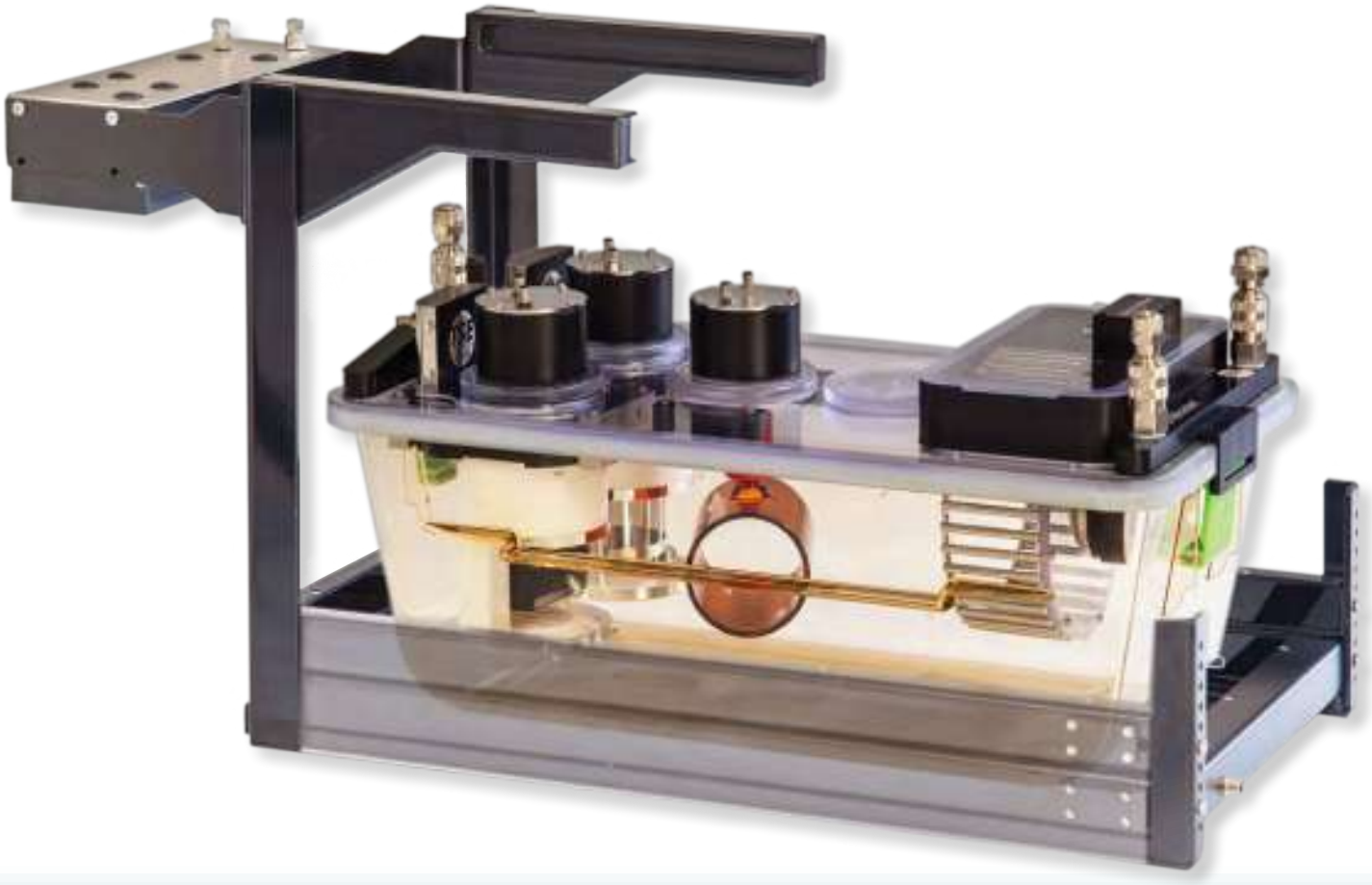
Sophisticated Life Science Research Instrumentation

PhenoMaster^{NG}

Next Generation Phenotyping



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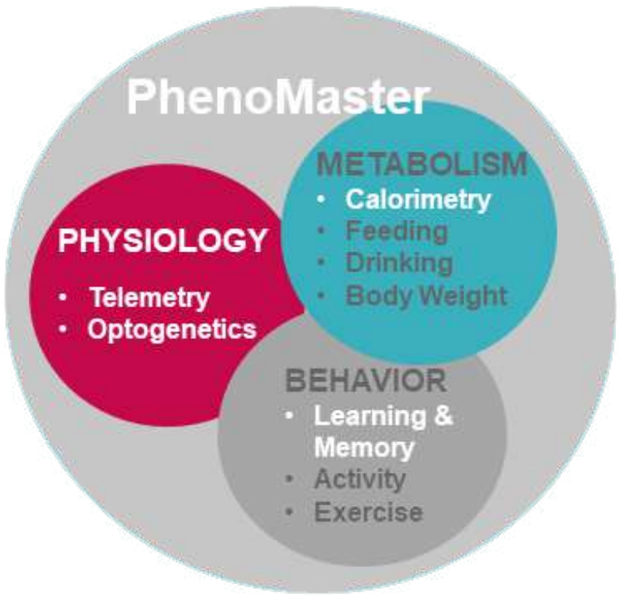
PhenoMaster^{NG}

Metabolism
Behavior
Physiology

INSPIRING. Three disciplines combined within a single fully automated home cage phenotyping system. Metabolic, behavioral and physiological high definition data continuously captured. Unsurpassed precision, minimal human intervention, highest animal welfare. The new standard in Metabolism Research.

