Piezoelectric sensors for noninvasive breath rate tracking in a cage setting

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BACKGROUND

Noninvasive detection of respiratory output enables longitudinal collection of breathing data in rodents and is useful for studying respiratory control, tracking disease progression, response to treatment, and drug induced respiratory abnormalities. A breath sensing method in a cage setting could be used to automatically track certain breathing parameters continuously over extended periods of time, allowing simultaneous collection of data from a large number of animals, with minimal stress to the animals.

Piezoelectric sensors produce voltage in direct response to physical pressure, and relay information related to animal movements, including breathing, from within a cage. Signal Solutions' **PiezoSleep™** system uses a piezoelectric sensor placed at the bottom of the cage to noninvasively track sleep and wake in rodents without the need for EEG. A low amplitude, relatively regular frequency piezo signal is one feature used to identify periods of sleep. This signal is presumed to be from movements related to breathing, and a breath rate estimate is provided from the **PiezoSleep™** software. To date, breath detection from the piezoelectric signal has not been validated with a second method. Plethysmography is the gold standard for noninvasive respiratory detection, providing accurate measurements of breath frequency and volume, however, confines the animal to a small chamber, limiting data collection to a few hours. In this study, breath rate estimates from piezoelectric signals were directly compared to breath rate estimates from plethysmography signals in a validation study for piezoelectric based breath tracking.

METHODS

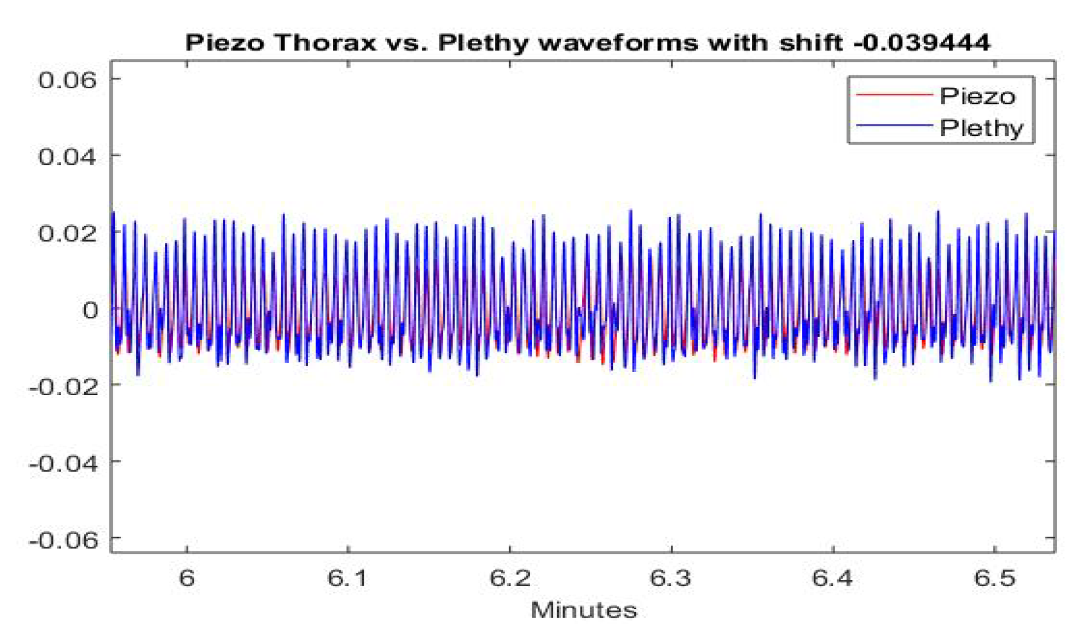
Respiratory output was collected from male and female AKR and C57BL/6 mice, weighing 25-41 grams, in a 160 ml. plethysmography chamber outfitted with a piezoelectric film sensor. Chamber air pressure was measured with a TSD160A Biopac differential pressure transducer and sampled and recorded with Biopac Acknowledge software at 100HZ, with constant airflow supplied at 300 mls/min. Mechanical pressure from a piezoelectric film sensor placed underneath the mouse was sampled at 120HZ and recorded using **PiezoSleep™** data acquisition software. Animal behavior was also recorded by video.

