TSE
Technical & Scientific
Equipment GmbH

TSE Non-Invasive Blood Pressure Monitoring System

209002series

Automatic Multi-Channel System for the Determination of Systolic Blood Pressure and Heart Frequency

Contents

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1. General information

Measuring blood pressure non-invasively in **laboratory animals** (mice, rats, dogs etc.) has now become easy using the fully computerized microprocessor-based **TSE Non-Invasive Blood Pressure Monitoring System, 209002series**.

Measurement is performed ***non-invasively*** on the tail of the conscious, unanesthetized animal with the aid of a pressure cuff ("Tail-Cuff Method“) and an animal-specific pulse transducer.

The system accurately and reliably determines heart rate and systolic arterial blood pressure in up to 72 measuring channels simultaneously facilitating rapid screening of large animal populations.

6-channel system for mice with measuring platform

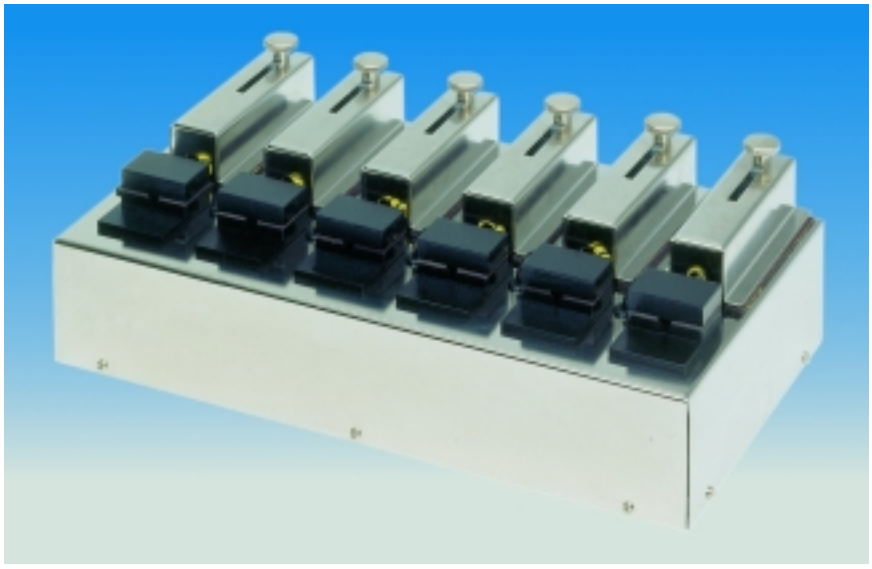
1.1. The rodent system

The rodent system (mice & rats) is based on an **opto-electronic** detection mechanism. The newly-designed opto-electronic transducer is the heart of the system, which is designed for use with IBM-AT compatible computers (486 or higher). Its components are:

- the measuring setup in **advanced** or **basic** configuration,
- pressure cuffs with pressure tubing,
- a control unit with built-in amplifier and pressure generator; in the advanced setup with integrated temperature control,
- a special BP-interface **or** BP-PCMCIA card for use with a space-saving laptop as well as
- the BP software for Windows.

1.1.1. Advanced system setup

During measurement the animals are fixed in restraining units and mounted onto a special **measuring platform** with **integrated heating**.



6-channel platform for mice

The tail is placed in a tail groove restricting motoric activity (tail movements) that could disturb the correct identification of the SAP values. The special construction also ensures easy placement of the pressure cuff and the opto-sensor combination.

Heating is performed by warming up the platform base via a heating element and an electronic temperature control that is part of the control unit. In most cases a short warming up time is sufficient (5...10 minutes).

This measuring platform is available with 1 up to 72 measuring places. Several smaller platforms can also be combined to form a modular multi-station setup.

1.1.2. Basic system setup

The opto-electronic rodent system is also available ***without measuring platform***. In this case the pulse sensor combination is mounted into a ring-shaped cuff. The animals are placed into stand-alone restrainers (different sizes available) and usually placed into a warming box for measurement.

In the **TSE Heating Box** with built-in electronic temperature control and continuous fresh air supply up to 6 animals can be warmed up simultaneously.

1.1.3. Measuring principle

An **optical pulse sensor** is used for pulse signal recognition. A highly sensitive infrared LED combination (emitter/receiver) measures the light transmission through the tail.

Advanced sensor configuration

The alterations in the diameters of the arteries caused by variations in blood pressure result in an altered light transmittance, which is recognized by the sensor and converted into an electrical signal. After electronic amplification and filtering to eliminate interference this signal is available for display and evaluation (**pulse curve**).