BEST GETS BETTER - PhenoMaster^{NG} - the next generation with improved sensor technology, even higher animal welfare standards and highest data density on the market!



Unique features

Flawless Metabolic Studies

Continuous Calorimetry for Highest Resolution

Complete Environmental Control

Modular Design for Maximum Flexibility

Full Data Transparency

Superior Standardization & Reproducibility

Modules
Overview

Calorimetry

Climate Chamber

Microbiome Activity Monitoring

Feeding, Drinking, Body Weight

Food & Liquid Access Control

ActiMot3 Activity Frame

Running Wheel

Operant Wall

Swivel

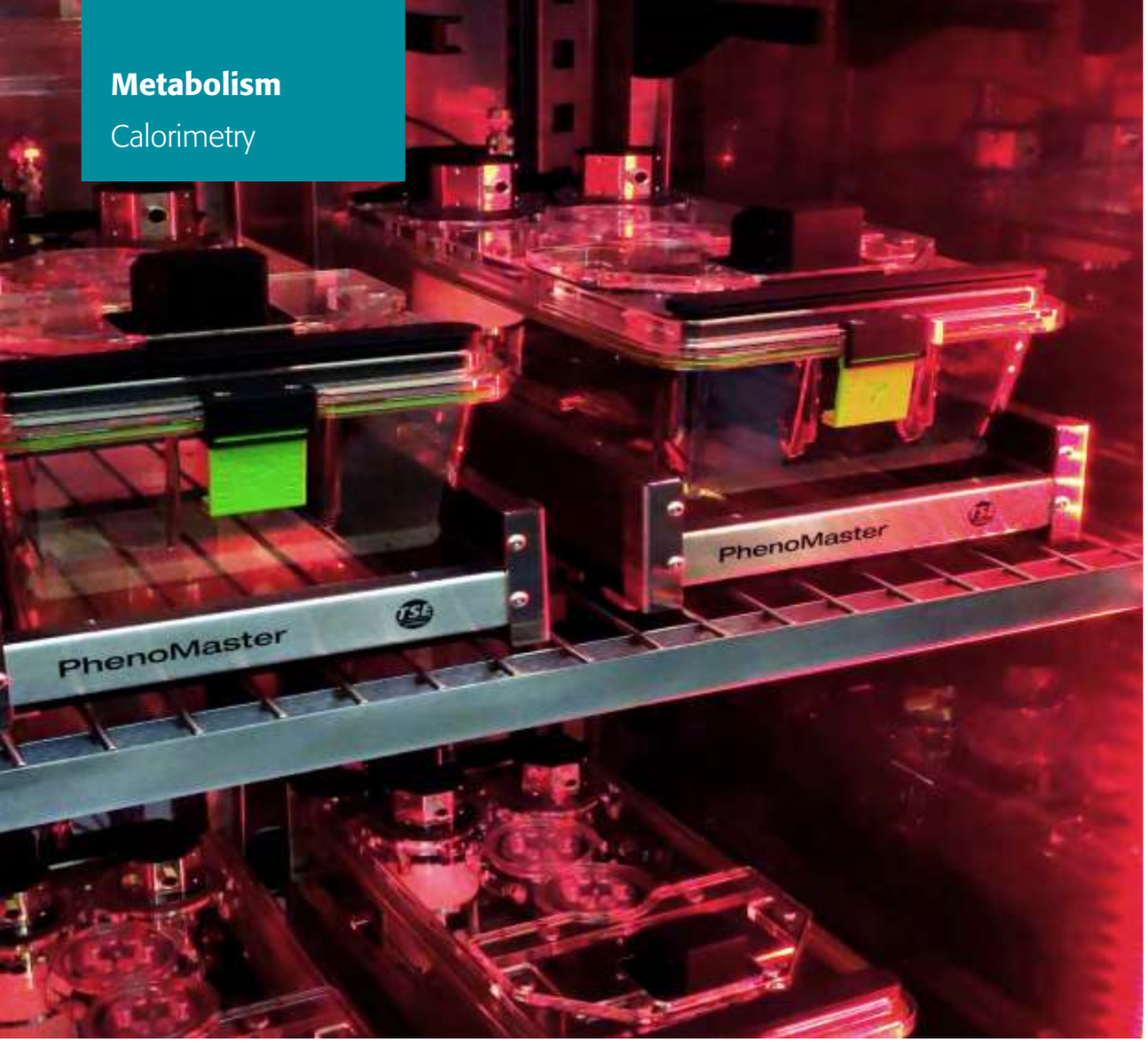
Implantable Telemetry

PhenoMaster^{NG}

Pioneer and Market Leader

Thinking ahead is what drives the PhenoMaster^{NG} development & evolution. The result is unparalleled flexibility and unique capabilities. Obesity, diabetes, microbiome studies, cardio-metabolic studies & energy expenditure. We've got you covered.

