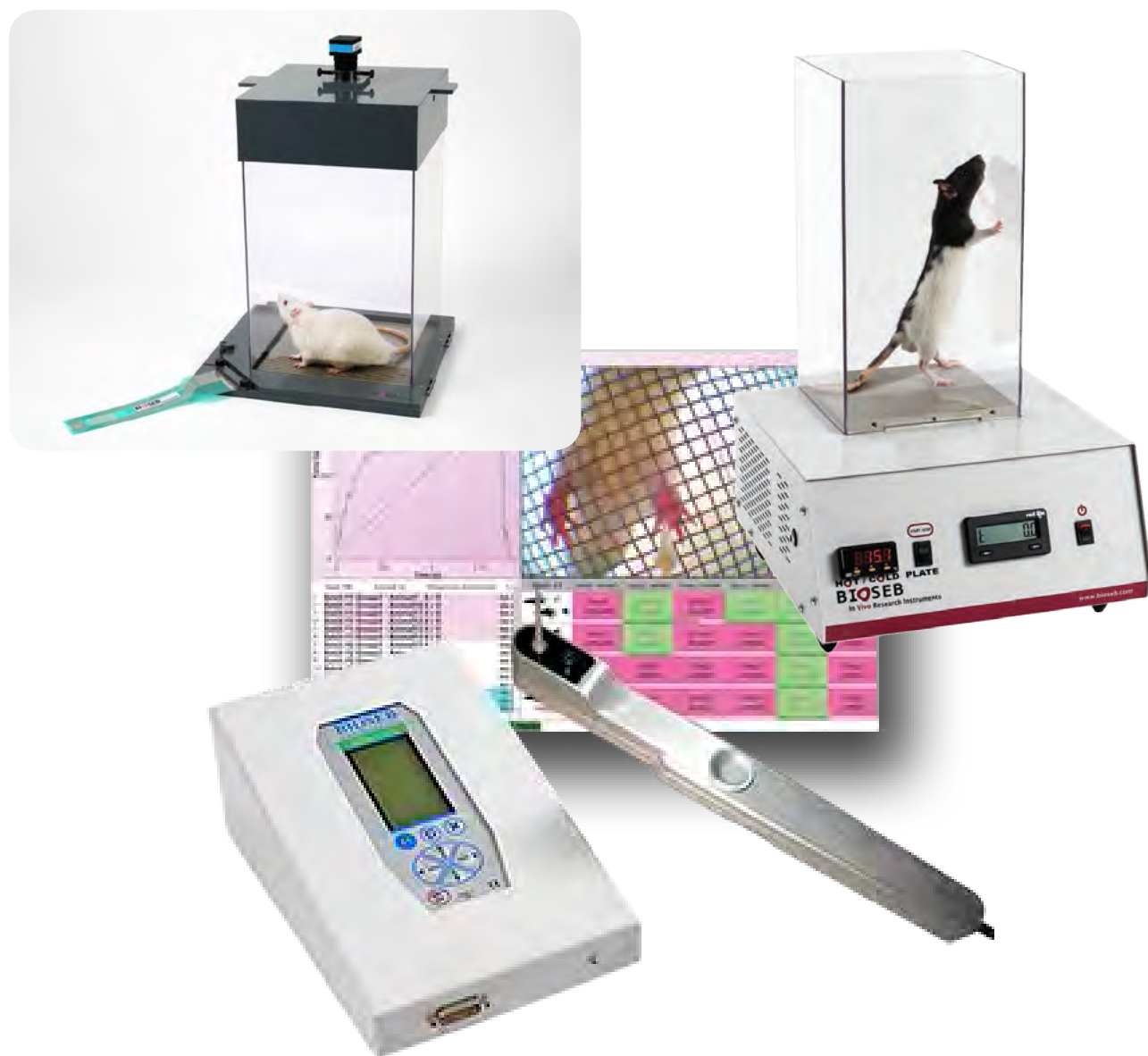


MEETING YOUR NEEDS BY DESIGNING INNOVATIVE AND HIGH-QUALITY SOLUTIONS FOR YOUR RESEARCH



STUDIES ON PAIN



MAIN INSTRUMENTS

- Dynamic Weight Bearing
- Electronic Von Frey
- Cold/Hot Plate Test

AN EFFICIENT AND ADVANCED ALTERNATIVE TO TRADITIONAL INCAPACITANCE TESTS FOR ASSESSING PAIN SENSITIVITY



DWB: Advanced Dynamic Weight Bearing 2.0

INSTRUMENT OVERVIEW

Bioseb's Advanced Dynamic Weight Bearing Test is the result of years of R&D based on the principles of early incapacitance instruments, which we evolved from Static Weight Bearing to the new Advanced Dynamic Weight Bearing 2.0

Thermal and mechanical stimulators are often used to assess pain in rodents, however, ethical considerations as well as the necessity to study comfort and evoked pain levels on rodents lead to the development of **tests avoiding any stimulation on the animals**. Therefore, Weight Bearing assessment of rodents is now well known and largely used for assessing pain sensitivity in rodents.

Among a variety of instruments that allow to measure Weight bearing on the hind paws of rodents, Bioseb's Dynamic Weight Bearing test is **the only rodent evoked pain test not requiring animal restraint**. It is also the only instrument allowing you to precisely measure changes in Postural Equilibrium in rodents by assessing their weight distribution on each one of their 4 paws.

