioning experiments, including various stimulus, response and reinforcement elements, and flexible operative integration of other functional modules.



PHYSIOLOGY

Implantable Telemetry

Stellar Telemetry is the next generation of implantable telemetry technology opening new possibilities for detailed monitoring of (blood)pressure, heart rate, ECG, EMG, gross motor activity and core body temperature in complex cage systems in metabolic studies. Fully programmable & scheduled autonomous recording to on-board data storage permit data collection with high fidelity (up to 1 kHz), no dropouts, and user scheduled read-out.

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PhenoMaster: Metabolism

Indirect Gas Calorimetry Module (CaloSys)

- Standard PULL with optional PUSH mode for application of defined gas mixtures for hypoxia or toxicity studies
- Standard multiplex with sharing of gas sensors between two or more cages. Seamless upgrade to more sensors for increased time resolution up to continuous mode calorimetry with a dedicated O_2/ CO_2 gas sensor pair per cage. Optional 'tri-gas' mode with humidity (H_2O water vapor) sensor
- Samples are analyzed with a temporal resolution of up to 40 s per animal per cage, clean physical measurements
- Programmable mass-flow controllers for each cage create optimized flow rates for different animal sizes/weights/species
- Variable influence of water vapor is effectively eliminated from gas measurements by a first-pass physical drying unit – **no mathematical corrections, clean and precise raw data!**
- Maintenance-free gas sensors, periodically auto-calibrated

Environmental Chamber

- Retracting shelves allow easy and ergonomic cage access
- Four integrated fans and a ventilation plate ensure constant air circulation and stable distribution of heat
- Whole-chamber temperature and humidity are tightly regulated and kept constant
- Execution of fast temperature shifts up to 2 Kelvin/min
- Ideal for experiments under thermoneutral conditions or to invoke temperature challenge conditions
- Lights are fully dimmable and allow definition of customized light/dark cycles under software control

The PhenoMaster CaloSys metabolic measurement module is exceptionally versatile. Next to its application in home cage metabolism monitoring, it can be coupled to other specialized cage systems.

Metabolic PhenoCage

- Special closed cage that automatically separates urine and feces
- High-precision weighing sensors quantify urine and feces by time and amount
- Optional high-speed freezing unit conserves the sample for later analysis
- Fast and simple extension with CaloSys, Feeding & Drinking & ActiMot modules

CaloTreadmill & CaloWheel

- Two fully computerized systems for exercise calorimetry with embedded motor coordination and performance monitoring
- Both systems can be closed with an air-tight cover; integrated tubing ports allow the flexible integration of a (continuous mode) CaloSys module for exercise calorimetry studies

Treadmill: optimal belt grip, user-defined speed profiles with acceleration & deceleration phases, adjustable incline/decline, optional light stimuli, air puff and electric shocks

CaloWheel: motorized wheel with computerized speed control for user-defined exercise schedules

Feeding & Drinking Module

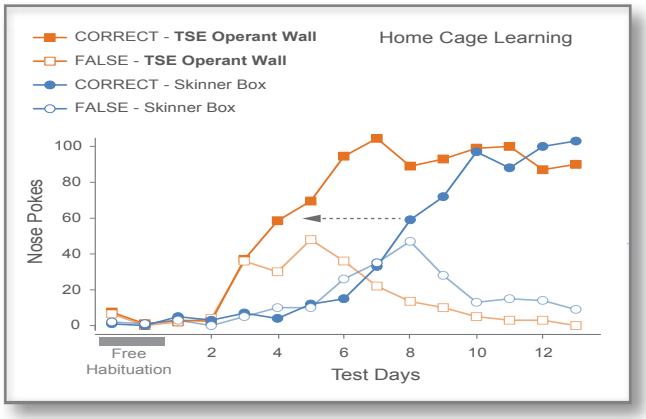
- Food containers and liquid bottles are designed with validated Spill & LeakProtect Technology to prevent content loss; transparent material allowing fast content level evaluation and sufficient daylight getting into the cage
- Containers and bottles are leaving sufficient space for exploratory activity, optionally inside the cage to save lab space
- Highly sensitive weighing sensors register food and liquid consumption
- Several weighing stations can be modularly installed per cage (e.g, 2 diets, liquid, body weight)
- Optional access control unit restricts feeding/drinking by time, duration, or amount consumed and can be made conditional to performance (running wheel activity) or behavior (operant wall task)

PhenoMaster: Behavior & Cognition

Next to home cage modules for metabolic and physiological testing, the PhenoMaster System offers extensive options for behavioral and cognitive screening of mice and rats. All modules can be used individually or in combination – in perfect synchrony.