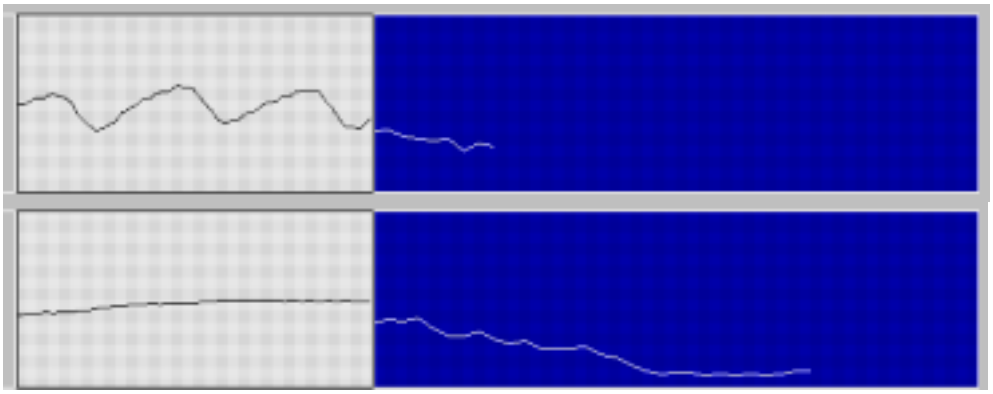
The heart rate (Bpm) is obtained by continuous calculation from the pulse signal.

Occluding pressure on the tail is provided by a pressure pump built into the control unit. The air coming from the pump is led through thin flexible plastic tubing into an inflatable **pressure cuff** placed around the animal's tail. This cuff consists of a short plastic tube with

variable inner diameter to which a rubber membrane is connected forming a closed system indifferent to changes in atmospheric pressure.

Pressure cuff

Due to the continuous pressure rise in the cuff the blood flow in the tail artery is gradually occluded. When the artery is closed the pulse wave can no longer be picked-up by the sensor: the corresponding pressure value is recorded as systolic pressure SAP1. If desired the system subsequently also monitors the returning of the pulse wave with the onset of pressure release (cuff deflation). The pressure in the cuff at the moment of the first reappearance of the pulsation is recorded as systolic pressure SAP2. Both cuff inflation and deflation run at a user-defined speed.



Pulse curve **Amplitude curve**

During the measurement the waveform of the **maximum pulse signal amplitude** is displayed on the computer screen. The tail cuff pressure is continuously shown as a bar graph.

The measuring values can be printed out and stored in an export file for further statistical evaluation.

1.1.4. Notes

- At normal room temperature the blood flow in the tail is normally reduced so that pulsations cannot be measured reliably. In order to achieve satisfactory results rats and mice usually have to be **warmed up** prior to recording. This will provoke a temperature-induced dilation of the caudal arteries since these vessels serve as the principal outlet for body temperature control. The increased blood flow results in a reliable and strong pulse wave. Please note that some mouse strains show good curves at room temperature!

- In order to obtain reliable and reproducible results it is important that the animals are **trained** to adapt them to the experimental conditions (handling, heating and restraint) and to the tail cuff procedure (cuff pressure increasing and decreasing).

- **Stress** has to be avoided at all costs since stress is known to influence the SAP measurements negatively. Stress usually provokes a strong cardioacceleratory response; on top of that vasoconstriction invariably occurs leading to a delayed reappearance of a pulse signal with a smaller amplitude. Therefore care must be taken to avoid any unusual background noise, uncomfortable handling or any deviation from normal routine.

1.2. The measuring system for larger animals

The system can also be configured for **larger animals** such as dogs. In this case ring-shaped **piezo-electric** transducers are generally used to record the pulse signal. No heating is required in these animals. The sensor is attached to the tail of the animal distal from the pressure cuff. This highly sensitive transducer transforms the pressure waves in the tail artery into an electrical signal.

Apart from the different sensor technology the measurement corresponds to the rodent system as described in chapter 1.1.3.

1.3. Sizes of pressure cuffs and sensor rings

The pressure cuffs and sensor rings* are available with the following standard diameters:

Pressure Cuff (mm)	Sensor Ring (mm)
6,5	3 ... 20 in steps of 1mm
9,5	
13	
25	

** only in the basic rodent system and the system for larger animals*

Other sizes can be manufactured on request.

The sizes of the pressure cuff and sensor have to be chosen depending on the tail diameter of the animal examined. The diameter of the cuff should be larger than that of the selected sensor.