After 10 years of development the new version DWB2 offers unprecedented improvements increasing both speed and software user experience while optimizing results accuracy and reliability such as :

- **Fast and reliable**, automatic postural analysis algorithms
- **New 3-tab interface**: Settings/ Experiment/ Analysis. Simple and Straightforward
- **Group management** module and animal lists for GLP procedures

HOW DOES IT WORK?

The DWB relies on two different technologies :

A **matrix comprising around 2000 high precision force sensors** to measure the weight distribution on each of the four paws of the animal in grams. The instrument uses different sensors for rats or mice in order to provide a suitable sensitivity level (0-4g for mice and 0-40g for rats).

A **video monitoring** : the animal is filmed from above using a high definition camera. The video feed is analyzed in real-time during the test thanks to our tracking software allowing a precise analysis of the animal's posture.

Eventually, our software can accurately analyzes the animal's position during the entire duration of the test in order to automatically identify the location of each of the four paws on the force sensors.

KEY FEATURES

- User friendly software
- Operator-independent test with automatic scoring
- No stress induced on the animal (rat or mouse)
- Unique assessment of the 4 paws

TECHNICAL SPECIFICATIONS

Camera 640x480 USB-based camera high resolution delivered with its lens

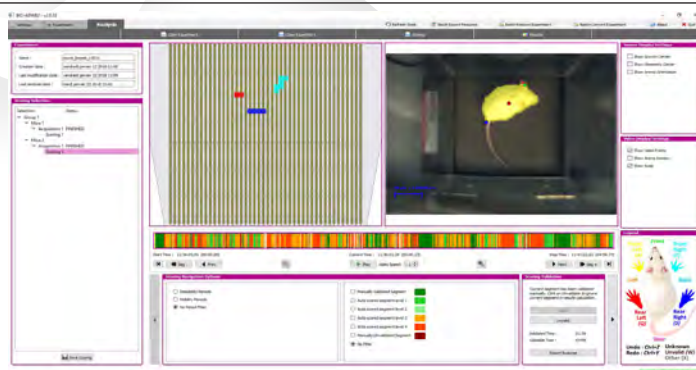
Versions available 3 versions: rat, mouse, combined rat+mouse

