

# TOWARDS REPRODUCIBLE WHOLE BODY PLETHYSMOGRAPHY OUTCOMES IN MICE

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## BACKGROUND

- » Whole body plethysmography (WBP) is used to non-invasively record breathing patterns in conscious subjects.
- » Chambers are typically transparent, with low side-walls.
- » Two parallel pneumotachs are generally used for flow measurements and ambient noise cancellation.
- » Experiments are usually conducted during day time in mice and rats.
- » Study outcomes are often associated with a large subject-to-subject variability.
- » Mice are prey animals, active at twilight, that naturally tend to avoid open well-lit areas.
- » Exposure to an unnatural environment with no possibility to hide can be a source of stress.



## HYPOTHESIS

- » WBP measurements in mice can be improved through design features related to both mechanical and subject-specific aspects.

## OBJECTIVES

- » To build new WBP chambers for mice based on an innovative design.
- » To evaluate the flow signal measurement robustness to ambient noise.
- » To acquire preliminary experimental data in naive mice considered to have a normal vision.

## METHODS

### EQUIPMENT

- » Pneumotach evaluation set-up
  - » Identical volumes
  - » Varied geometry
- » Newly designed mouse WBP chambers
- » Bias flow pump (emka VENT4)
- » Manometer
- » IOX2 software



### MECHANICAL TESTS

- » Ambient noise test
  - » Induced mechanical noise
  - » Varied pneumotach assemblies
  - » Varied noise amplitude
- » Leak assessment
  - » Pressurization to 30 cmH<sub>2</sub>O
  - » Hold period of 30 seconds
- » Calibration
  - » 2-point calibration method
  - » 10 mL over 5 seconds
  - » 8 units, 5 repeats per unit
  - » Coefficient of variation (SD/Mean)

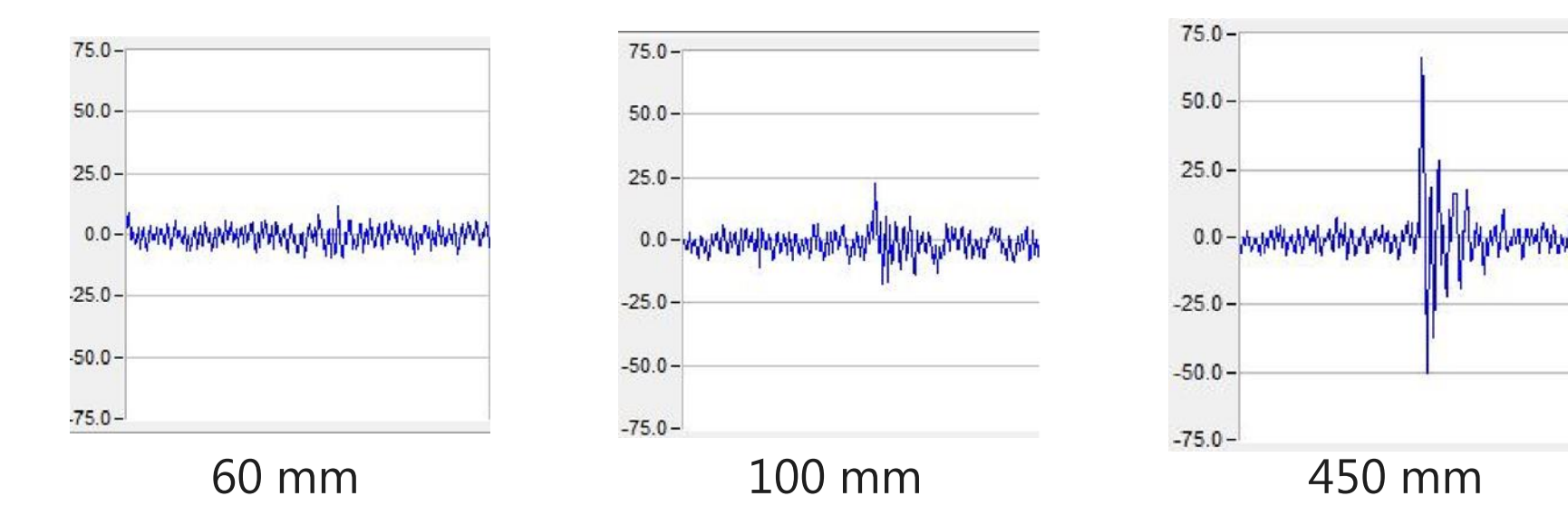
### PRELIMINARY IN VIVO TESTS

- » Naive female C57BL/6 mice
- » No prior acclimation
- » 20 minutes of recording - AM
  - » Outcome: Average respiratory rate over last 5 minutes
- » Clear & coloured WBP units
- » Repeated measurements over consecutive days

