Product Presentation

SONOTRACK

Content

- ❑ Company overview

- ❑ SONOTRACK

- ❑ SmartChamber

Company Overview


❑ Metris was established in 1994 and has a market presence of 23 years & customers in more than 50 countries across Europe, America and Asia

❑ Metris develops, sells and supports innovative products and solutions to assess laboratory animal behavior & animal vocalizations.

❑ Metris differentiates itself by finding new solutions that are increasing efficiency, throughput and are completely non-invasive (animal friendly)

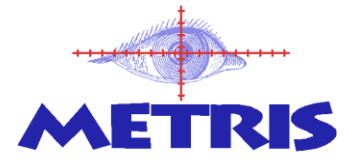❑ Our customers include Corporates, Academic Institutions, CRO's and Government Agencies
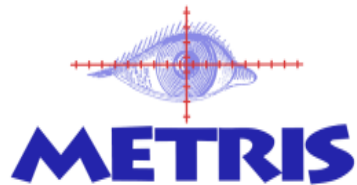
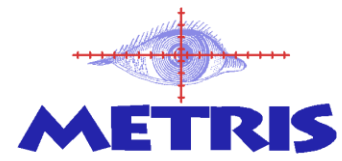# Company Overview

- ● Offices
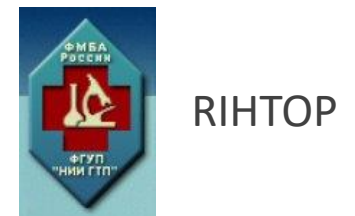- ● Exclusive Distibutors
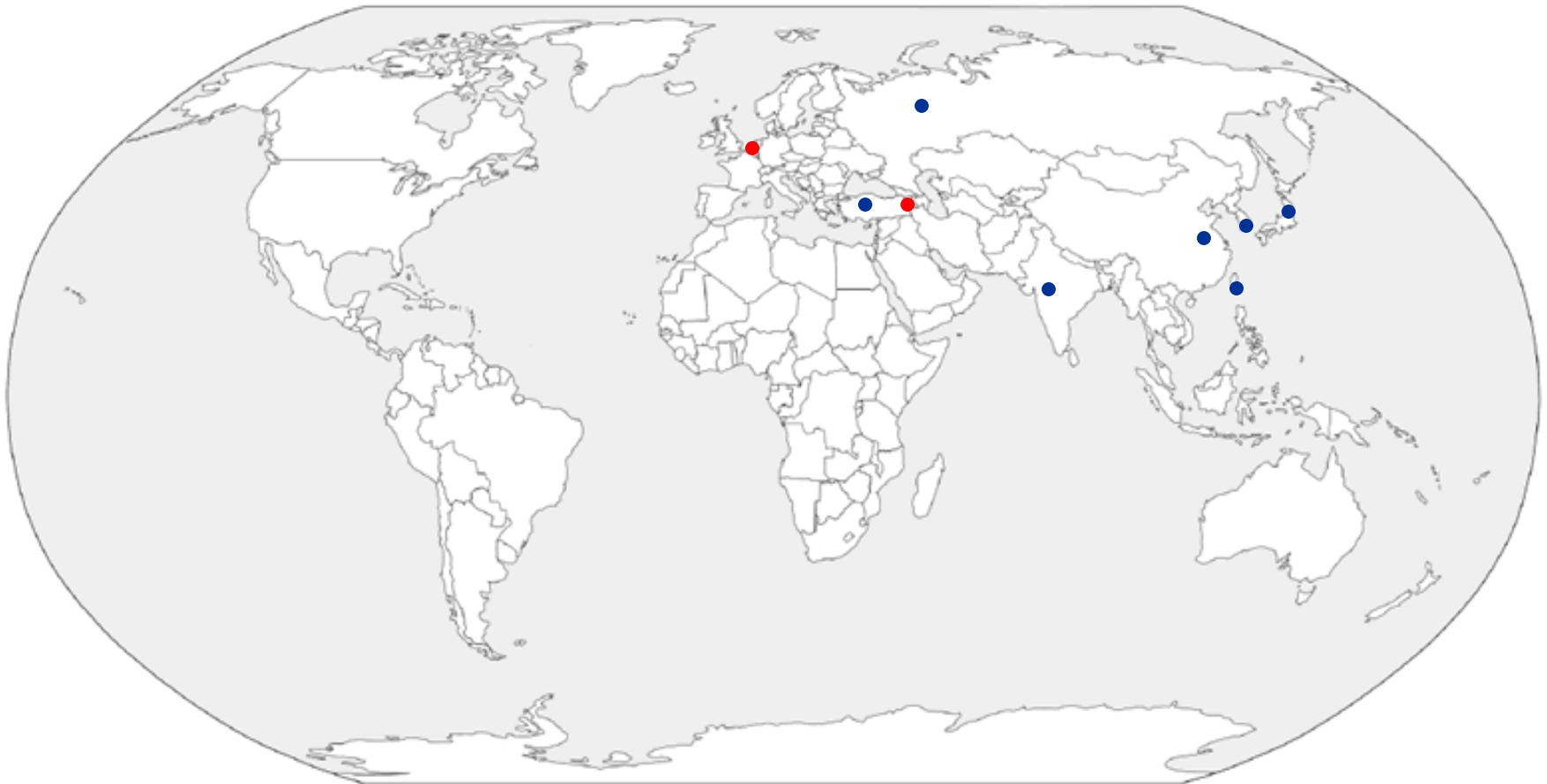
Our Strategic Partners