DWB: Advanced Dynamic Weight Bearing 2.0 - New Incapacitance Test

DEDICATED SOFTWARE

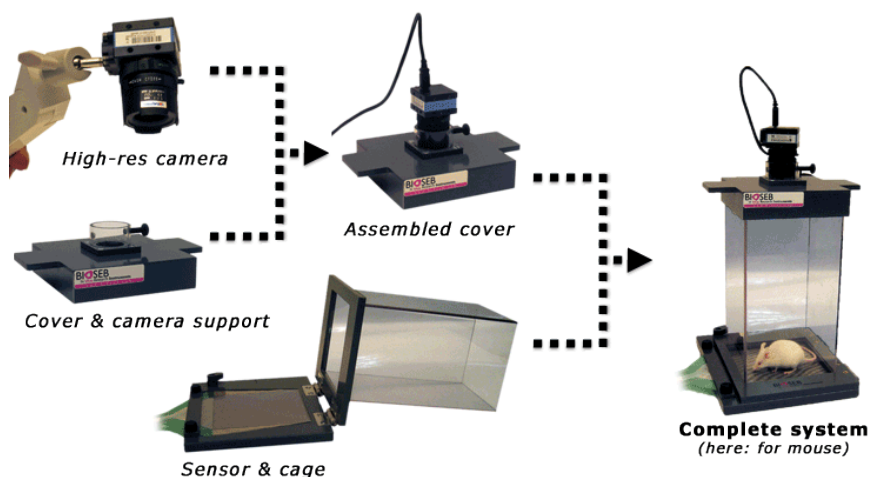
Parameters measured:

- Weight for each paw (g and % total animal weight)
- Weight for grouped front and rear paws (g and % total animal weight)
- Left/Right and Front/Rear weight ratio
- Surface for each paw (mm²)
- Surface for grouped front and rear paws (mm²)
- Variability (standart deviation/mean) for each parameter
- Parameters given for each posture and as a mean for the whole experiment
- Total time spent on each paw over the whole experiment (s)
- Duration of different postures (4 paws, rearing...) over the whole experiment (s)
- Total time spent on each paw over the whole experiment (s)



Screenshot of Bioseb's Advanced DWB Software: Dual video + sensor approach

SYSTEM OVERVIEW: CAMERA, COVER, CAGE



DOMAINS OF APPLICATION

Pain - Nociception/Analgesia

- Bone cancer models
- Neuropathic models
- Inflammation model
- Post surgery models
- Osteo-arthritis models
- Arthrose models
- Pelvic pain models

Physiology

- Peripheric ischemia
- Cerebrovascular accident models

Neurology

- Spinal cord injuries recovery process

Other research applications

- Calcaneal tendon disease
- Crucial ligaments disease
- Vestibular disorders

HIGHLIGHTED BIBLIOGRAPHY Exhaustive list on our website



Methods Used to Evaluate Pain Behaviors in Rodents, *Frontiers in molecular Neuroscience* (2017), J.R. Deuis, L.S. Dvorakova, I. Vetter et al, DOI: 10.3389/fnmol.2017.00284 - *Domain of application: Pain*

Adjustment of the dynamic weight distribution as a sensitive parameter for diagnosis of postural alteration in a rodent model of vestibular deficit, *PLOS One* (2017), B Tighilet et al, DOI: 10.1371/journal.pone.0187472 - *Domain of application: Sensory systems*

Polytherapy with a combination of three repurposed drugs (PXT3003) down-regulates Pmp22 over-expression and improves myelination, axonal and functional parameters in models of CMT1A neuropathy, *Int Orphanet J Rare Dis.* (2014), Chumakov I et al, DOI:10.1186/s13023-014-0201-x - *Domain of application: Muscular systems*

Peripheral sensitization and neuropathic pain in the rat medial meniscal tear model of post-traumatic osteoarthritis, *Osteoarthritis and Cartilage* (2018), M.S. O'Brien et al, DOI: 10.1016/j.joca.2018.02.708 - *Domain of application: Joints*