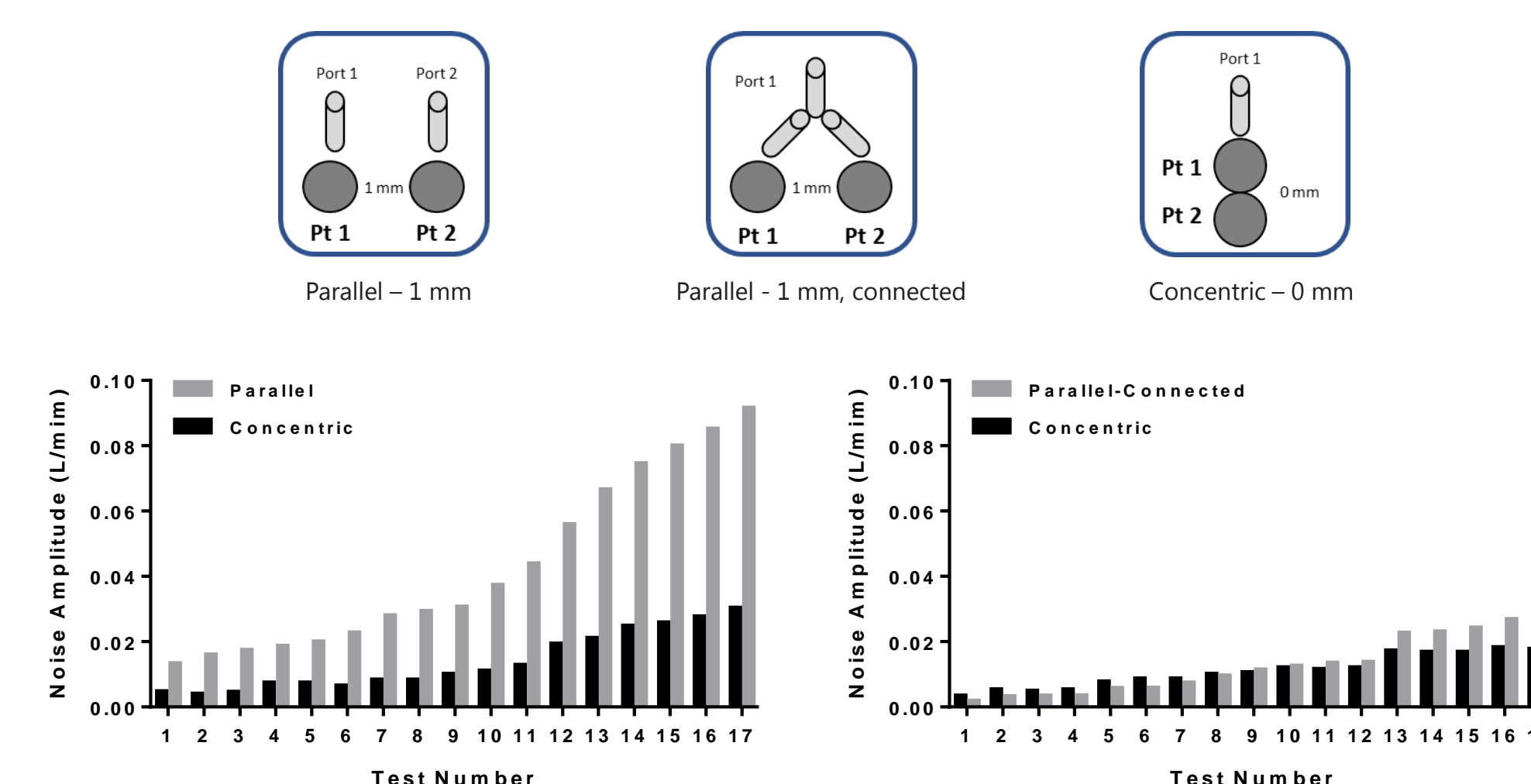
## RESULTS

### AMBIENT NOISE CANCELLATION

Disturbance by ambient noise increases with pneumotach separation



Ambient noise effect is improved with novel concentric pneumotach



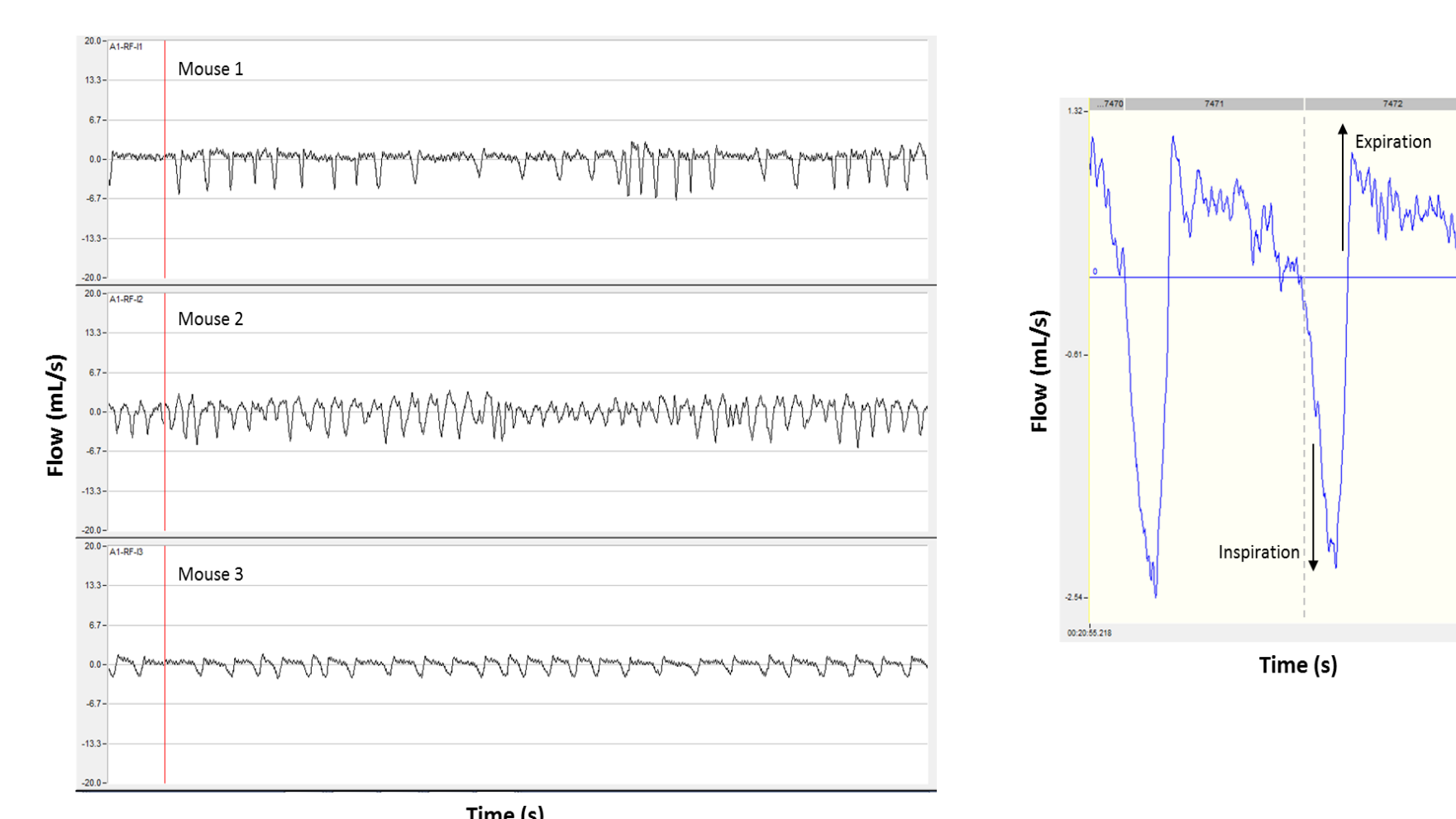
### LEAK ASSESSMENT & CALIBRATION

Absence of leak up to 30 cmH<sub>2</sub>O & consistent calibration values

| WBP Unit # | Calibration Range          | Leak Assessment                     |  |
|------------|----------------------------|-------------------------------------|--|
|            | Coefficient of variation % | Applied Pressure cmH <sub>2</sub> O | Pressure Drop at 30 s cmH <sub>2</sub> O |
| 1          | 2.30                       | 30                                  | 0  |
| 2          | 0.28                       | 30                                  | 0  |
| 3          | 3.20                       | 30                                  | 0  |
| 4          | 2.11                       | 30                                  | 0  |
| 5          | 1.38                       | 30                                  | 0  |
| 6          | 1.77                       | 30                                  | 0  |
| 7          | 1.48                       | 30                                  | 0  |
| 8          | 2.05                       | 30                                  | 0  |
| Mean (SD)  | 1.82 (0.84)                | 30                                  | 0  |