Metabolism
Calorimetry



CaloSys

For truly flawless metabolic studies fast, precise, sensitive, reproducible

CaloSys indirect gas calorimetry measures the animal's oxygen consumption and carbon dioxide production to calculate key metabolic parameters, incl. the respiratory exchange rate (RER), energy expenditure (EE), substrate utilization (fat reserves vs. carbohydrate catabolism).

CaloSys does both, PULL or PUSH mode

- Only PUSH mode permits hypoxia studies, experiments under germ free conditions and exposure to defined gas content

NEW Sensor Technology

- CaloSys is as fast as you need - it adapts to your needs
- Continuous high speed calorimetry in every cage
- Or... Multiplex calorimetry with sharing of gas sensors between two or more cages with seamless upgrade to continuous mode
- Sampling rate of 1s per cage

HIGH SPEED CONTINOUS CALORIMETRY

NEW Microbiome Activity Monitoring

- Extension with H2, CH4, VOCx, 13isoC sensors
- Combination with IVC / IsoCages housing germ free or immunocompromised animals

Unparalleled Accuracy

- NEW Continuous simultaneous measurement of pressure, humidity and temperature at (individual) cage level for industry most accurate real-time correction of gas concentration measurement and analysis
- Variable influence of water vapor is effectively eliminated & measured from gas measurements by a first-pass physical drying unit (water condensation trap) - no toxic chemicals
- High precision custom developed gas sensors are calibrated against standardized gases - in contrast to room air, which is fluctuating constantly
- Gas sensors are maintenance-free & periodically auto-calibrated
- Programmable mass-flow controllers for each cage create optimized flow rates for different animal sizes / weights / species, fully temperature compensated for use in climate chambers
- Additional monitoring of surrounding & room - human activity, CO2, H2O, temperature, room light, barometric pressure

Unique Transparency and Adaptability

- True raw sensor output data are directly available and accessible
- Metabolic parameter calculation formulas are accessible and changable
- Open data format

Climate Chamber

Full Environmental Control Engineered & Optimized for Animals

- Thermoneutrality & temperature challenge
- Full control over temperature, humidity and lighting - stable & reliable
- Constant air circulation and even distribution of heat or cold air
- Fast execution of programmed temperature changes
- Multiple cages - high throughput, high efficiency

Metabolism
Calorimetry

CaloSys

Most versatile and flexible

CaloSys combines and synchronizes with the worlds largest choice of home cage test modules. In addition, it is compatible with out of home cage test devices; such as:

CaloTreadmill

- Computerized air-tight system for exercise calorimetry
- Optimal belt grip, user-defined speed profiles with acceleration/deceleration phases, adjustable incline / decline, optional light stimuli, air puff or electric shock

CaloWheel

- Air-tight motorized exercise calorimetry wheel with computerized speed control for user-defined running schedules

NEW Design Metabolic PhenoCage

- Special glass cage with improved urine and feces separation and quantification in standard lab tubes
- Re-designed freezing unit conserves urine and feces instantly for later analysis
- Feeding and drinking module quantifies intake parameters
- Integration of new extra gas sensors (H2, CH4, VOCx)
- Easy assembly and improved animal welfare (AAALAS & FELASA) with new floor design & optional resting platform

Feeding, Drinking, Access Control

Don't miss a sip / nip! Superior weighing sensors capture every feeding & drinking episode. No spillage or leakage. Detailed meal pattern analysis. Automated access restriction.

PRIME Sensitivity

PRIME Precision

Next Generation Weight Sensors

- High-precision sensors, capturing micro-feeding events!
- NEW Small & light plug-in sensor design - easy handling, space saving, universal for feeding, drinking & body weight
- UNIQUE Validated for temperature challenges
- Variable number of sensors per cage
- Multiple sensor configuration for discrimination experiments: e.g. two diets, water and body weight (free combination)

Validated Container Technology

- Food containers with SpillProtect technology
- Bottles with LeakProtect technology
- Easy assembly to weight sensors, easy refill
- NEW Container design and lid-fixation grant up to 30% more living space

Remote Control & Monitoring

- NEW Individual cage controllers allow for complete digital communication to a central acquisition computer with automatic error checking and encryption at sensor level of each individual cage.