Thirty-five Day Fluoxetine Treatment Limits Sensory-Motor DePcit and Biochemical Disorders in a Rat Model of Decompression Sickness, *Frontiers in Physiology* (2017), C Cosnard et al, DOI: 10.3389/fphys.2017.00604 - *Domain of application: Metabolism*

ORDERING INFORMATION

Reference	Description
BIO-DWB-AUTO-M	For mice
BIO-DWB-AUTO-R	For rats
BIO-DWB-AUTO-DUAL	Dual: for rats and mice

The ADVANCED DWB is available in three setups offering different dimensions and sensors, depending on the rodents being tested: **RAT** (BIO-DWB-AUTO-R), **MICE** (BIO-DWB-AUTO-M), **COMBINED RATS & MICE** (BIO-DWB-AUTO-DUAL).

FOR MORE INFORMATION, VISIT OUR WEBSITE: WWW.BIOSEB.COM/DWB

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A QUICK & EASY YET POWERFUL ELECTRONIC SOLUTION TO DETERMINE RODENTS' MECHANICAL SENSITIVITY THRESHOLD



Bioseb's New Electronic Von Frey instrument: overview

HOW DOES IT WORK?

The electronic model of Von-Frey filament combines **ease-of-use and rapidity** for the determination of the mechanical sensitivity threshold in rodent.

A tip is applied against the central edge of the animal hind paw. Paw withdrawal caused by the stimulation is registered as a response. The corresponding force applied is recorded by the system and displayed on the large backlit screen of the Von-Frey unit with a resolution of 0.1 grams. A different tip is used for **rat** (hard plastic tip) and **mice** (elastic spring tip).

Differently to the procedure using classical Von-Frey filaments, the **threshold value can be obtained in only one test**, and in a highly reproducible manner.

KEY FEATURES

- Non-corrosive tips: precision springs, no "touch-on" effect
- A lighter stimulator wand for more precise movement
- Stand-alone instrument: internal memory for up to 100 values



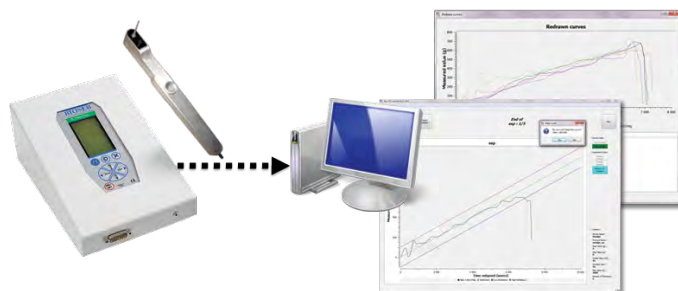
BIO-EVF4: Electronic Von Frey

INSTRUMENT OVERVIEW

Bioseb's new Electronic Von Frey unit EVF is an **easy-to-use** instrument allowing you to quickly determine the mechanical **pain sensitivity threshold** in rodents (both rats and mice).

This value can be measured in one single application, and offers a high accuracy and repeatability. Sensibility threshold result is displayed on a large backlit LCD. The sensor can be used with a wide variety of species (mice, rats, etc.).

Thanks to 16 years in marketing electronic Von Frey instruments, Bioseb has designed what will be the next standard for reflex testing on freely moving rodents.



DEDICATED SOFTWARE: BIO-CIS

The BIO-CIS Software reduces inter-operator variability and can be used in two different ways with the EVF:

Direct measurement: When the Electronic Von Frey is connected to the BIO-CIS software during stimulation, the software displays the real-time graph of applied force vs time in real-time and store the value in an Excel spreadsheet

Indirect measurement: Transfer of internal memory of the EVF to the computer as an Excel spreadsheet.