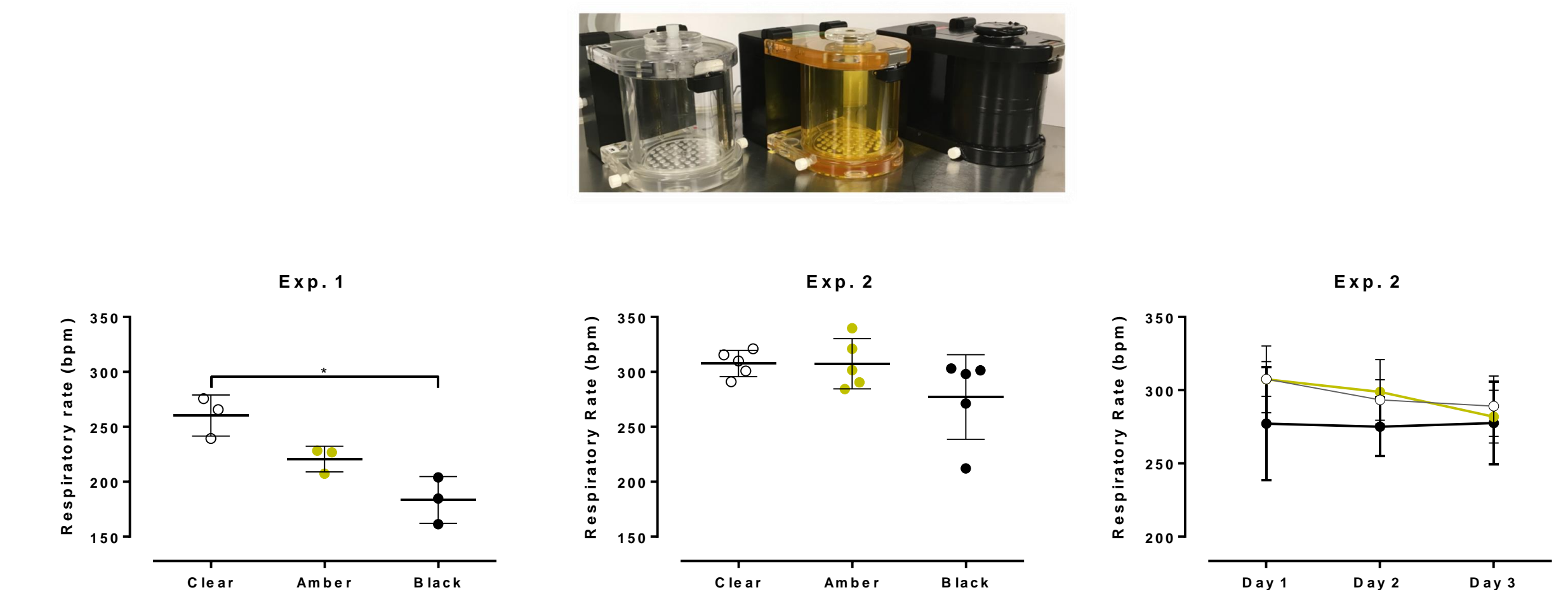
### PRELIMINARY IN VIVO TESTS

Example of experimental flow signal traces in three naive mice



### PRELIMINARY IN VIVO TESTS

Respiratory rate of naive C57BL/6 female mice in clear & coloured WBP chambers



## DISCUSSION

- » A new mouse WBP design is proposed, with the objective of improving signal quality while reducing subject disturbances during measurements.
- » The concept employs:
  - » An innovative pneumotach geometry that improves ambient noise cancellation.
  - » An adequate sealing mechanism that ensures a sensitive signal detection and stability.
  - » Features to enable the subjects to better cope with the environment of the measurement device.
- » Feedback is welcome on the design as well as on the preliminary mechanical and *in vivo* tests.

## CONCLUSION

- » Areas of respiratory research rely on WBP for studies related to sleep apnea, respiratory depression, or neuromuscular diseases.
- » Improvement to the measurement technique could potentially have overall beneficial effects on group sizes and separation, as well as on WBP result repeatability and reproducibility.

## DISCLOSURE

At the time of the study, AR, SA, SR, and PG were employed by SCIREQ Inc., a commercial entity with interests in a subject area related to the content of this presentation. SCIREQ Inc. is an emka TECHNOLOGIES company.



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