Exclusive Distribution in
CIS countries (e.g. Russia)
for:

Our Strategic Partners

Scientific Partners
(global alliances)

METRIS

National Institutes of Health
Turning Discovery Into Health

TNO innovation for life

Porsolt & Partners Pharmacology

trans pharmation

RIHTOP
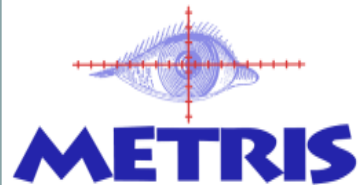
Product portfolio

- LABORAS (behavior analysis)

- SONOTRACK (vocalization analysis)

- SLEEPSIGN (sleep analysis)

- SMARTCHAMBER (controlled environment)

SONOTRACK

Contents

- ❑ Meaning of Ultrasound Vocalizations (USV)

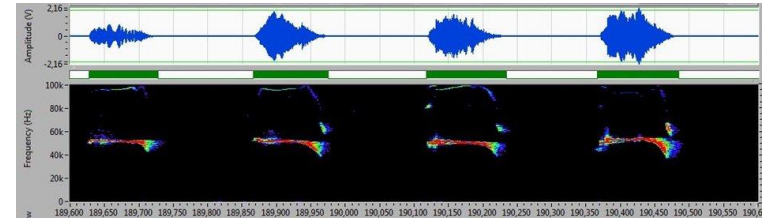- ❑ History of USV measurements

- ❑ Applications and trends

- ❑ Sonotrack functionality

- ❑ Sonotrack configurations

- ❑ Planned Developments

Meaning of Ultrasound Vocalizations (USV)

❑ Ultrasonic Vocalizations are sounds that are created by a number of species that are beyond the hearing range of humans (typically 15 kHz and higher)

❑ Animals creating ultrasonic vocalizations are amongst others:

- Rodents (15kHz - 125 kHz)
- Bats (30kHz – 75 kHz)
- Some Primates (15kHz – 75 kHz)
- Insects (15kHz - 300 kHz)
- Some whales and dolphins

❑ Powerful indicator of animal wellbeing and emotional state

Examples of USV

❑ Mouse

❑ Marmoset

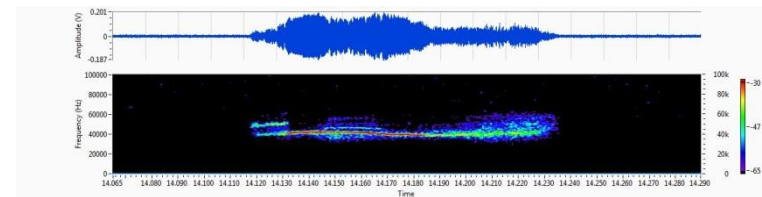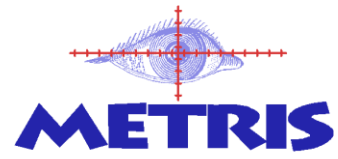

❑ Hamster

❑ Rat

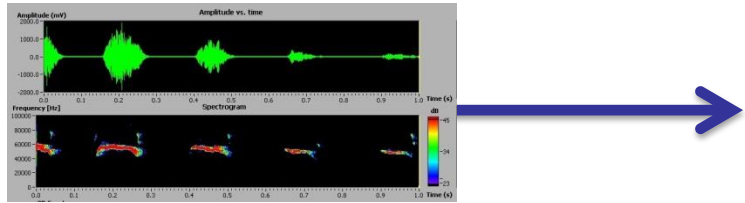# History of USV measurement

Playback of USV
(Metris 2007)

Automatic call counting
(Metris 2004)

Full Spectrum Digital Analysis
(e.g. Avisoft, Metris)

Wide scale use of heterodyne
bat detectors in laboratories
(e.g. Petterson, Noldus)

First rat US vocalizations
measured (1954)

1950   1960   1980   2000   2010

SONOTRACK Applications

❑ SONOTRACK can be used to monitor animal well-being and interaction between animals based on the ultrasonic vocalizations of the animals

❑ Typical research areas:
  – Pain Research
  – Anxiety Research
  – Stress Research
  – Memory Studies
  – Depression Studies
  – Sexual Interaction
  – Social interaction (mother-pup, male-female, etc.)
  – Developmental toxicity
  – Animal Welfare Studies

Modular and Multi-purpose system with

9

different research applications

SONOTRACK Applications

❑ High throughput screening using USV
in drug development, toxicology & safety studies
(could become mandatory)

❑ Improved method to measure emotional parameters such as Anxiety, Fear, Pain, Stress and animal welfare research

❑ Novel disease models using USV for amongst other
- Autism
- Inflammation
- Alzheimer (speaking deficits)

❑ Integrated measurement of USV with behavior and physiology

❑ *Phenotyping studies of Knockout and transgenic mice & rats*

SONOTRACK Applications

number of scientific publications in
ISI Web of Knowledge (May 2012)