After a period of acclimation, signals were recorded over 1-2 hours. Twenty-three individual recordings were used to assess breath rates, after removing recordings with minimal sleep or technical issues. From each recording, signals were aligned, and breath rates were estimated over 4 second overlapping windows with 2 second increments, using an autocorrelation-based method. Breath periods were determined from peaks in the autocorrelation function, which correspond to the breath periods. The height of the fundamental peak indicates how well correlated consecutive breath intervals are. Estimates were made only in intervals where sufficient periodicity was detected based on the autocorrelation peak height. Error is taken as the difference between the estimates from the plethysmography and piezoelectric signals and broken into 2 categories: The root mean square error (RMSE) of the breath rate in Hz; and anomalous error, which is the result of not selecting the fundamental peak associated with the breath interval (i.e. RMSE greater than 50%). Anomalous intervals were usually the result of noise or motion interference and are reported in terms of percent over all the test samples for each group. Breath rate estimates at 2 seconds intervals could then be averaged over larger intervals, reducing resolution, but improving robustness.

RESULTS

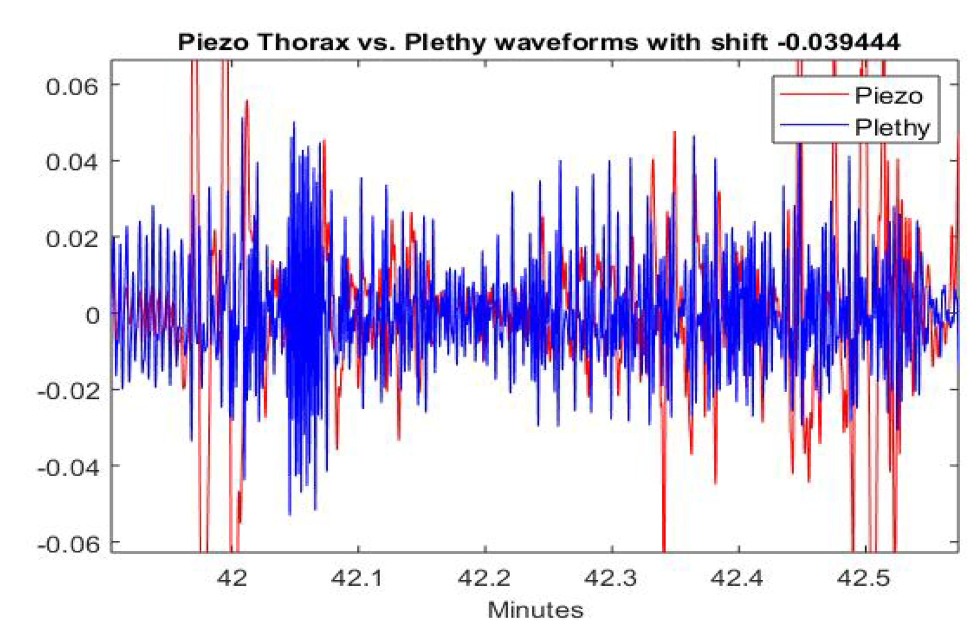
PIEZOELECTRIC AND PLETHYSMOGRAPHY SIGNAL OVERLAYS