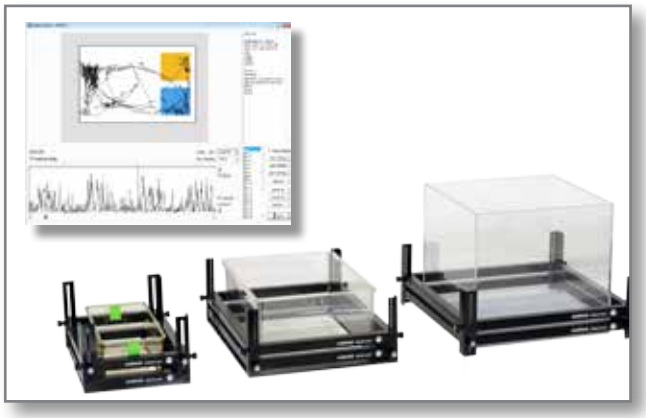
Learning & Memory Module

- Fully automated Operant Wall
- Integrated into the home cage while preserving minimally required living space
- Extra-slim design saves valuable space for exploratory activity
- User-defined advanced learning and memory paradigms according to Skinner
- Stimulus elements: house light, sound/noise generator and speaker, stimulus lamps (all tailored to customers' needs)
- Response elements: nose pokes, levers (optionally retractable), running wheel
- Reinforcement elements: dispenser for dustless precision pellets or for liquids, air puff
- Various combination possibilities with the feeding & drinking access control module and running wheel – for example access is conditional on completed task at the operant wall



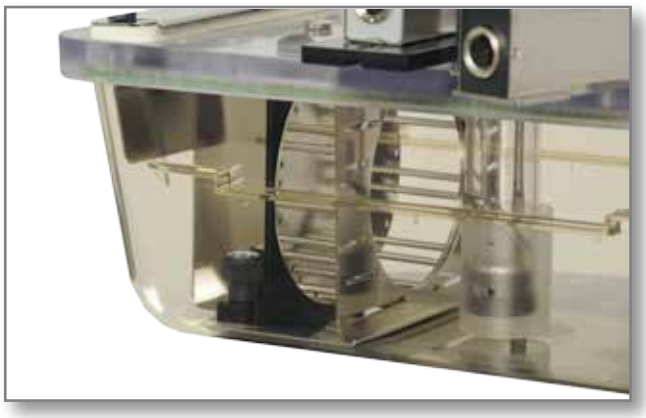
Advantages over conventional Skinner Box

- Learning in stress-free home cage environment occurs faster
- The animal performs at will across light and dark phases
- Allowing accurate circadian performance analyses
- 5-choice serial reaction time paradigm within the home cage



Activity Module

- Two infrared light beam sensor frames surround the home cage and can be used for other test arena (e.g., open field) as well
- A fine maze of infrared light beams detects all ambulatory (XY plane) and rearing (Z plane) movements in 3 dimensions
- 10 ms temporal resolution enables detection of jumping behavior
- Effective spatial resolution of 7 mm, spatial averaging filters increase the resolution further to 1 mm
- Regions of interest and detection thresholds can be user-defined
- Over 100 parameters and various display options related to: movement type, position, timing, and path



Exercise Module

- Diverse voluntary home cage running wheels allow:
  - Time-, and distance-, running with an enabled/disabled mode
  - Paired running (running profile of control animal is imposed on test animal)
  - Motivated running (running for food/liquid in combination with access control unit)
  - Indirect voluntary exercise calorimetry
  - Motor skill testing with a complex wheel (variable distance between crossbars, removable rungs)