SONOTRACK functionality

USV Recording, Playback and Analysis

- 1, 2 or 4 channel Full Spectrum USV recording
- Advanced Manual and Automatic analysis
- 1 or 2 channel USV playback *(optional)*
- Synchronization with 3rd party system, TTL start pulse or level change *(optional)*
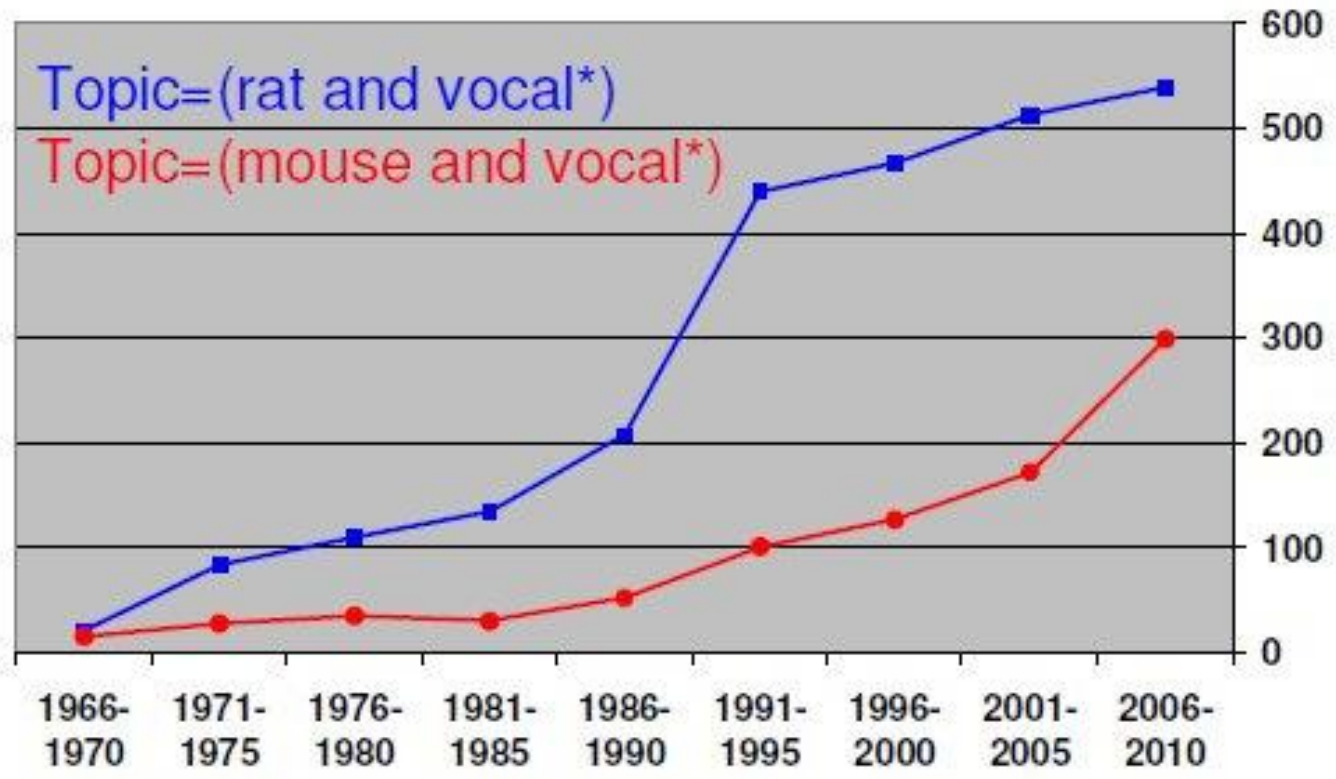
SONOTRACK functionality

- ❏ Full Spectrum recording (15kHz -125 kHz)

- ❏ Recording on 4 independent ultrasound channels simultaneously

- ❏ Long term experiments (24 hours or more)

- ❏ Automatic call counting Ultrasonic Vocalizations in user definable frequency bands

- ❏ SONOTRACK can easily be adjusted to experimental environment and is very easy to use

- ❏ SONOTRACK offers new approaches for animal characterization

Manual Analysis Features
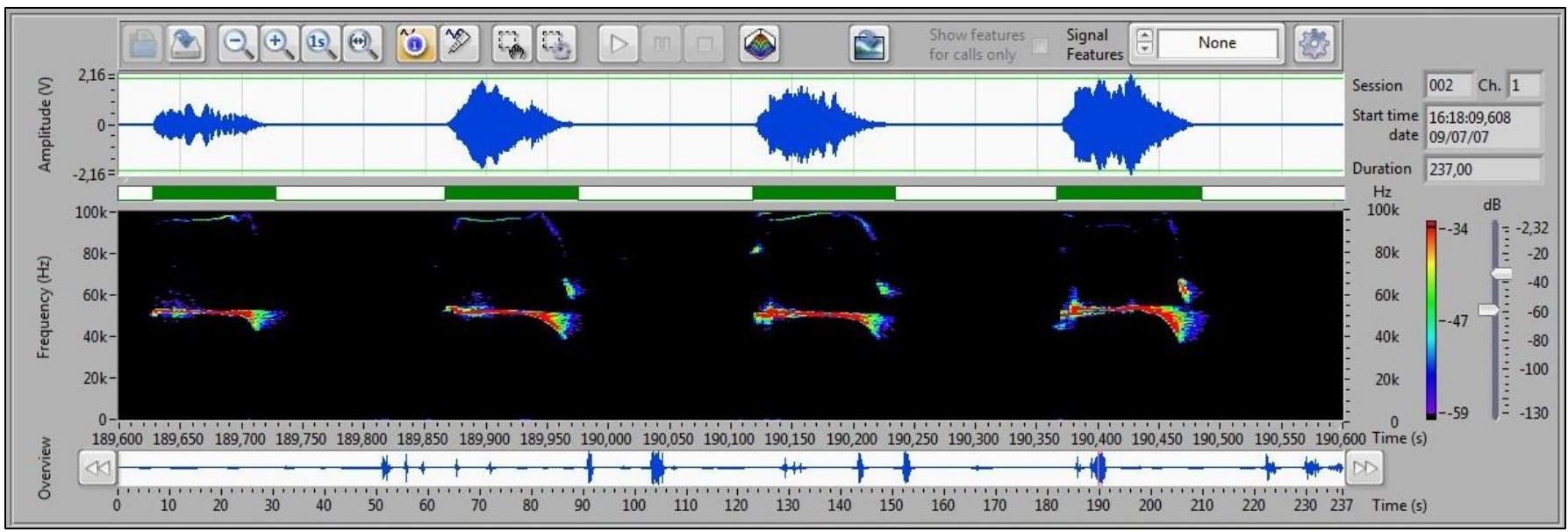
- ❏ Overview of complete recording and selection from overview
- ❏ Quick zooming and de-zooming in Spectrogram
- ❏ Automatic detection display (green bars)
- ❏ Graphical display of Power, Entropy, THD, SINAD, etc.