Automated Access Control

- Simple design, supreme functionality
- Automated restriction of food/liquid availability by time, intake duration or amount consumed
- **The only home cage system, where** access to food / water can be made conditional on defined performance parameters, e.g. running for food (in combination with a wheel)

Paired / Yoked Feeding

- Impose feeding / drinking patterns (time, duration, amount) of control animals onto assigned experimental animals, thereby creating highly controlled physiological conditions

Body Weight

Voluntary body weight screening. Assess weight gain in response to high fat diet or drug exposure or simply monitor animal well being.

UNIVERSAL Sensor Technology

No Handling. No Stress.

- Same universal sensor technology as for feeding and drinking
- Red tubular housing, invites animals to rest and groom in
- Body weight measurements every time the animal enters
- Home cage enrichment, premium animal welfare

Metabolism

Feeding & Drinking

Body Weight

Behavior
Learning & Memory

Operant Wall

NEW FEATURES

- Nose poke holes can be closed with automated doors to prevent extinction effects and soiling
- Liquid dispensers can now be combined with lickometers to quantify the actually consumed amount of liquid
- 5-choice serial reaction time paradigms can be conducted within the home cage by combining operant walls

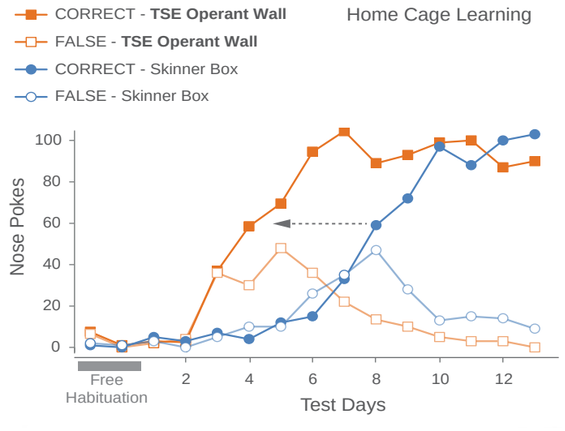
Operant Wall

We bring the experiment to the animal

The only home cage integrated operant wall permitting fully automated operant conditioning experiments. No human interference, reduced stress levels, long-term self-motivated learning, customized experiments & other significant advantages.

Smart Tools for Smart Research

- Stimulus elements include: house light, stimulus lights, sound/ noise generator and speaker (all tailored to customers' needs)
- Response elements include: nose pokes, levers (optionally retractable), running wheel
- Reinforcement elements include: dispenser for dustless precision pellets or liquids, air puff
- Various combination options with other modules extend the functionality, e.g. automated food/liquid access control unit restricts food/liquid intake prior to a learning session, or a running wheel as reward or response element, compound infusion or optogenetics via the swivel port



Advantages

- Habituation to the test module occurs much faster in a stress-free home cage environment, thus reducing the time of experiment
- The animal performs at will across light and darkphases according to innert motivation
- Allowing accurate circadian performance analyses
- Less human interference, reduced workload
- Saves costs and space

ActiMot3

Capture every move! Rearing, jumping, fine & ambulatory movements

MORE than 100 Output Parameters

ActiMot3 infrared light beam sensor frames monitor animal locomotor activity highly effective and reliable, registering even most subtle movements in the home cage or another test arena (e.g. open field, hole board, light/dark or place preference arena).

Finest Infrared Technology

- The XY frame spans a dense net of infrared light beams across the XY plane at the bottom of the cage/arena to monitor ambulatory and fine movements
- The Z frames (up to 2 per cage/arena) with light beams in the Z plane register rearing and jumping
- Beam status is queried every 10 msec; this temporal resolution of 100Hz is much higher than that of any video tracking system - allowing detection of subtle and fast movements!
- NEW **Physical spatial resolution is 5 mm for both, mouse and rat frames**
- Spatial averaging filters increase resolution further to 1.25 mm
- Smallest footprint, optimized for use in climate chambers

Uniquely Rich Analysis

- Definition of regions of interest allow zone-specific analysis
- Customized detection thresholds fine-tune acquisition
- Flexible start conditions (mouse click or animal detection)
- Real-time animal and data monitoring
- UNIQUE Up to 125 output parameters related to: movement type, position, timing
- Actograms, activity tracks, histograms, 2D & 3D display options

Unsurpassed Flexibility

- Frames are available in different sizes and geometries
- Flexible use with home cage, hole board, ligh/dark box, place preference box
- Adjustable height matches the physical size of the animal and amount of bedding
- Frames operate in any lighting condition, incl. darkness

Behavior

Exercise

Running Wheel
Turn your research around

TSE Systems pioneers the development of sophisticated voluntary home cage running wheels that can do much more than just “turn”.