2. Setting the system up

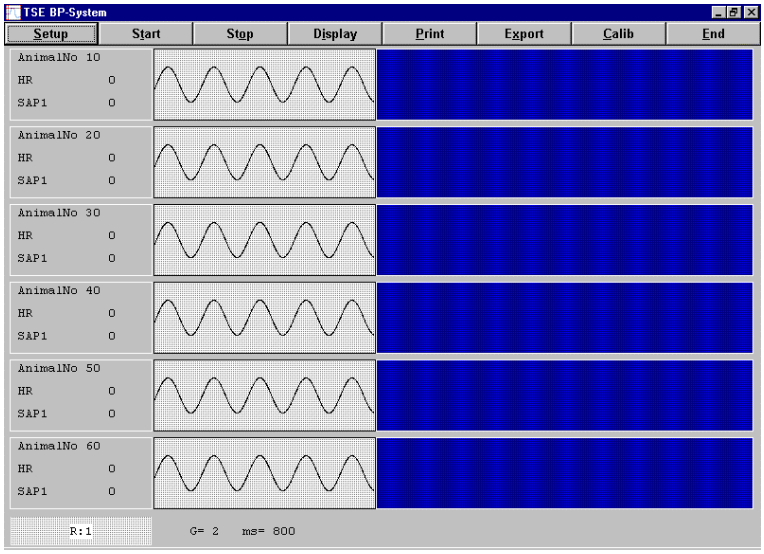
- The control interface is built into the computer or the PCMCIA card connected to the laptop.
- The control unit is connected to the interface. If several control units are included an adapter box is provided.
- The measuring platform is placed on top of the control unit and temperature control connection is made.
- The pressure tubings from the cuffs are connected to the pressure generator (in the platform configuration via a common connector tubing).
- In addition electric connection of the pulse sensors is performed.

3. Performing measurements

3.1. Program start

In this description the 6-channel software is described as an example. The software is identical for all automatic system configurations.

After starting the program you see the main menu:



Display mode shown with artificially generated signal

The **switches** at the upper screen margin are used to activate the individual program functions.

The **numerical display window** on the left is reserved for output of the animal number, the heart rate, the pressure value(s) as well as the mean pressure value. The exact configuration varies according to the measuring mode.

A large display window shows 2 waveforms:

- In the **left-hand** window the pulse signal which the sensor recognizes appears. Before the measurement this display can be used to check the quality of the signal and to adjust the amplification optimally.
- In the **right-hand** window the maximum amplitude of the pulse signal is shown while the measurement is being carried out. In the display mode before the start of the measurement this window is empty.

In the **status line** the following information is displayed:

- phase information (such as “Dummy”, “E-Delay” etc.),
- the running number of the measurement series in the file (**R**),
- the running number of the trial (**N**),
- the amplification factor **G** and
- the width of the pulse window in **milliseconds**.

3.2. Entering all parameters in the software setup

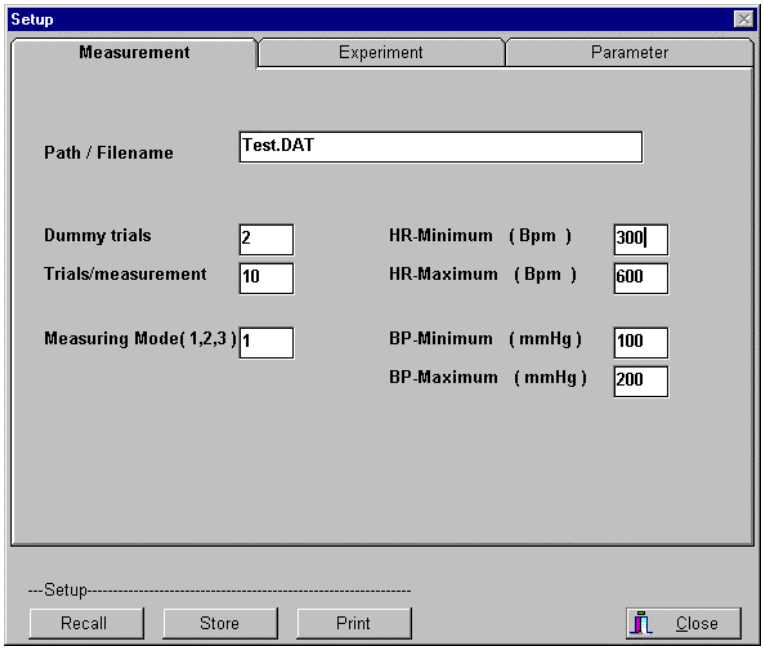
Before the start of a measurement a series of settings must be made in the **Setup**. Different setup configurations can be stored as files so that they can be recalled for subsequent tests.

3.2.1. Setup/Measurement

A measurements consists of 1...20 single trials which are carried out automatically one after the other (**trials/measurement**). The trials are carried out either directly after each other or after an operator-defined pause has elapsed.

The number of trials which have to be carried out in order to obtain a meaningful mean value for the blood pressure should be determined by making test measurements.

The measuring data of these trials are stored in a results file that is given a name by the user (**Path/File name**).



For training the animals or during the warming-up phase before the measurement itself is started so-called **dummy trials** *can* be carried out whose data are **not** stored in the results file.