Manual Analysis Features
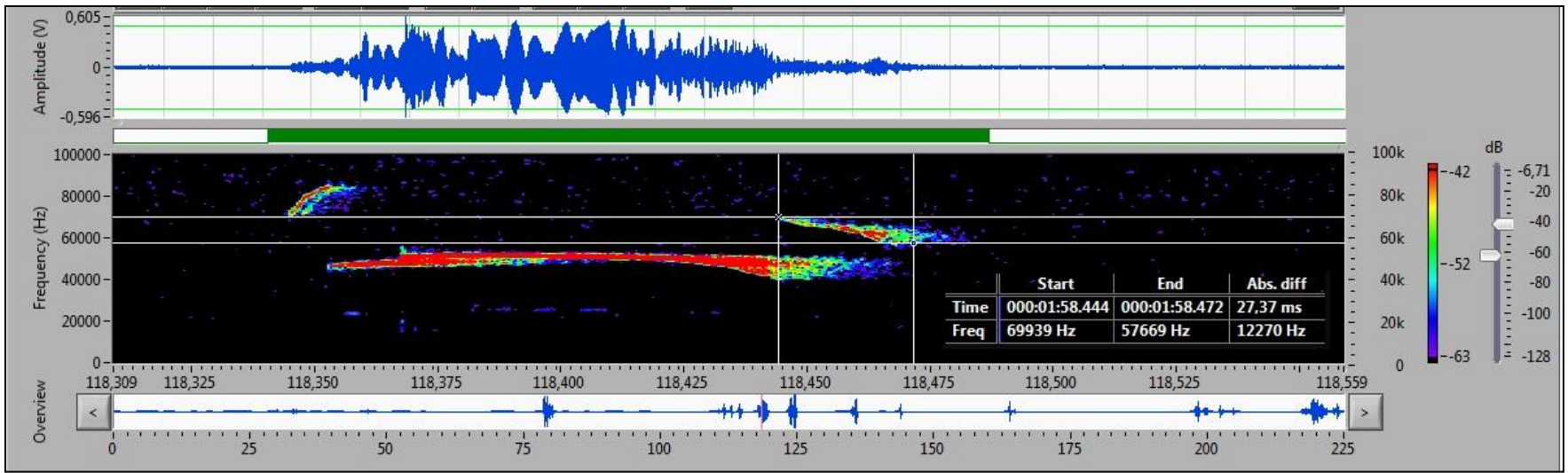
- ❑ Select and save:
  - – Points of Interests (POI's)
  - – Selections
  - – Measurements
- ❑ Export of images (.jpg, bmp, gif) for publications / presentations
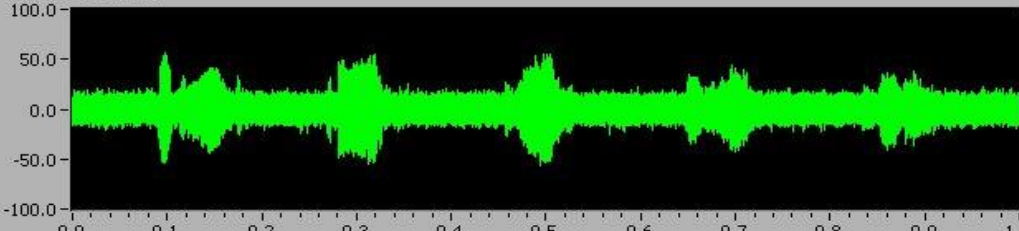- ❑ Export of audio (wav. Files) for presentations

Automatic Analysis Features

Automatic Callcounter (set to detect individual parts of calls)
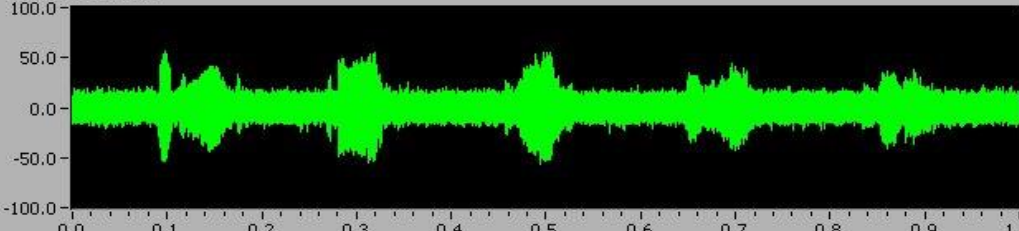
Automatic Analysis Features