NEW Design

- Slim wheel design and lid-fixation grant maximum space for movement - over 30% more living space
- Smart and easy plug in module - quick removal for cleaning

Diverse Functionalities

- Time- and distance-controlled running with enable/disable function
- Programmed progressive exercise routines
- Paired running (running profile of experimental animal is imposed onto a control animal)
- Motivated running (running for food / liquid in combination with the food / liquid access control unit)
- UNIQUE Motor skill evaluation wheel (variable distance between cross bars by removing selected rungs) for highly sensitive and reliable detection of motor skill deficits
- UNIQUE Combination with operant wall for complex learning tasks
- Perfect home cage enrichment for better animal welfare

EXTRA...

slim space functionality

Motor Skill Wheel

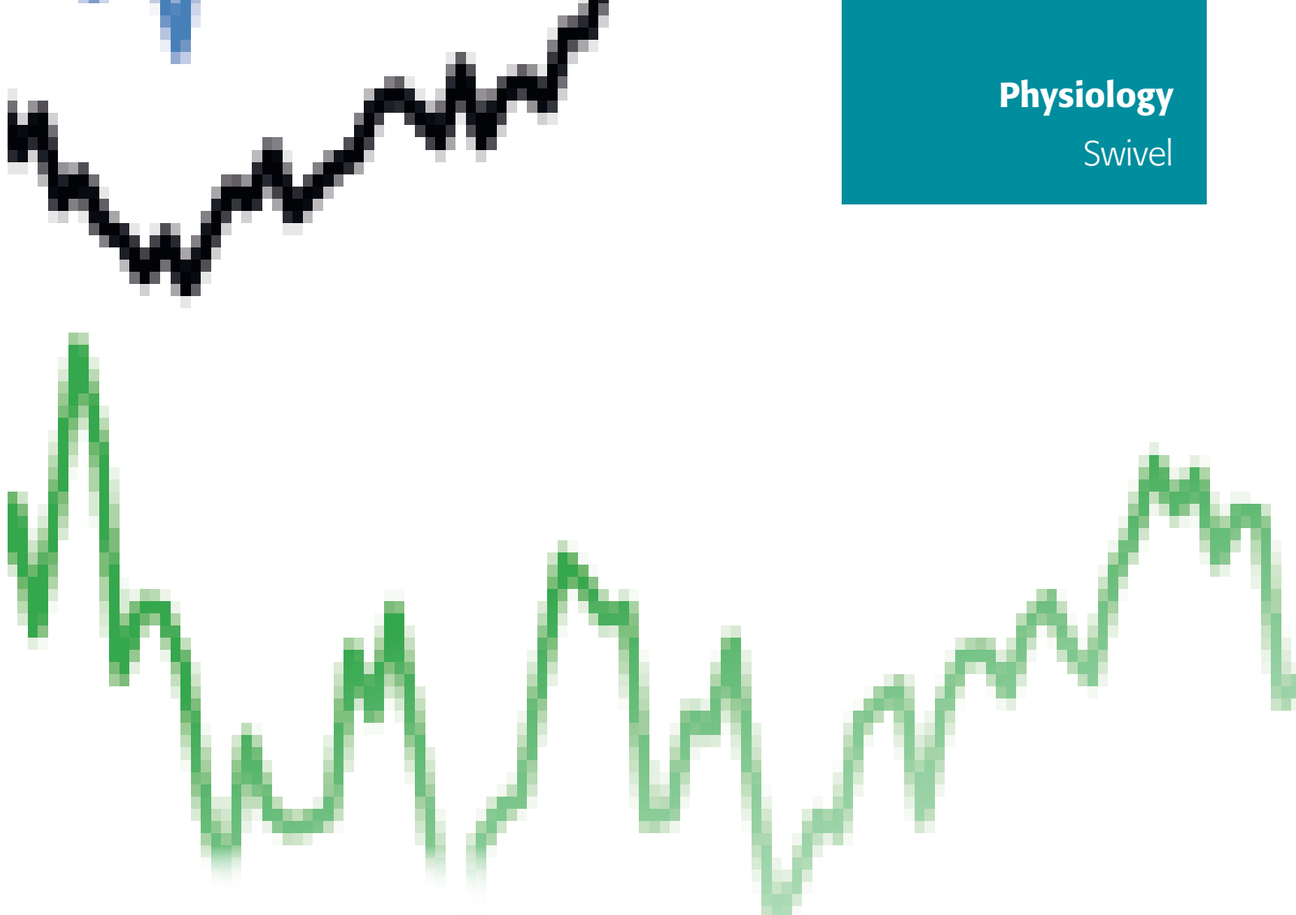
(...) “The new automated wheel-running apparatus reported provides a powerful and discriminative tool for the reliable and reproducible assessment of motor function, as evidenced by its cross-validation (...) Encouragingly, the system can detect early-stage motor deficits that cannot be detected using the rotarod test” (...); (Mandillo et al., Dis Model Mech, 2014)

Swivel

Think outside the box!

Unique Functionality

Exclusive to PhenoMaster



With TSE's Swivel module, home cage testing is brought to exciting new levels. Optogenetics, compound infusion, microdialysis and more - in freely moving animals - fully automated, no more handling, no more stressful procedures in the familiar home cage environment.