3 different **measuring modes** are available:

Mode **1**	SAP determination while pressure in the cuff is rising (**standard method**)
Mode **2**	SAP determination while pressure in the cuff is decreasing
Mode **3**	SAP determination during rising **and** decreasing pressure

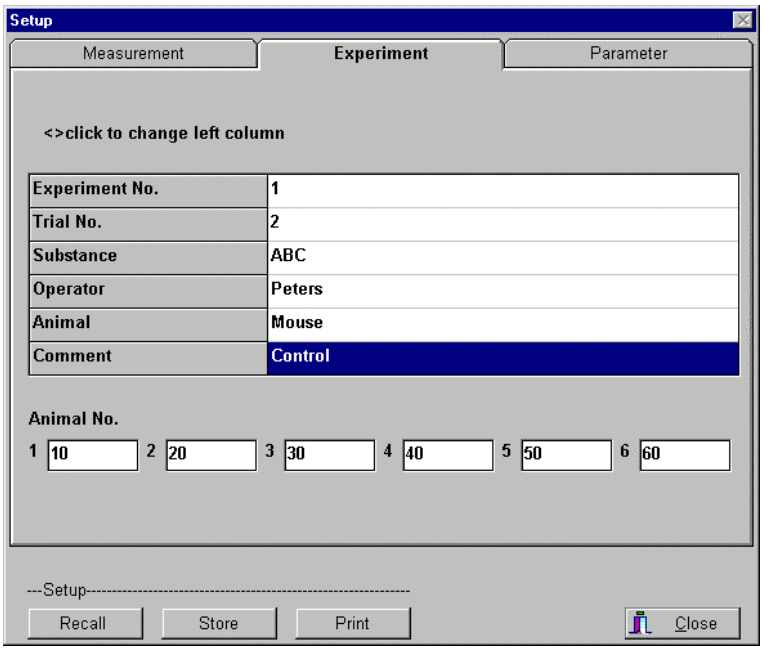
The limits for the detection of the heart rate are entered in the fields **HR-Minimum/Maximum (Bpm)**. The values should be set *as close as possible* to the expected heart frequency of the animal. In this way the determination of the heart rate and therefore the measurement of the blood pressure is accelerated.

BP-Minimum is the pressure level in the cuff at which monitoring the pulse signal amplitude starts during the measurement in modes 1 and 3 and at which the decreasing pressure curve ends in modes 2 and 3. At the start of a trial in modes 1 and 3 the cuff is inflated **rapidly** from zero to **BP-Minimum**. Pressure increase beyond the **BP-Minimum** is carried out with the operator-defined steps (*pressure steps*).

BP-Maximum is the upper cuff pressure limit during measurements in modes 1 and 3. In mode 2 the starting pressure at which the step-by-step pressure reduction starts is determined by BP-Maximum. The value must be slightly higher than the expected systolic pressure.

3.2.2. Setup/Experiment

- Several entry fields are available for identifying the measurement. The name of the entry fields can be edited by the operator.
- The **animal identification entry** is shown in the numerical display window during the measurement.



3.2.3. Setup/Parameter

The measuring procedure is defined by a variety of control parameters.

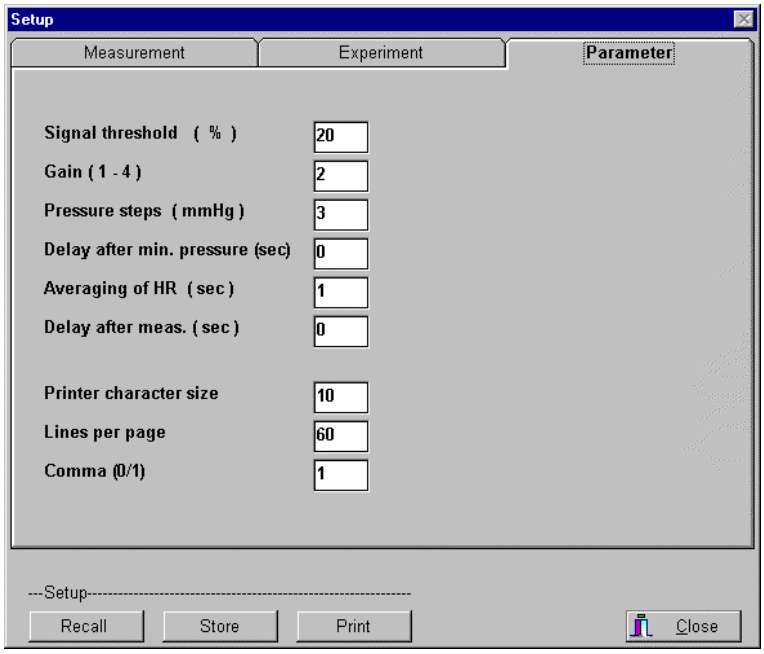
Signal threshold (%)

Range: **5...50%**. The signal threshold determines the percentage level which the amplitude of the pulse signal must have during pressure alteration compared with the initial pulse signal before the measurement (=100%) so that the conditions

- "no more signal“ (for pressure increase) or
- "signal present again“ (for pressure decrease)

can be detected and therefore the SAP value can be determined. The ideal value must be determined in test measurements and depends on the signal quality.