30 second period of sleep



Minute 6-6.5: asleep
BR piezo 2.60-2.68 piezo; BR plethy 2.63-2.80

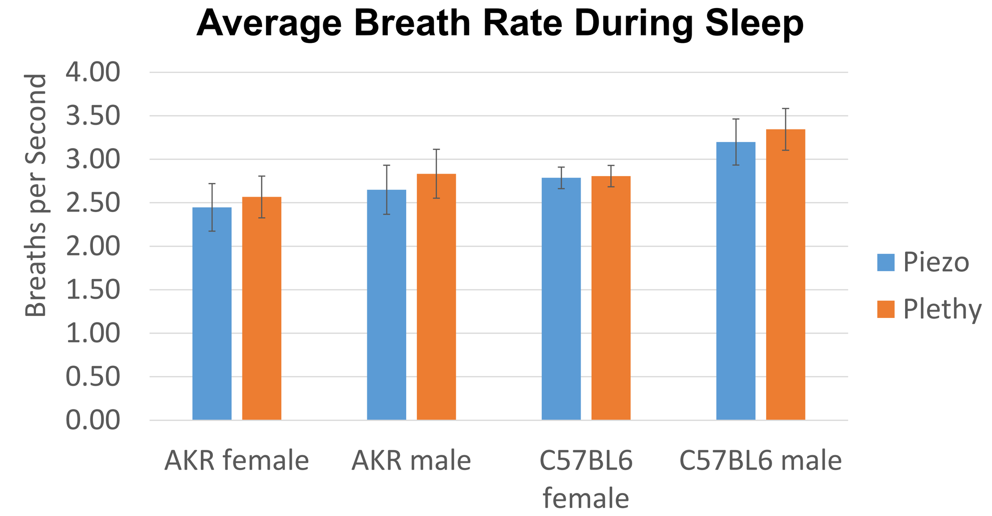
30 second period of wake



Minute 42-42.5: Observed awake/grooming
BR piezo: NaN BR plethy: 2.4 - 5.7

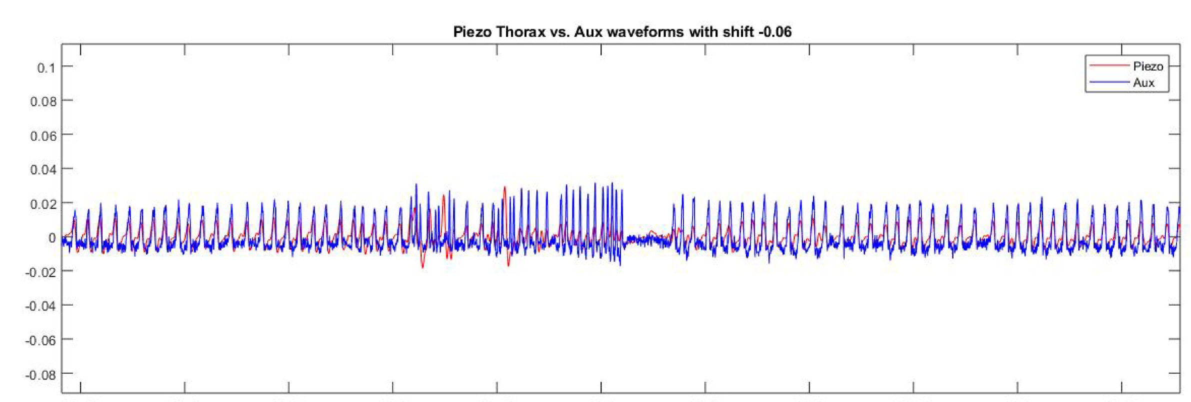
BREATHING DURING OBSERVED SLEEP

Average Breath Rate During Sleep



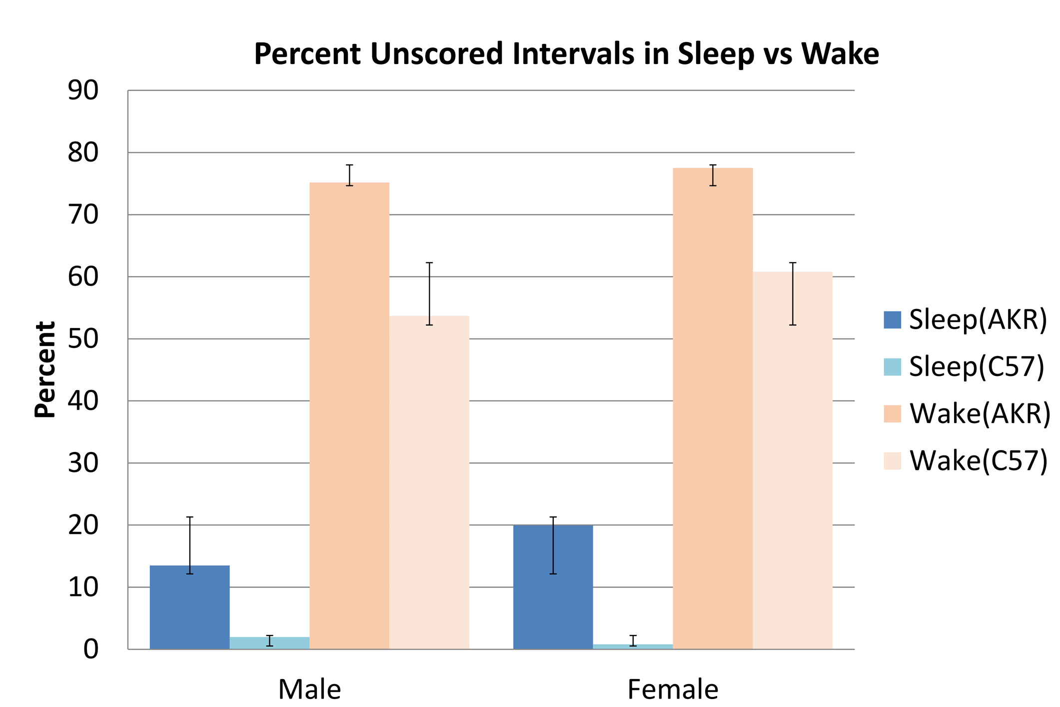
Breath Rates calculated from piezoelectric sensor and plethysmography during sleep. Percents shown are averaged from scored intervals of collective recordings of either male or female C57BL/6 or AKR mice.