Automatic Callcounter (set to detect parts of calls single calls)

SONOTRACK Result Summary

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
1	**TEST RESULT SUMMARY**																	
2								TOTAL	BAND 1	BAND 2	BAND 3	AVG	MIN	MAX	AVG	MIN	MAX	
3	WINDOW	T-BEGIN	T-END	SESSION	CHANNEL	ANIMAL ID	TREAT-CODE	CALLS	CALLS	CALLS	CALLS	DURATION	DURATION	DURATION	FREQ	FREQ	FREQ	
4	1	0	60	1	channel_1	pup 1 test 1	0	63	0	30	33	47.75	23	73	65031	52760	84913	
5	2	60	120	1	channel_1	pup 1 test 1	0	11	0	7	4	42.64	27	59	63620	54725	78878	
6	3	120	180	1	channel_1	pup 1 test 1	0	11	0	1	10	51.55	24	85	75622	57075	83958	
7	1	0	60	2	channel_1	pup 2 test 1	0	80	0	69	11	56.39	23	103	57132	50738	82417	
8	2	60	120	2	channel_1	pup 2 test 1	0	78	0	61	17	66.72	23	118	58282	49009	83935	
9	3	120	180	2	channel_1	pup 2 test 1	0	51	0	43	8	66.47	26	116	55734	47066	78727	
10	1	0	60	3	channel_1	pup 3 test 1	0	35	0	34	1	86.66	36	128	54213	48302	78611	
11	2	60	120	3	channel_1	pup 3 test 1	0	4	0	4	0	69.5	50	99	51240	49865	52465	
12	3	120	180	3	channel_1	pup 3 test 1	0	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A	
13	1	0	60	4	channel_1	pup 4 test 1	0	9	0	3	6	46.44	30	63	67884	54077	78000	
14	2	60	120	4	channel_1	pup 4 test 1	0	23	0	19	4	44.65	23	66	60507	55054	84522	
15	3	120	180	4	channel_1	pup 4 test 1	0	20	0	19	1	50.2	23	78	56607	46542	77200	
16	1	0	60	5	channel_1	pup 5 test 1	0	116	0	110	6	54.09	23	88	55296	49552	80473	
17	2	60	120	5	channel_1	pup 5 test 1	0	74	0	70	4	70.05	23	131	53793	45297	69302	
18	3	120	180	5	channel_1	pup 5 test 1	0	31	0	31	0	77.29	33	123	51798	46402	55583	
19	1	0	60	6	channel_1	pup 6 test 1	0	43	0	41	2	75.98	32	120	53280	47179	77029	
20	2	60	120	6	channel_1	pup 6 test 1	0	71	0	63	8	75.21	23	122	55413	49467	84652	
21	3	120	180	6	channel_1	pup 6 test 1	0	91	0	71	20	88.79	29	133	57243	47500	85360	
22	1	0	60	7	channel_1	pup 7 test 1	0	34	0	26	8	54.24	26	77	58269	51462	73946	
23	2	60	120	7	channel_1	pup 7 test 1	0	57	0	46	11	53.95	23	92	58344	51606	81444	
24	3	120	180	7	channel_1	pup 7 test 1	0	14	0	11	3	46.5	25	70	58546	54540	76486	
25	1	0	60	8	channel_1	pup 8 test 1	0	6	0	4	2	38.83	32	47	59927	51250	77383	
26	2	60	120	8	channel_1	pup 8 test 1	0	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A	
27	3	120	180	8	channel_1	pup 8 test 1	0	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A	
28	1	0	60	9	channel_1	pup 1 test 2	0	5	0	4	1	44.8	40	49	60268	54163	79295	
29	2	60	120	9	channel_1	pup 1 test 2	0	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A	
30	3	120	180	9	channel_1	pup 1 test 2	0	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A	
31	1	0	60	10	channel_1	pup 2 test 2	0	3	0	1	2	57	38	81	68078	58062	73421	
32	2	60	120	10	channel_1	pup 2 test 2	0	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A	
33	3	120	180	10	channel_1	pup 2 test 2	0	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A	
34																		
35																		

Ultrasound Playback features

❑ Playback of Ultrasounds to the animal (stimulus signal)
   - selecting and playing back parts or complete recordings
   - defining and playing back artificial frequency patterns

❑ Synchronized simultaneous recording and playback

❑ Playback system can be used for normal sounds too
   - Amplifiers (20 Hz .. 200 kHz)
   - Speakers (1 kHz – 125 kHz)

Synchronization features

❑ Sonotrack offers optional start synchronization with other 3rd party systems

  - Sonotrack can start another system or
  - Sonotrack can be started by another system

❑ Synchronization is done through a so-called TTL signal of which the properties can be adjusted:

  - TTL level change (high to low ⌐_ or low to high _⌐
  - TTL pulse (with adjustable duration) _⌐_

❑ Start synchronization requires:

  - Accurate timing sources of both connected devices
  - Minimum delay between TTL initiation and application start

Synchronization features

❑ Connection between systems through shielded cable:

– Shielded HDMI plug on Sonotrack Control Unit (interface enables other digital signals to be send out in future)

– Other side of cable can be supplied with appropriate connector (depends on 3rd party system)
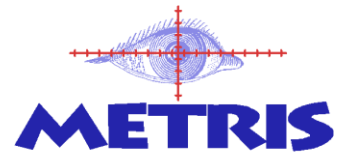
– Cable length 1.5 meter (length can be adjusted on customer request)

Automated Call Classification

❑ Why Automated Call Classification:

– Mice can generate 1000+ Vocalizations in less than 5 minutes

– Manual Call Classification and analysis requires about 2 minutes per call for an experienced analyst. Long duration recordings (several hours or more) are therefore not manageable.