Note: The larger the % value set for the signal threshold, the lower the pressure value which will be determined for the SAP value, as a lower cuff pressure is needed to achieve the required pulse signal amplitude! Once a setting has been made it should not be altered during a series of measurements as otherwise the results will no longer be comparable with each other.



Gain

The amplifying factor for the pulse transducer sets the required amplitude of the pulse signal.

Pressure steps (mmHg)

Range: 1...5 mmHg. Pressure alteration values, i.e. the smallest step by which the pressure is increased or decreased during the measurements. A small value slows down the measurement but increases the accuracy.

The measuring process consists of a sequence of **phases** whose lengths are determined by the operator.

Delay after min. pressure (sec)

Range: 0...10 seconds. Pause between reaching the starting pressure and the start of the step-by-step pressure alteration.

Mode 1/3 If the minimum pressure (BP-Minimum) has been reached than a pause of the defined length will be allowed to elapse before the step-by-step increase in pressure is started (measurement).

Mode 2 If the maximum pressure (BP-Maximum) has been reached than a pause of the defined length will be allowed to elapse before the step-by-step decrease in pressure is started (measurement).

Averaging of HR (sec)

Range: 1...120 seconds. Time for averaging the heart rate before the start of the measurement. The program measures the intervals between the individual signals in the

pulse window and calculates the mean interval for the set time (**BPM** phase). This value is converted to **Bpm** (beats per minute) and shown in the display window.

Delay after measuring (sec)

Range: 0...10 seconds. When a trial has been completed the pressure in the cuff is released completely and a pause of the selected time is then allowed to elapse; after this pause the next heart rate determination is carried out. The pause (**E-DELAY**) is used for the ***regeneration*** of the pulse signal after occlusion. The necessary length must be determined in preliminary tests. At the end of the pause the pulse signal in the left-hand window should again show the full amplitude.

The remaining parameters influence the output of the protocol on the connected printer and the decimal separator in the export file.

3.3. Preparation

3.3.1. Preheating

- Preheat the measuring platform or the warming box if included in the system. The temperature control allows to enter a minimum and a maximum temperature. With mice a temperature range of **33 - 37°C** is recommended. The temperature is displayed with 0.1°C accuracy.

3.3.2. Preparing the animals

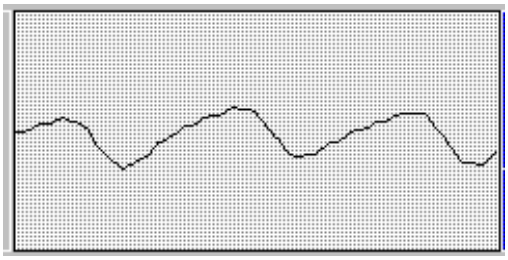
- Rodents: Place the animals in the restrainers and place the restrainers on the preheated measuring platform or in the warming box.
- Pass the tails through the pressure cuffs (to be placed at the base of the tail). Slide the pressure cuff up the tail until it is fixed gently in position. Do not clamp it firmly!!
- On the measuring platform place the tails into the tail groove and fix the end of the tail with adhesive tape. Place the upper sensor unit on top of the lower one (magnetic adhesion).
- In the ring-shaped configuration slide the sensor cuff on the tail.

3.4. Measurement

The following procedure describes a measurement in **measuring mode 1** (i.e. pressure determination only as pressure increases).

3.4.1. Before starting the measurement (display mode)

- Start the program and switch on control unit.
- Enter all parameters in the ***Setup***.
- Before the start of the measurement the **pulse signal** recorded by the pulse sensor is shown in the left window. The quality of the curve should now be checked. A clear pulse curve with no interference should be recognizable. Interference could be caused, for example, by movement of the animal



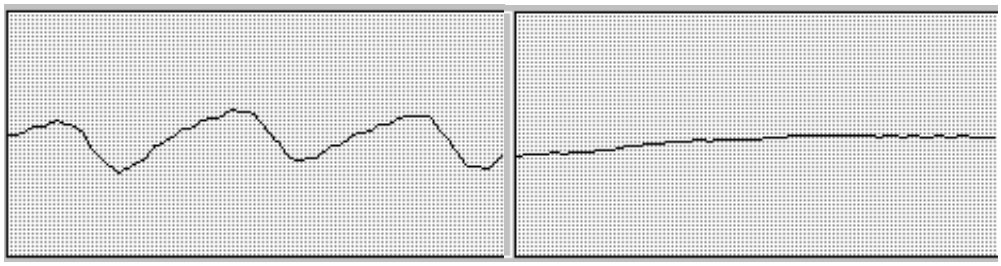
- It may be necessary to correct the **amplification factor**. The pulse curve should occupy approx. 50% of the window height.
- The **heart rate** is now calculated continuously from the pulse signal and shown in the numerical display window.