TECHNICAL SPECIFICATIONS

Measurement range	0 to 500 grams (5N)
Resolution	0,1gram
Sensor protection	120 % of full range with alarm avoiding overload
Backlit Extra-Large LCD	Easy to read, display peak, current value and Bargraph
Statistical functions	Average value and standard deviation for each subject
Result	Sensitivity threshold at paw withdrawal, MNT Mechanical nociceptive threshold
Internal Memory	Up to 100 values
Power supply	110-220V
Included with every EVF	Case, footswitch, dedicated tips

INCLUDES AN EMBEDDED CAMERA INSIDE THE STIMULATOR & A DEDICATED SOFTWARE REVOLUTIONIZING THE EXPERIMENT



BIO-EVF5: Electronic Von Frey with Embedded Video

INSTRUMENT OVERVIEW

We know that one of the main issue with Electronic Von Frey instruments is the necessity for the operator to bend into an uncomfortable posture in order to stimulate under the rodents' paws.

In order to solve this issue, we embedded a camera inside the stimulator handle, which allows you to record and display video directly from underneath the paws.

Plus, we added a dedicated software matching every requirements for the Von Frey Test.



Video with target pointer

No discomfort for stimulation. Just look at the video to perform the stimulation. Thanks to the target on the screen, it will be easy to know where you will stimulate.



Real-time curve display

Immediate display of applied force over time. The curves will help you to validate your measurements and to improve reproducibility. Every video and curves can be replayed during analysis!

Batch #2	Group2_Armal01	Group2_Armal20	Group2_Armal01	Group2_Armal10	Group3_Armal10	Group3_Armal17

Quick value assignation

A table allowing you to assign each measurement to the corresponding paw by directly clicking on the touch screen. Fast validation in 1 touch with animal list management.

TECHNICAL SPECIFICATIONS

Measurement range	0 to 500 grams (5N)
Resolution	0,1gram
Sensor protection	120 % of full range with alarm avoiding overload
Backlit Extra-Large LCD	Easy to read, display peak, current value and Bargraph
Statistical functions	Average value and standard deviation for each subject
Result	Sensitivity threshold at paw withdrawal, MNT Mechanical nociceptive threshold
Internal Memory	Up to 100 values
Power supply	110-220V
Included with every EVF	Case, footswitch, dedicated tips

INCLUDES AN EMBEDDED CAMERA INSIDE THE STIMULATOR & A DEDICATED SOFTWARE REVOLUTIONIZING THE EXPERIMENT

BIO-EVF4 & EVF5: Options, domains of applications & publications

OPTIONS

- A **patient switch** allows to freeze the displayed value when the threshold is reached
- A USB connexion allows to transfer the displayed value onto a computer
- New, robust and modular cages to gently hold rodents (rats or mice) during nociceptive and analgesic tests including Hargreaves and Von Frey protocols: an innovative, solid, practical and user-friendly design by Bioseb.



New stand for Bioseb's Electronic Von Frey

DOMAINS OF APPLICATION

- Phenotyping
- Neuropathy
- Inflammation
- Post-operative pain
- Phantom pain
- Diabetic neuropathy
- Nerve Regeneration

HIGHLIGHTED BIBLIOGRAPHY Exhaustive list on our website



Monoaminergic descending pathways contribute to modulation of neuropathic pain by increasing-intensity treadmill exercise after peripheral nerve injury, *Exp Neurol.* (2018), Lopez-Alvarez VM et al., DOI: 10.1016/j.expneurol.2017.10.007, (**Mechanical allodynia & Hyperalgesia**)

Group I metabotropic glutamate receptor plasticity after peripheral inflammation alters nociceptive transmission in the dorsal horn of the spinal cord in adult rats, *Mol. Pain* (2017), Radwani H et al., DOI: 10.1177/1744806917737934., (**Inflammatory pain**)

Minocycline attenuates the development of diabetic neuropathy by modulating DREAM and BDNF protein expression in rat spinal cord, *J Diabetes Metab Disord.* (2019), Ismail CAN et al., DOI: 10.1007/s40200-019-00411-4., (**Neuropathic pain**)