– Automated Call Classification is <u>more consistent</u> and provides <u>more additional parameters</u> of the vocalization

– Only Automated Call Classification will enable use of USV for animal models in pharmaceutical research.
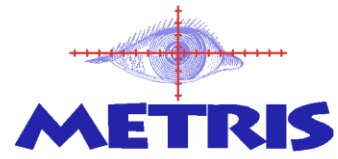
Automated Call Classification

❑ International subsidies on Automated Call Classification have exceeded 5 million in the last 3 years, including:
  - DoD (SBIR)
  - NIH Initiatives
  - EU 7th frame work
  - Local Initiatives (Netherlands, Japan, USA)

❑ Limited to no results, because of:
  ❑ Lack of standardization
  ❑ Lack of combined application and technical knowledge

❑ Metris is the first company offering fully automated call classification *(starting in May 2017)*
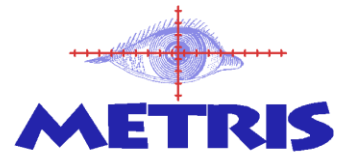
Automated Call Classification
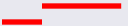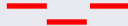
- ❑ Challenges
  - – No fully accepted definition yet for call classes
  - – Different vocalization structures between species and for different strains within the same species
  - – Different vocalizations based on age and gender

- ❑ Metris approach
  - – Use call classes that are quite generic
  - – Give user some possibilities to adjust the boundaries of the parameters that define the call class
  - – Calculate various bio-acoustic parameters of each component in a call
 - – Present all data in easily accessible Excel table

Automated Call Classification

Continouos USV mouse		Discontinuous USV mouse	
Short (very short duration)	—	**Trailing** (flat with short interrupt)	— —
Flat (frequency constant	—	**Step up** (freq. step up)	— —
Up (frequency increase)	/	**Step down** (freq. step down)	— —
Down (frequency decrease)	\	**Step double (split)** (2 frequency steps)	— — —
Chevron (freq. up & down)	∩	**Complex 3** (mix of 3 components)	— — —
Reversed Chevron (freq. down and up)	∪	**Complex 4** (Mix of 4 components)	
		Complex 5 (mix of 5 components)	