PhenoMaster: Physiology – Stellar Telemetry

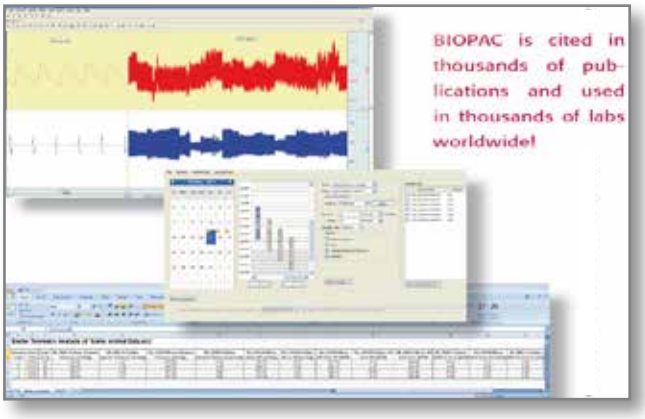
Continuous monitoring of key physiological vital signs in complex cage environments while performing metabolic, behavioral, or even inhalation studies anytime and anywhere within your facility with **Stellar Telemetry** – the new generation of implantable telemetry technology. A logical added capability to your PhenoMaster.

Transmitters

- Allow measurement of electromyogram (EMG), electrocardiogram (ECG), heart rate, (blood) pressure, respiratory rate, tidal volume, electroencephalogram (EEG), electrooculogram (EOG), temperature, and activity (different combinations possible)
- Solid state pressure-tipped sensor for various pressure measurements throughout the body (brain, lung, heart, (blood)vessels or in the GI tract)
- High fidelity and high frequency responses, no head pressure or animal movement noise

Receiver

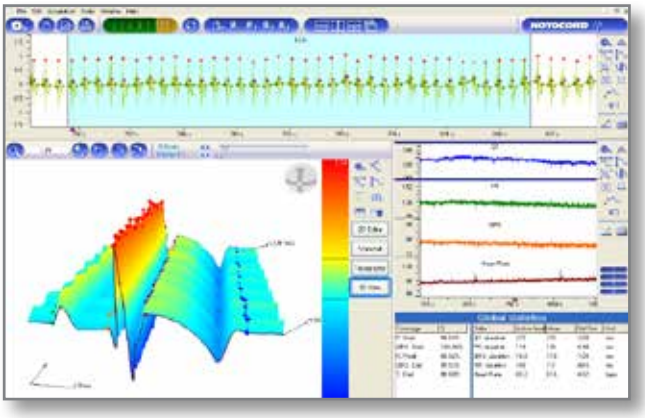
- One single antenna/receiver monitors thousands of animals
- Data are received anywhere in the lab (limit ca. 5 m)
- Stellar's unique on-board self-scheduling and storing capabilities guarantee ongoing data collection even if the animal is out of the receiver range
- Receiver can be positioned on the wall, ceiling or in another room (5 m range)



Stellar Telemetry can be operated with both, BIOPAC Acq*Knowledge* or NOTOCORD-hem™ Evolution software!

BIOPAC Acq*Knowledge*

- Seamless animal scheduling with intuitive calendar interface
- Powerful display options – view data in multiple formats simultaneously
- Signal conditioning tools incl. filtering options and artifact removal
- Multi-animal, multi-channel simultaneous automated analysis



NOTOCORD-hem™

- Simultaneous acquisition from different sources and systems
- Compatible with various experimental setups and animal species
- Extensive library of signal processors and analyzers
- Real time review of data and results during acquisition
- GLP / 21 CFR Part 11 compliant

E-Mitter Telemetry

- E-Mitter implantable transponders for:
  - temperature
  - gross motor activity
  - heart rate data

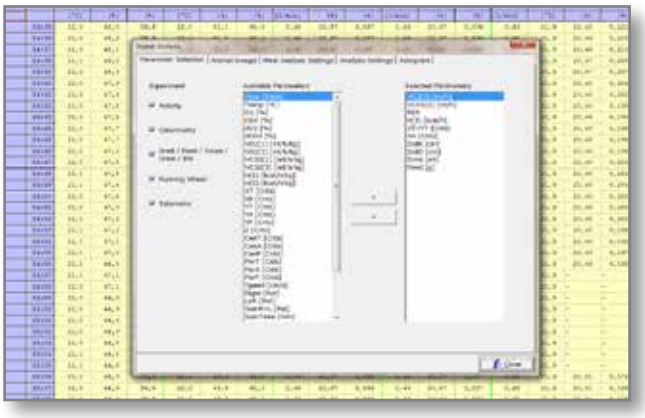
An E-Mitter is a small implantable transponder that is powered by an external Energizer/Receiver under the cage. This allows the E-Mitter to operate without batteries and remain implanted indefinitely to monitor the subject's temperature, activity or heart rate. The data are captured in the PhenoMaster software.