Cholesterol Depletion Regulates Axonal Growth and Enhances Central and Peripheral Nerve Regeneration, *Front Cell Neurosci.* (2019), Cristina Roselló-Busquets et al., doi: 10.3389/fncel.2019.00040, (**Nerve regeneration**)

ORDERING INFORMATION

Feature	BIO-EVF4	BIO-EVF5
Handle stimulator	Without camera	With camera
Dedicated Software	Bio-CIS (Optional)	BIO-EVF (included)
Curves drawing	With optional BIO-CIS software	Yes
Experiments management	No	Yes
Animal list management	No	Yes
Video replay	No	Yes
Statistics	Basic	Advanced

FOR MORE INFORMATION, VISIT OUR WEBSITE: WWW.BIOSEB.COM/EVF

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AN INNOVATIVE, ACCURATE AND EASY-TO-USE INSTRUMENT FOR YOUR RESEARCH ON ANALGESIA



BIO-CHP: Cold/Hot Plate

INSTRUMENT OVERVIEW

Bioseb's Cold and Hot Plate Test is an innovative instrument opening **new investigation fields for your analgesia research** by allowing you to test animal's sensitivity to pain resulting from exposure to heat or cold.

Thermal stimulation is a common technique to assess peripheral sensitivity threshold. It is a standard test along with mechanical stimulation for a large spectrum of pain related research and to control for other behavioural assays.

Bioseb's Cold Hot Plate (CHP) is a **user-friendly device** to measure thermal pain resistance / sensitivity resulting from **exposure to heat or cold**. An electronic thermostat maintains the plate's temperature within the broad range of -2°C to 50°C (European recommendations) with an accuracy of $\pm 0.5^{\circ}\text{C}$ and a surface temperature uniformity of $\pm 0.2^{\circ}\text{C}$. For special applications, our extended version (BIO-CHP-ER) allows setups in the range of -5°C to $+65^{\circ}\text{C}$. Bioseb Cold/Hot plate is also **the fastest on the market**.

Equipped with transparent enclosure, a front panel digital thermometer that displays the current plate temperature, and a chronometer to count the stimulation duration, it is a perfect stand-alone solution.

HOW DOES IT WORK?

Set the plate to the chosen temperature and wait for the thermometer to display it has been achieved. Place the subject on plate within the enclosure and start the built-in chronometer using the button on the front panel or the foot pedal.

The operator stops the chronometer when the animal demonstrates a nociceptive response, such as paw lick, hind paw withdrawal, or jump. Reaction time remains displayed in seconds on the front panel until zeroed.

Bioseb designed the CHP as a stand-alone instrument. Its capacity can be augmented by optional software for programming temperature ramps and looping protocols.

KEY FEATURES

- Standard CHP works from -2 to 55°C
- Extended CHP works from -5 to 65°C
- Homogeneity all over the plate, at any temperature
- Fastest on the market to reach target temperature
- Embedded thermometer and timer
- Optional red colored transparent cage (BIO-CHP-CAGES-R)
- Expandable to thermal preference testing

DOMAINS OF APPLICATION

- Neuropathic pain
- Chronic pain
- Allodynia/Hyperalgesia
- Phenotyping
- Neurodegeneration
- Nerve injury
- Mood disorders

TECHNICAL SPECIFICATIONS

Dimensions - Enclosure	350 x 170 x 170 mm
Dimensions - Plate	165 x 165 mm
Temperature range	-2°C . to 55°C (in 20 to 25°C ambient environment, 50% RH)
Extended temperature range	-5°C . to 65°C (in 20 to 25°C ambient environment, 50% RH)
Temperature accuracy / uniformity	Accuracy: $\pm 0.5^{\circ}\text{C}$. ; Uniformity on plate: $\pm 0.2^{\circ}\text{C}$.
Time to reach target temperature	Ambient to 4°C : less than 10 min. ; 4°C to 55°C : 5 min.
Weight	6.7 kg