Swivel Technology

- Swivel connects the cathetered animal in the home cage to external devices
- The counter-balanced lever arm moves vertically and horizontally with the animal to prevent slack in the tether
- Unique sensitivity makes it ideal for awake-animal optogenetics, microdialysis and all types of infusion studies
- The swivel features an adjustable spring counter-balance, which increases responsiveness to quick movements
- Suited for all cage lids

Integrated Device Control

- Swivel-connected external devices are driven by PhenoMaster Software
- Timed triggering
- Conditional triggering - dependent on performance parameters (e.g. in combination with learning with the operant wall)

Swivel & Operant Wall

(...) "Operant conditioning system: Computer-controlled operant conditioning was conducted in 12 identical conditioning chambers equipped with a swiveling infusion device (PhenoMaster, TSE Systems)" (...); Cansell et al., Mol Psychiatry 2014

PhenoMaster Software

Powerful, flexible, user-friendly

Pheno*Master* your Experiments

Acquisition

- NEW Webbrowser based system, platform indepent (Windows, MacOS, iOS, Android, Linus) operable with any device (desktop, note-book, tablet, smart-phone)
- NEW Capability to create virtual large screening clusters by "combining" multiple PhenoMaster systems in different labs with no geographical restriction (high-speed internet & intranet connection is required)
- All hardware modules are easily operated in a single main menu with intuitive navigation
- Large selection of configuration options for each module
- Synchronized data acquisition for all modules
- 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 space for tremendous diversity in experimental designs
- Real time monitoring and display of ongoing experiments; in graph, table and numerical form

Analysis & Batch Processing

- NEW Separate fully programmable and configurable data analysis package powered by Microcal Origin with among other features: C++, Matlab, Python and Rscript interfaces for client customization
- NEW Output and export filters for Mathematica, SPSS, Statistica and other packages
- Open real-time read/write database, Protocol and Database based on industry standard InfluxDB, SQL and CSV files.
- Easier to customize Report Tables in graphs
- NEW Statistics such as 3-way ANOVA, Partial Correlation, etc.
- Raw sensor data are always stored for each module (e.g., status of each light beam at every time point, O_2 or CO_2 values for each cage and time point)
- Various integrated alarm functions (animal welfare monitoring

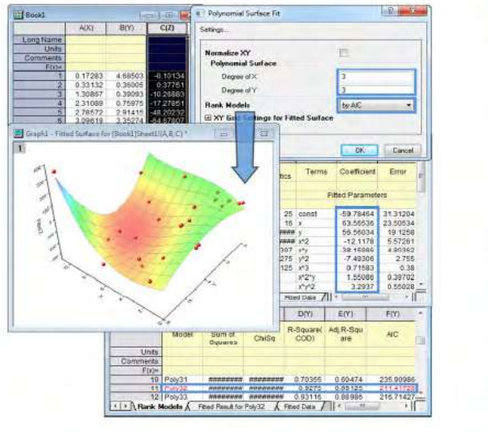
Programming

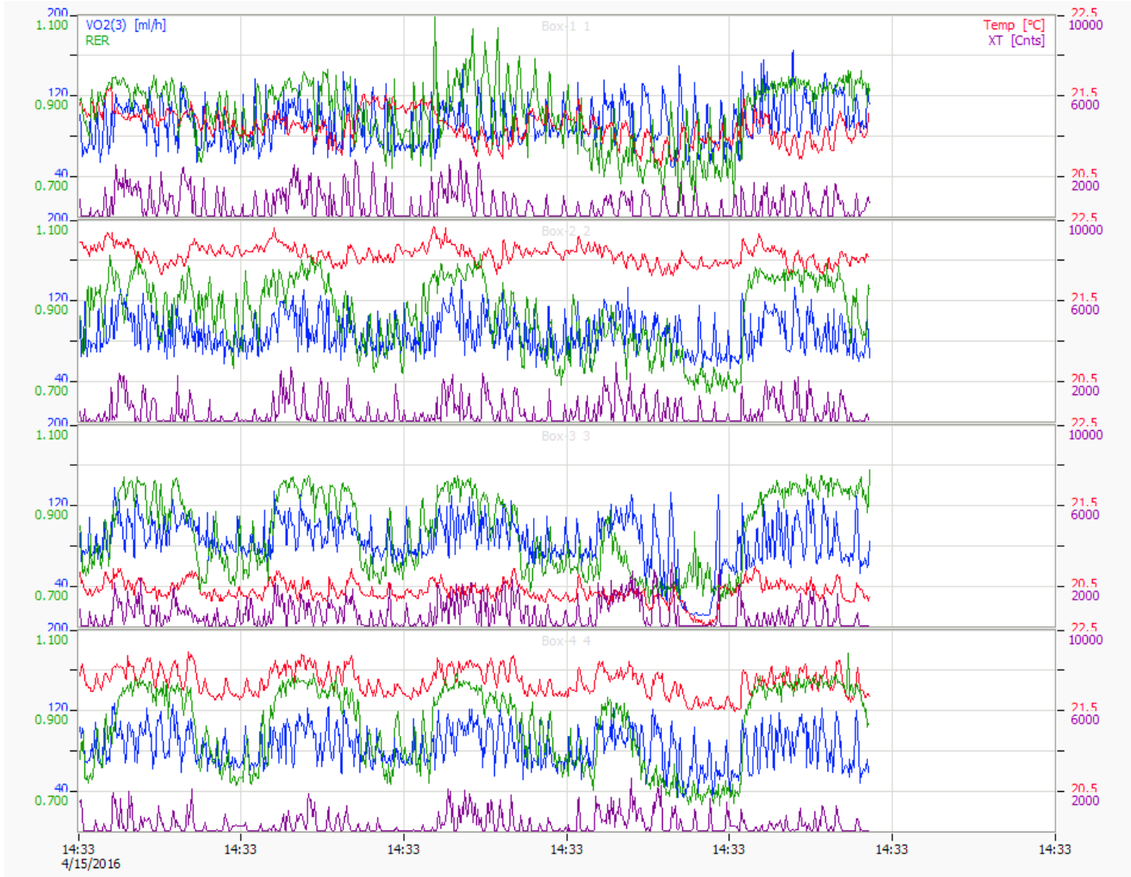
- NEW R Console and support for R serve to exchange data between Origin and R