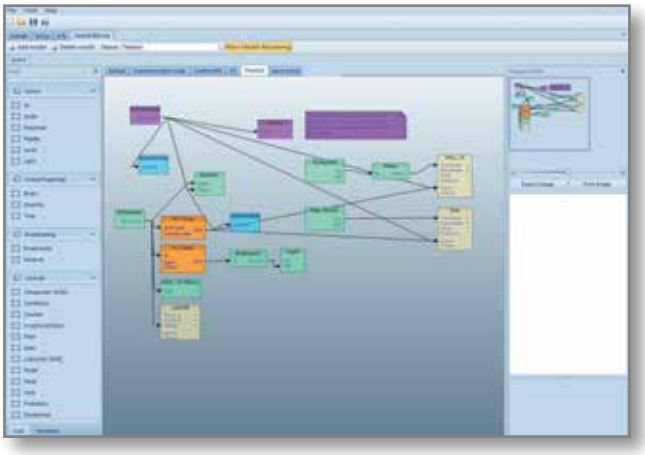
PhenoMaster: Data Handling & Software

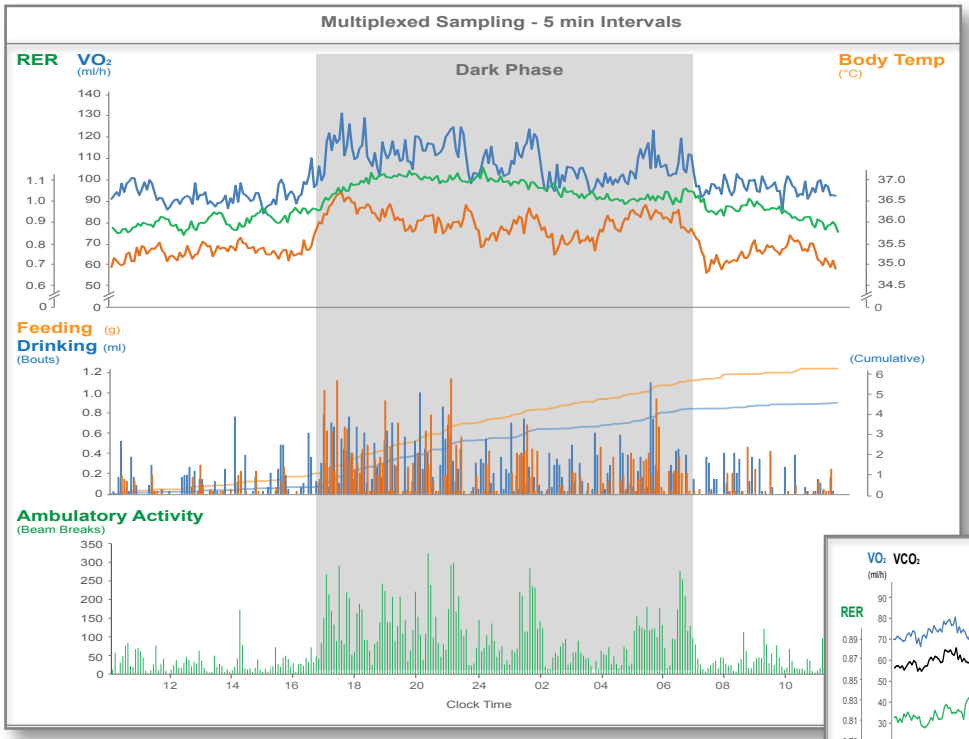
The TSE PhenoMaster software is designed as simple user-friendly, highly integrative platform that manages the synchronous operation and data acquisition of all PhenoMaster hardware modules and associated external devices.