Automated Call Classification
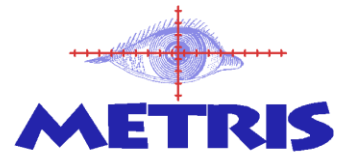
Part 1 : Presentation of raw data
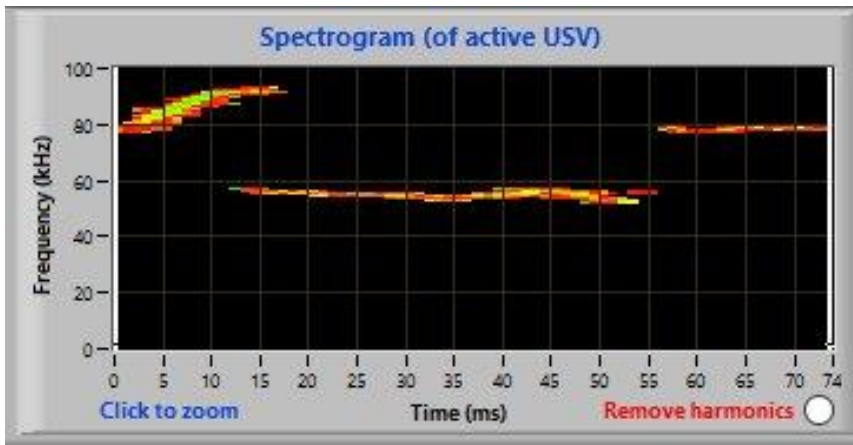*(each graph can be expanded)*
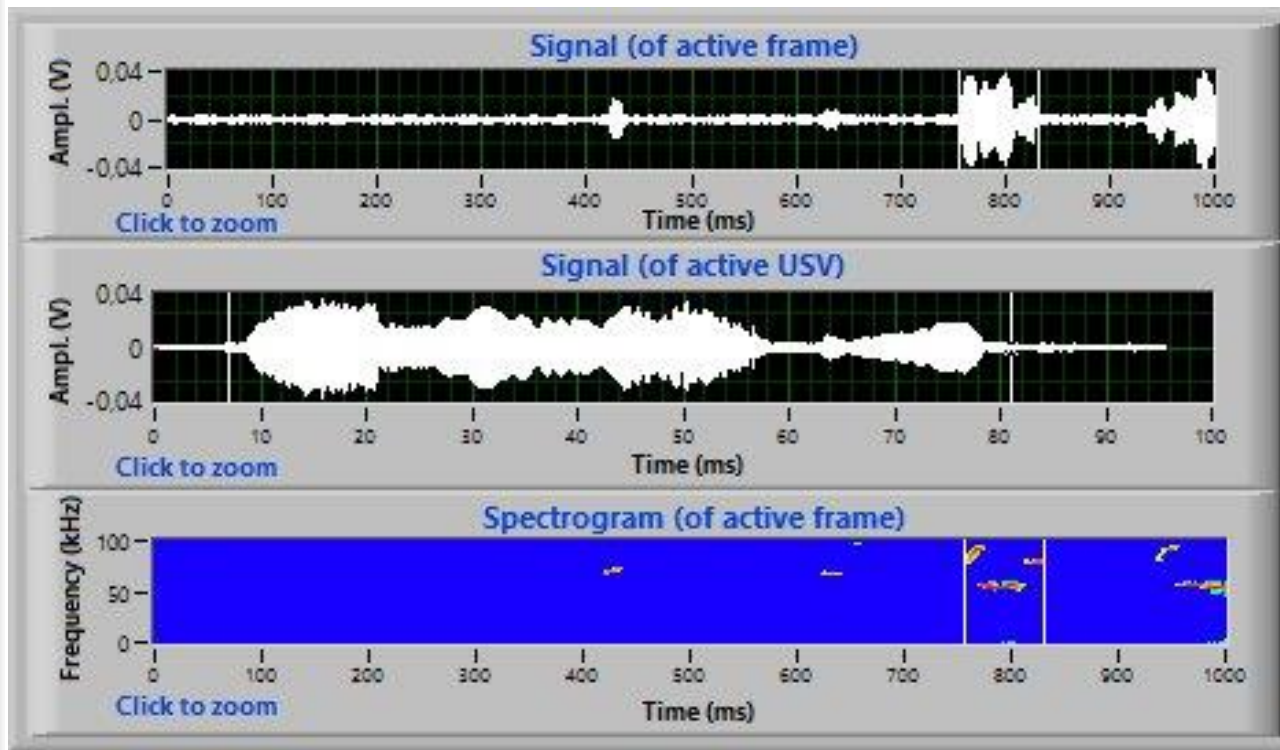
Amplitude vs. time (1-second of data)
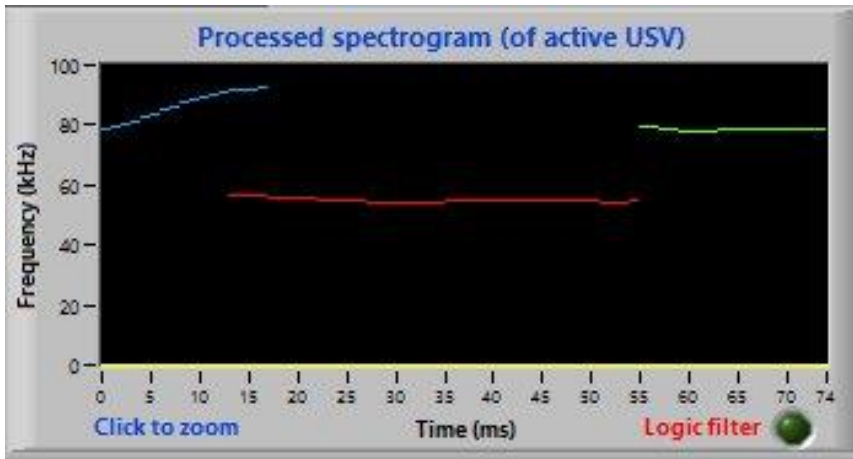
Amplitude vs. time (identified USV)

Spectogram (1-second data)
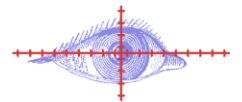
Automated Call Classification

Part 2 : Presentation of identified USV
(each graph can expanded)

Spectogram of identified USV

Simplified Spectogram of USV
(filtered and processed)

Automated Call Classification

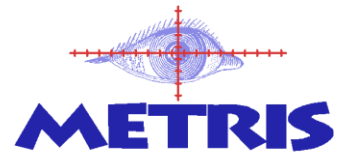## Part 3 : Presentation of USV parameters

Key parameters of the USV

Start time	End time	Duration
2,757 s	2,831 s	0,074 s

Type of USV | Step double

	Frame	ID. of USV
USV detected	1	3

Wave file name

Key parameters of USV

Key parameters per component of the USV

Component	Start time ms	End time ms	Duration ms	Freq. start kHz	Freq. end kHz	Freq.Min kHz	Freq.Max kHz	Freq. Avg kHz	Power Max dB	Power Avg dB
Base-1	0,00	17,00	17,00	78,22	91,89	78,22	91,89	148,29	134,99	-19,96
Base-2	55,00	74,00	19,00	79,49	78,52	77,83	79,49	142,12	137,91	-17,04
Base-3	13,00	55,00	42,00	56,05	54,49	54,30	56,15	157,22	146,97	-7,97