3.4.2. Carrying out a series of measurements

- If the quality of the pulse signal is adequate and if the heart rate is sufficiently stable then the **measuring mode** is started.
- A display axis for the cuff pressure now appears. The scale starts with the BP-Minimum and ends with the BP-Maximum.
- The cuff pressure now increases **rapidly** to **BP-Minimum**.
- If "Delay after min. pressure“ has been defined then when the minimum pressure has been achieved a pause of the defined length will be allowed to elapse (**DELAY** phase).
- The pressure cuff will now be inflated step-by-step with the step entered under *pressure step in mmHg*. This is the **DUMMY** or **MEASURE** phase.
- In the *left-hand* small screen window the recorded pulse signal continues to be displayed.
- In the right-hand window the maximum amplitude of this pulse signal is shown as a curve.
- During the measuring process a check is made each time the pressure is increased as to whether the pulse signal is still existent (amplitude > signal threshold).
- From a certain pressure onwards it can be seen in the left-hand window that the pulse signal – as a result of the increasing occlusion of the artery – is smaller. The reduced amplitude is shown on the right as a decreasing curve.

- When the pulse signal amplitude falls below the signal threshold the corresponding pressure value is identified as **SAP1** and output in the left-hand display field.

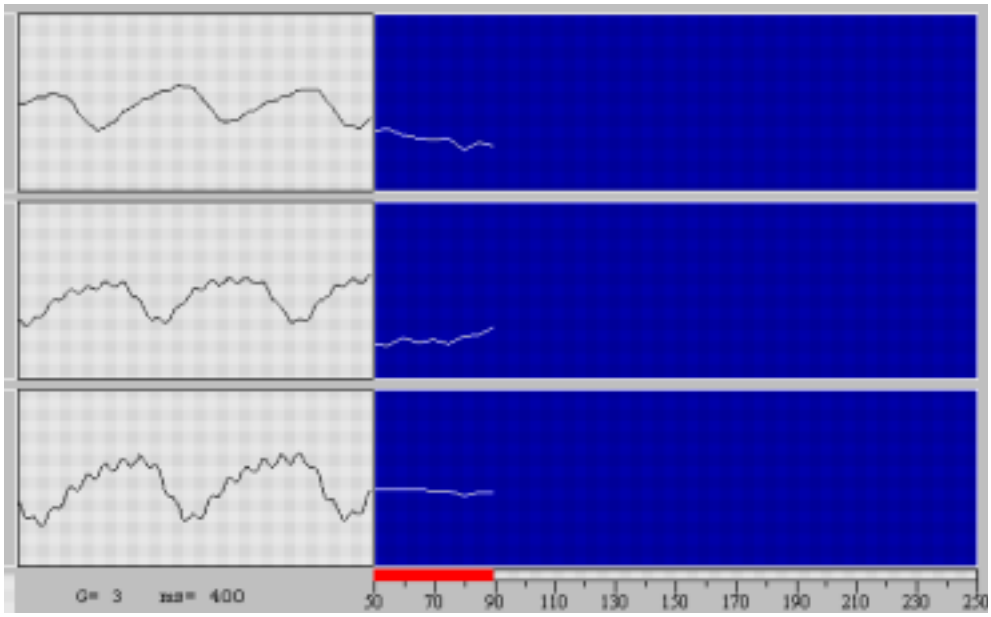
The amplitude level above which "No signal“ is recognized depends selection of the ***Signal threshold*** parameter. If *no* SAP can be determined it may necessary to change this parameter.