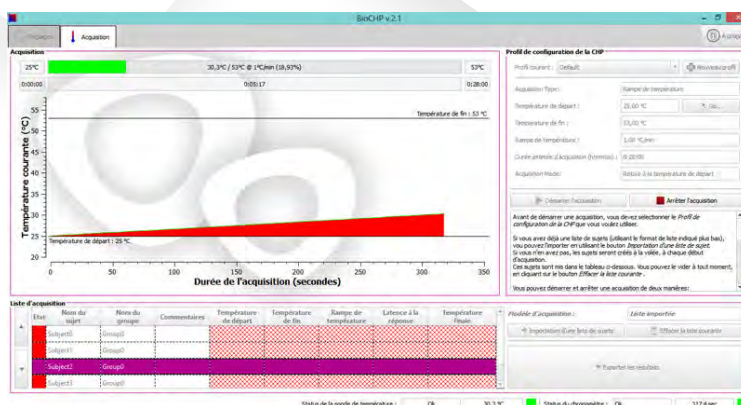
BIO-CHP: Cold/Hot Plate



DEDICATED SOFTWARE

Though it is functional as a stand-alone instrument, the Cold Hot Plate Test Analgesia Meter can also be used with optional software, allowing the user to define temperature «ramps» and «Loops».

- Software controls the temperature for generation of a continuous and reproducible ramp or loop
- Ramps allow for identification of the precise nociceptive behavior-inducing temperature for each subject
- Loop protocol design is useful for subject acclimation
- Pre-set temperature limits can be programmed to prevent damage to animal's paws and minimize pain/stress to animal

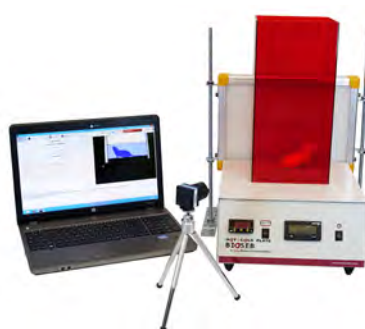


THE CORE OF A SUIT OF THERMAL PREFERENCE & EVOKED PAIN EVALUATION TOOLS



Two Temperature Choice Test

Track animal position while experiencing two temperature paradigms.



Jump Test

Evaluate the escaping behaviour of mice experimenting a ramp of cold and hot temperatures over a plate.



Thermal Gradient Test

Automatically track the position of a rodent exposed to a gradient of temperature.

HIGHLIGHTED BIBLIOGRAPHY Exhaustive list on our website



Effect of 1-hydroxy-1,1-ethylidenediphosphone acid, bis(2-pyridyl-1,2,4-triazolyl-3)propane and their adduct on the pain sensitivity of rats pyridyl-1,2,4-triazolyl-3)propane and their adduct on the pain sensitivity of rats, Scientific notes of the Crimean Federal University (2019), Cheretaev I. V. et al.

Wider range of allodynia in a rat model of repeated dural nociception compared with infraorbital nerve chronic constriction injury, Neurosci Lett. (2018), Hu G. et al., 10.1016/j.neulet.2017.12.048.

Effects of resveratrol in the signaling of neuropathic pain involving P2X3 in the dorsal root ganglion of rats, Acta Neurol Belg. (2019), Guo J. et al., DOI: 10.1007/s13760-019-01126-2.

Huachansu suppresses TRPV1 up-regulation and spinal astrocyte activation to prevent oxaliplatin-induced peripheral neuropathic pain in rats, Gene. (2019), Huao Y. et al., DOI: 10.1016/j.gene.2018.09.035.

ORDERING INFORMATION

Reference	Description
BIO-CHP	Dynamic Cold hot plate for mice or rats (-2 to 55°C)
BIO-HP	Dynamic Hot plate for mice or rats (30 to 55°C)
BIO-CHP-ER	Dynamic Cold Hot Plate Extended Range (-54 to 65°C)
BIO-CHP-RAMP	Software for Dynamic Cold/Hot plate

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