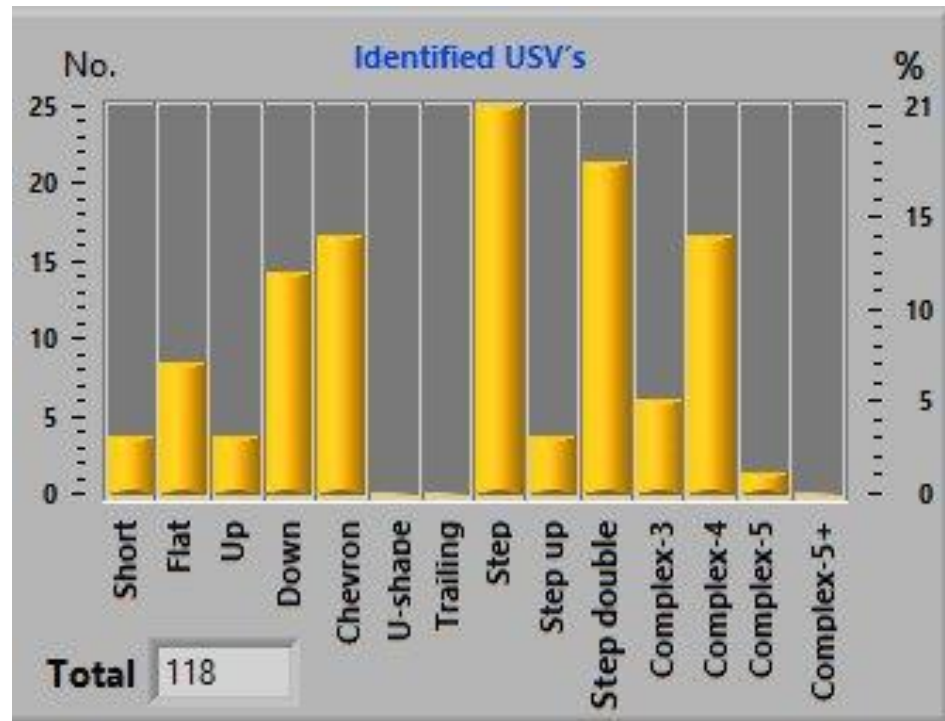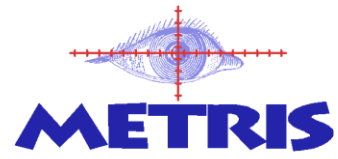**Key parameters of each USV component**

Automated Call Classification

Part 4: Number and percentage of USV per call type

Identified USV's

| Short	Flat	Up	Down	Chevron	U-shape	Trailing	Step down	Step up	Step double	Complex-3	Complex-4	Complex-5	Complex-5+	Total
3	8	3	14	17	0	0	25	4	21	6	16	1	0	118
3	7	3	12	14	0	0	21	3	18	5	14	1	0	100%

Automated Call Classification

❑ Information per USV
- ❑ Start time (relative to start of recording)
- ❑ End time (relative to start of recording)
- ❑ Duration

❑ Per component of the USV
- ❑ Start time (relative to start of USV)
- ❑ End time (relative start of USV)
- ❑ Duration
- ❑ Freq. at Start
- ❑ Freq. at End
- ❑ Freq. Min
- ❑ Freq. Max.
- ❑ Freq, Avg.

- ❑ Power Max.
- ❑ Power Avg.
- ❑ Power at Freq. Max.
- ❑ Power at Freq. Avg.

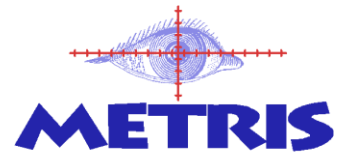# Automated Call Classification
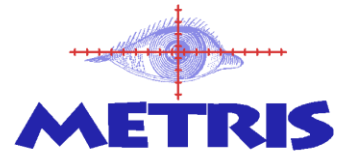
Call Classification Application demo

Sound Attenuation Chambers

❑ Sound Attenuation Chambers strongly improve the quality of the recordings by removing background noise and echo

❑ Metris SmartChamber^{TM} has the following advantages:
- (Ultra) sound isolation
- Elimination of echo's
- Reduction of Magnetic field
- Build in Sonotrack microphone (placed at optimal position)
- Ultralow noise ventilator (mounted outside measurement chamber)
- Integrated Video (displayed on tablet)
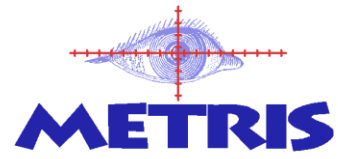- Tablet control of light, ventilator & door

Sound Attenuation Chambers

4 stacked Smartchambers

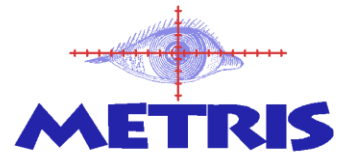# SONOTRACK Configurations

❑ Recording only
   - 1 channel
   - 2 channels
   - 4 channels

❑ Playback module
   - 1 channel playback
   - 2 channels playback
   - 4 channel playback *(in development)*

❑ Data acquisition through
   - USB (integrated in Sonotrack Control Unit)

SONOTRACK Configurations

Options and accessories

❑ Extra license (uses Dongle, for analysis only)

❑ Synchronization with 3rd party systems (using TTL-pulse)

❑ Wave file export (to process and analyze Sonotrack data in other applications

❑ Fully Automated Call Classification application for mice

❑ Sound Attenuation Chambers

SONOTRACK Configurations

❑ Sonotrack Mobile (special field version)

in water & dust tight Explorer case, battery powered

2-channels recording unit

1-channel playback unit

Place for 1 speaker

Place for 2 microphones

External connector panel

Developments

METRIS

Detection of calls of multiple animals in a cage (2017-2019)

Automated Call classification for mice (2015 – 2017)

Call classification mouse / rats (Dbase initiative NIH (2014 -2016)

Improved noise removal in USV data (2013-2015)

Improved call detection (2012-2014)

2012   **2014**   **2016**   **2018**   **2020**

More information

For more information please contact Metris b.v.

Info@metris.nl   ●   www.metris.nl