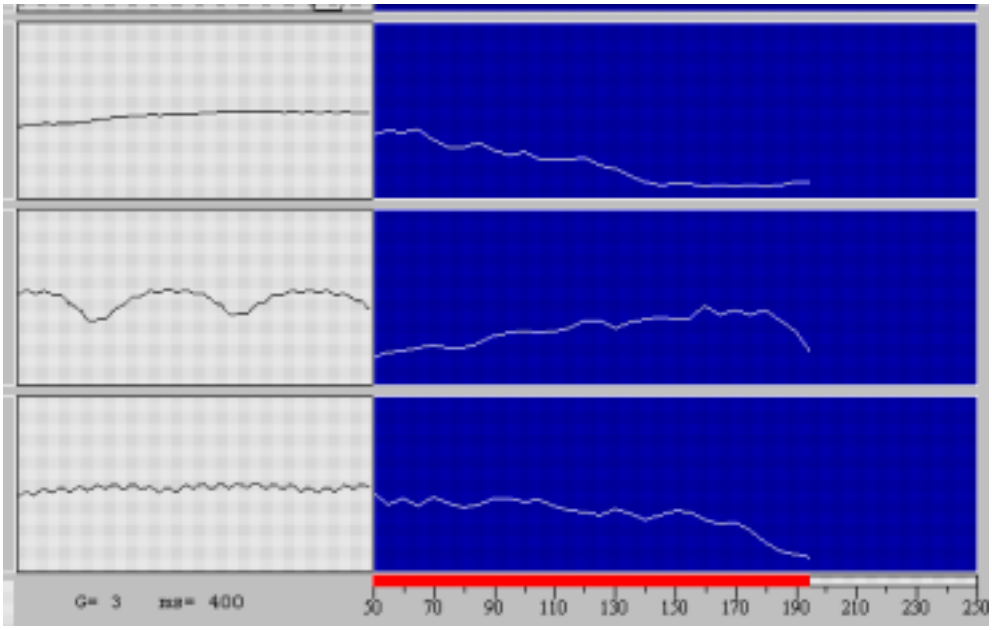
Before occlusion **After occlusion**

- The pressure is increased until **BP-Maximum** is reached.
- Pressure is then completely released from the cuff.
- If only 1 trial was to be carried out the measurement is now finished. With more than 1 trial or with previous dummy trials the system is then in a measuring pause, the **E-DELAY** – if one has been defined. The next heart rate determination is then carried out (**BPM** phase). Then the next blood pressure measurement is carried out, maybe with a previous DELAY phase. Measurements within the series are numbered consecutively (**N**).

Example of a measurement in rats (3-channel-system)



After the start of the pressure increase (MEASURE phase)
The pulse signal appears in the left window. The cuff starts to inflate.



The pressure in channel 1 and 3 has already reached a level where the pulse signal cannot be recognized any longer. In channel 2 there is still a pulse signal.

3.5. Table of measurements

When the measurement is finished a **table of measurements** appears:

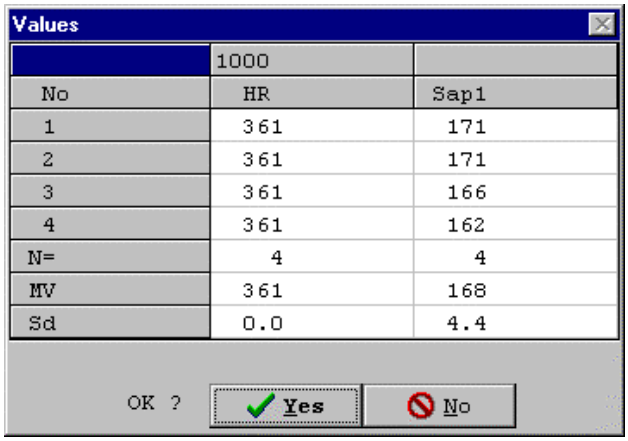


Table for Mode 1

Depending on the mode, SAP1 (Mode 1, 2) or SAP1+SAP2 (Mode 3) are listed as well as the heart rate. For a number of single measurements N>1 the table additionally contains the mean value (MV) and the standard deviation (Sd). After confirming with YES the values are stored in the raw data file.

4. Displaying the measuring values

Using the menu point **Display** the content of a stored file can be shown as a list.

```
0002    09:24          12.02.1999
         1000
           HR   Sap1
    1     361    171
    2     361    171
    3     361    166
    4     361    162
   N=       4      4
   MV     361    168
   Sd     0.0    4.4
```

The list is made up of the following information:

- Running number of the series of measurements in the file
- Starting time of series of measurements
- Starting date
- Animal number
- For each trial (running number) heart rate (HR) and the measured pressure value(s) SAP1 or SAP1/SAP2
- If the number of trials is >1 then the number (N), mean value (MV) and standard deviation (Sd) will be shown.