Signal Disruption During Sleep

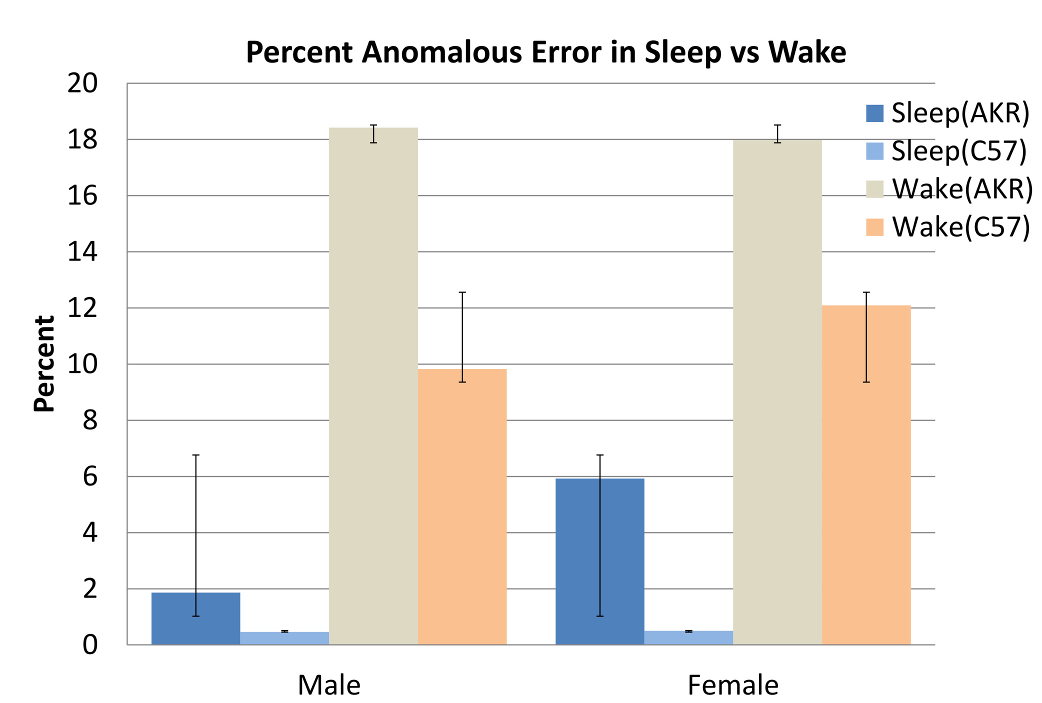


30 second interval of observed sleep with apnea like signal. Piezo red, plethy blue. C57BL6 male/04/12/19.

PIEZO BASED BREATH DETECTION DURING SLEEP AND WAKE



PERCENT OF UNSCORED TWO-SECOND INTERVALS DURING SLEEP AND WAKE. An unscored interval indicates that the piezo signal did not meet the periodicity criteria to be recognized as breathing. Unscored intervals were predictably higher during wake, when animal movements obscure breathing signals. Unscored intervals during sleep will be further investigated with goals of improving piezo based breath tracking and to include classification of non-regular breathing signals during sleep. Percents shown are averaged from all recordings of male and female AKR and C57BL/6 mice.



PERCENT ANOMALOUS INTERVALS DURING SLEEP AND WAKE. Anomalous intervals are intervals with scored breath rates that differ by more than 50% between piezo and plethysmography. Percents shown are averaged from all recordings of male or female AKR or C57BL/6 mice.

CONCLUSIONS

- Average breath rate estimates from piezoelectric sensors closely match breath rate estimates from plethysmography during sleep in male and female mice.
- Interruptions in breathing during sleep such as apnea appear to be identifiable by piezoelectric sensors.
- For appropriate indications, piezoelectric sensors should be useful as a high throughput method to continuously track important breathing parameters over extended periods of time within an animal's cage.

FUTURE WORK

- Assess ability to reliably detect other disease relevant breathing parameters with piezoelectric sensors, such as apnea and ventilatory stability during sleep, and estimate breath rates during wake, using appropriate animal models.
- Improve breath rate estimator and develop algorithms to include detection of breathing abnormalities such as apnea and irregular breathing.
- Test automated breath detection in Signal Solutions' custom cages and in new systems in commercial cages using animal models with breathing abnormalities.

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