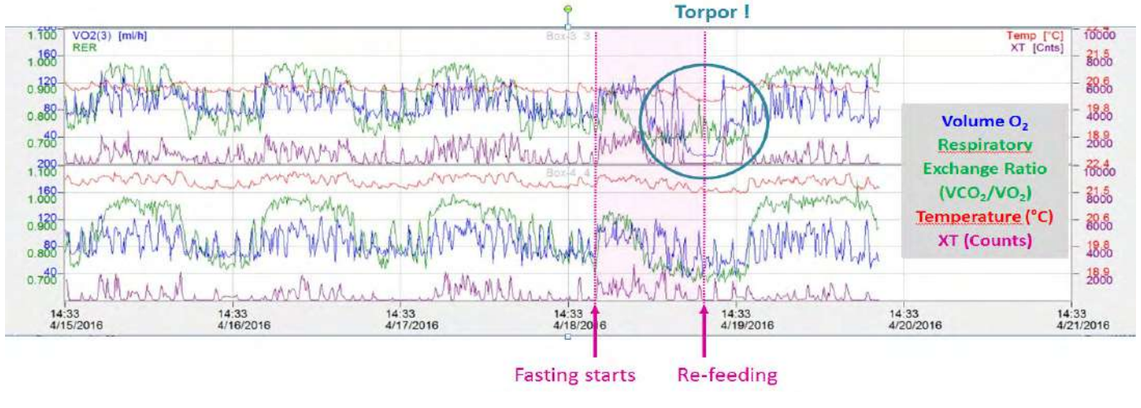
Reporting

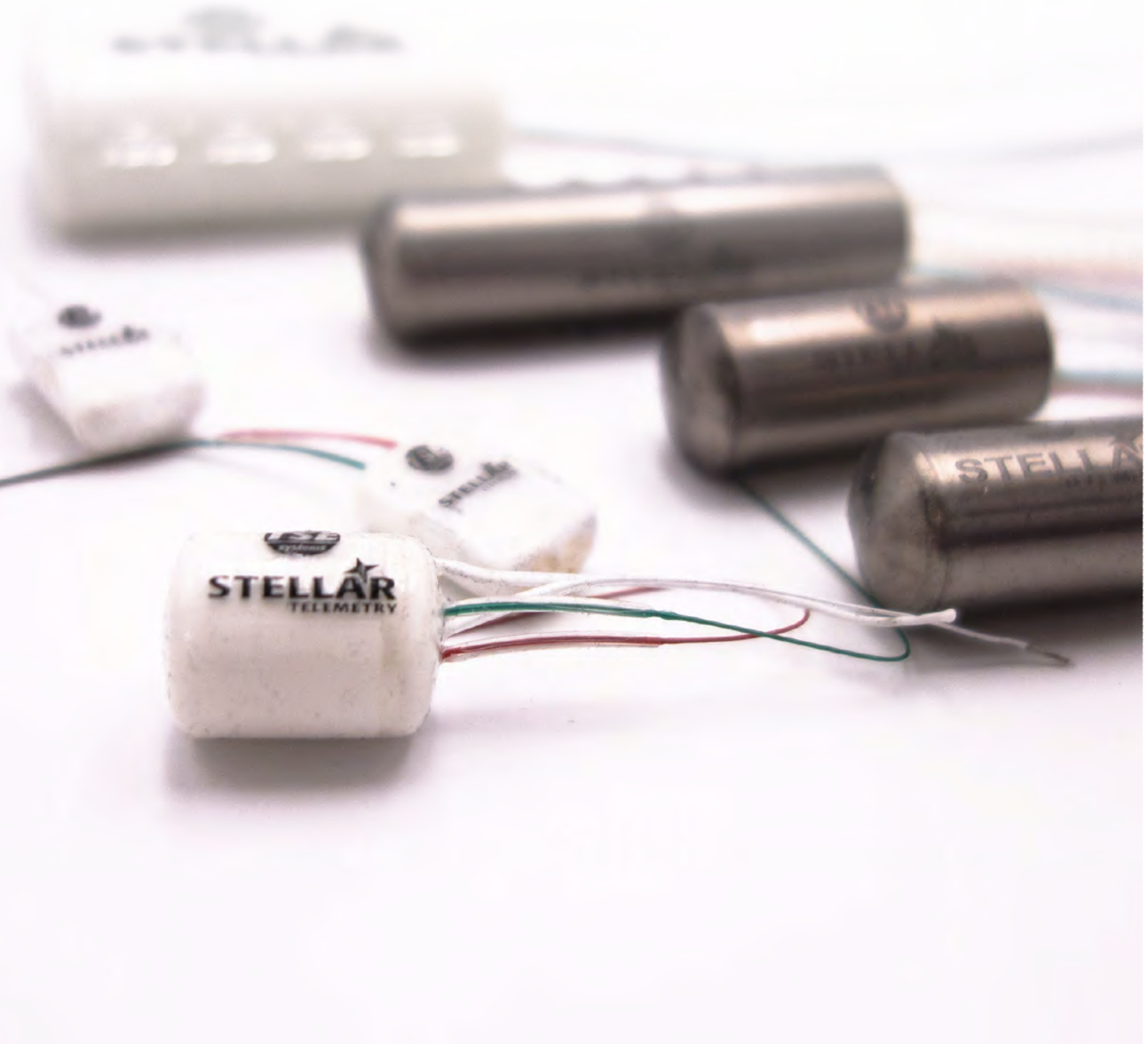
- NEW Word Template for Report Creation in Batch Processing
- NEW Smart Plotting with Cloneable Graph Templates