Software Features

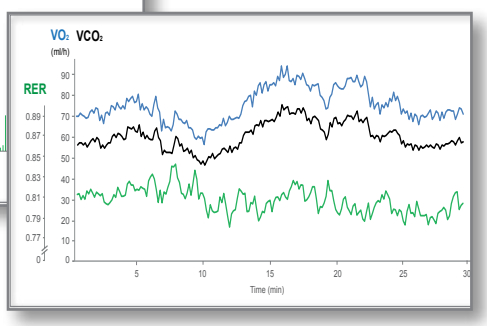
- Intuitive navigation
- Multiple modules are implemented into a single main menu
- Large selection of configuration options
- Multiple modules communicate and interact according to customized rules e.g., events detected in one module trigger actions in one or several other modules giving room to tremendous diversity in experimental designs
- Data acquisition is synchronous even for features and modules with distinct temporal resolution
- Real time monitoring and display of ongoing experiments; in graph, table and numerical form
- Various integrated alarm functions (animal welfare monitoring)
- Professional data base options allow flexible data handling
- Data can be conveniently exported to Excel or other data mining programs
- Integrated raw data storage
- Free software updates for two years
- Unlimited software licenses for data analysis on multiple computers







Simultaneous measurement of respiratory exchange ratio (RER), oxygen consumption (VO_2), food/drink intake, locomotor activity and core body temperature



Continuous calorimetry with 10 s intervals

Selected Publications

- Clemmensen C, Finan B, Fischer K, Tom RZ, Legutko B, Sehrer L, Heine D, Grassl N, Meyer CW, Henderson B, Hofmann SM, Tschöp MH, Van der Ploeg LH, Müller TD. Dual melanocortin-4 receptor and GLP-1 receptor agonism amplifies metabolic benefits in dietinduced obese miceDual melanocortin-4 receptor and GLP-1 receptor agonism amplifies metabolic benefits in dietinduced obese mice. **EMBO Molecular Medicine** 2015; 7(3): 288-98

- Han J, Li E, Chen L, Zhang Y, Wei F1, Liu J, Deng H, Wang Y. The CREB coactivator CRTC2 controls hepatic lipid metabolism by regulating SREBP1. **Nature** 2015; Epub ahead of print

- Finan B, Yang B, Ottaway N, Smiley DL, Ma T, Clemmensen C, Chabenne J, Zhang L , Habegger KM, Fischer K, Campbell JE, Sandoval D, Seeley RJ, Bleicher K, Uhles S, Riboulet W, Funk J, Hertel C, Belli S, Sebokova E, Conde-Knape K, Konkar A, Drucker DJ, Gelfanov V, Pfluger PT, Müller TD, Perez-Tilve D, DiMarchi RD, Tschöp MH. A rationally designed monomeric peptide triagonist corrects obesity and diabetes in rodents. **Nature Medicine** 2015; 21(1):27-36

- Tang C, Ahmed K, Gille A, Lu S, Gröne HJ, Tunaru S, Offermanns S. Loss of FFA2 and FFA3 increases insulin secretion and improves glucose tolerance in type 2 diabetes. **Nature Medicine** 2015; 21(2):173-7

- Urbach YK, Raber KA, Canneva F, Plank AC, Andreasson T, Ponten H, Kullingsjö J, Nguyen HP, Riess O, von Hörsten S. Automated phenotyping and advanced data mining exemplified in rats transgenic for Huntington's disease. **Journal of Neuroscience Methods** 2014; 234:38-53

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- Kim JG, Suyama S, Koch M, Jin S, Argente-Arizon P, Argente J, Liu ZW, Zimmer MR, Jeong JK, Szigeti-Buck K, Gao Y, Garcia-Caceres C, Yi CX,Salmaso N, Vaccarino FM, Chowen J, Diano S, Dietrich MO, Tschöp MH, Horvath TL. Leptin signaling in astrocytes regulates hypothalamic neuronal circuits and feeding. **Nature Neuroscience** 2014; 17(7):908-10

- Liu C, Bookout AL, Lee S, Sun K, Jia L, Lee C, Udit S, Deng Y, Scherer PE, Mangelsdorf DJ, Gautron L, Elmquist JK. PPARg in vagal neurons regulates high-fat diet induced thermogenesis. **Cell Metabolism** 2014; 19(4):722-30

Specifications subject to change without notice

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