5. Printing a protocol

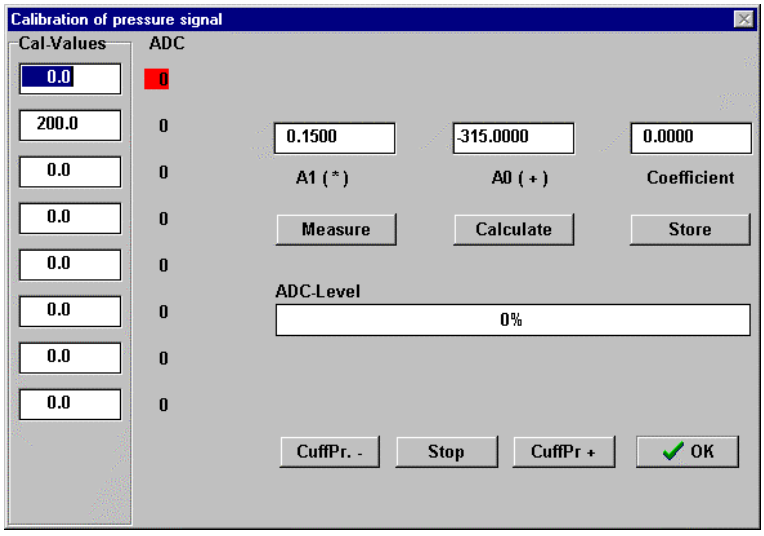
The list shown with the **Display** switch can also be printed out on a printer. Depending on the type of printer the optimal settings for the printout must be made under ***Setup/Parameter***.

6. Exporting the data

A measuring data file can be stored in an export file. The export file can be generated with the file extension **CSV** or **TXT**. This file can be imported into EXCEL directly for further statistical calculations. The decimal separator in this table can be selected by the operator in the menu ***Setup/Parameter*** (comma or point).

7. Calibration

The system is calibrated ex works. In case a recalibration is required, you need an external device (e.g. a mercury manometer) for measuring a defined static pressure, which is produced using the pressure generator built into the control unit. This instrument is connected to the tubing connection of the control unit. Calibration is done via linear regression. The calibration values are stored on the hard disk.



TSE BP-System

Experiment No.:	1
Trial No.:	2
Animal:	Mouse
Operator	B.

		05.03.99				
	1	15:39	b17		b18	
			HR	**Sap1**	**HR**	**Sap1**
		1	479	134	595	112
		2	533	127	572	104
		3	488	135	662	104
		4	501	127	554	104
		5	502	129	610	110
		6	447	128	576	107
		7	475	127	541	107
		8	612	134	569	110
		9	0	134	575	104
		10	429	135	518	104
		N	9	10	10	10
		Mv	496	131	577	107
		Sd	53.1	3.7	39.5	3.1
	2	15:44	b17		b18	
			HR	**Sap1**	**HR**	**Sap1**
		1	506	144	585	107
		2	441	145	588	110
		3	487	143	571	109
		4	468	141	616	100
		5	451	138	600	94
		6	483	136	619	107
		7	460	141	589	114
		8	505	139	590	107
		9	546	142	585	107
		10	512	138	647	104
		N	10	10	10	10
		Mv	486	141	599	106
		Sd	32.1	2.9	22.3	5.5
	3	15:50	b17		b18	
			HR	**Sap1**	**HR**	**Sap1**
		1	535	142	648	91
		2	534	139	658	120
		3	577	131	607	110
		4	523	136	620	110
		5	540	135	623	114
		6	520	126	566	0
		7	542	127	628	112
		8	567	127	645	107
		9	521	132	646	107
		10	529	132	616	107
		N	10	10	10	9
		Mw	539	133	626	109
		Sd	19.2	5.3	26.6	7.8

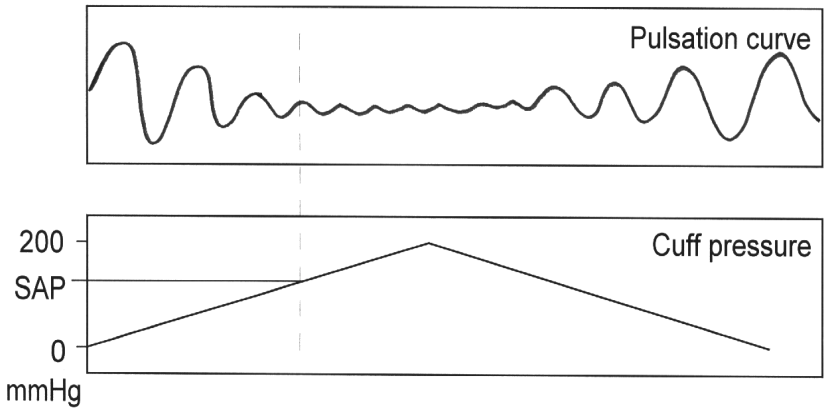
Appendix 1

The semi-automatic non-invasive system configuration

209001series

Semi-automatic 1-place system for rats

The **semi-automatic** low-cost system is ideal whenever smaller numbers of animals are to be measured. Pressure in the tail cuff is increased and decreased stepwise by the user. The control unit is ready for connection to a chart recorder in order to display the pulsation curve picked up by the sensor. The systolic blood pressure values can then be read off from the calibrated pressure waveform.



The semi-automatic system is available for all animal species (opto-electronic for small animals, piezo-electric for larger animals). When heating of the animals is required an optional heating box can be provided.