ORIGIN® 2018
Graphing & Analysis









Stellar Telemetry

As module of PhenoMaster, Stellar Telemetry allows scheduled or continuous monitoring of key physiological vital signs in complex cage environments while metabolic and behavioral measurements are acquired simultaneously - all modules perfectly attuned.

Transmitters

- Implants for any animal 15g - 3500+g
- 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 pressure measurements throughout the body, (brain, lung, heart, (blood)vessels or GI tract smallest on the market, virtually drift free!
- High fidelity and high frequency responses, no head pressure or animal movement noise
- Stellar adds on to all PhenoMaster modules - in the home cage or any other test environment, incl. social groups

Receiver

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

Software - It's Your Choice!

- Stellar Telemetry can be operated with both, BIOPAC Aq*Knowledge* Software and NOTOCORD-hem™ Evolution software and native within PhenoMaster

BIOPAC Aq*Knowledge*

- Seamless animal scheduling with intuitive calender intrerface
- 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™ Evolution

- 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/21CFR Part11 compliant

Selected Publications

- Ramachandran D, Clara R, Fedele S, Hu J, Lackzo E, Huang JY, Verdin E, Langhans W, Mansouri A. Intestinal SIRT3 overexpression in mice improves whole body glucose homeostasis independent of body weight. **Mol Metab.** 2017 Oct;6(10):1264-1273

- Laeger T, Baumeier C, Wilhelmi I, Würfel J, Kamitz A, Schürmann A. FGF21 improves glucose homeostasis in an obese diabetes-prone mouse model independent of body fat changes. **Diabetologia.** 2017

- Cains S, Blomeley C, Kollo M, Rácz R, Burdakov D. Agrp neuron activity is required for alcohol-induced overeating. **Nature Communications** 2017 Jan 10;8:14014

- Clemmensen C, Finan B, Fischer K, Tom RZ, Legutko B, Sehrer L, Heine D, Grassl N, Meyer CW, et al. Dual 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 F, Liu J, Deng H, Wang Y. The CREB coactivator CRTC2 controls hepatic lipid metabolism by regulating SREBP1. **Nature.** 2015 Aug 13;524(7564):243-6.

- Finan B, Yang B, Ottaway N, Smiley DL, Ma T, Clemmensen C, Chabenne J, Zhang L , Habegger KM, et al. 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 im- proves 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

- Mauer J, Chaurasia B, Goldau J, Vogt MC, Ruud J, Nguyen KD, Theurich S, Hausen AC, Schmitz J, et al. Signaling by IL-6 promotes alternative activation of macrophages to limit endotoxemia and obesity-associated resistance to insulin. **Nature Immunology** 2014; 15(5):423-30

- Kim JG, Suyama S, Koch M, Jin S, Argente-Arizon P, Argente J, Liu ZW, Zimmer MR, Jeong JK, Szigeti-Buck K, et al. 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 vagalneurons regulates high-fat diet induced thermogenesis. **Cell Metabolism** 2014; 19(4)