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Research Paper

IR thermography-based monitoring of respiration phase without image segmentation

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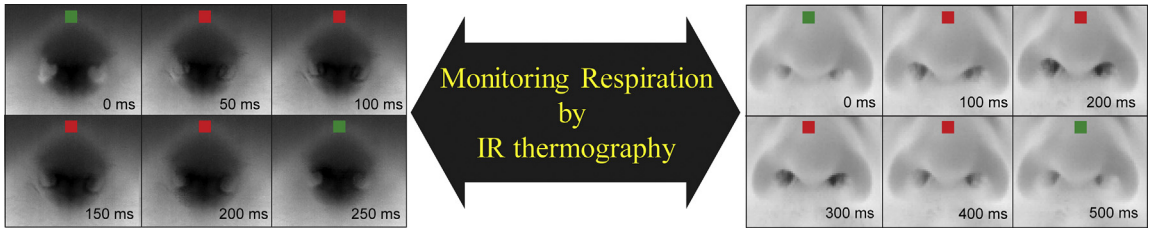
GRAPHICAL ABSTRACT



HIGHLIGHTS

- A new algorithm for improving non-contact monitoring of respiration withx IR thermography is established.
- Novel algorithm obviates the need for defining regions of interest, image segmentation and tracking of the nostril.
- Validation in a preclinical mouse model and human subjects confirm accurate, robust, user-friendly extraction of respiration phase.
- The novel approach facilitates wider application of IR thermography in biomedical and clinical research.

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ABSTRACT

Background: Respiratory rate is an essential parameter in biomedical research and clinical applications. Most respiration measurement techniques in preclinical animal models require surgical implantation of sensors. Current clinical measurement modalities typically involve attachment of sensors to the patient, causing discomfort. We have previously developed a non-contact approach to measuring respiration phase in head-restrained rodents using infrared (IR) thermography. While the non-invasive nature of IR thermography offers many advantages, it also bears the complexity of extracting respiration signals from videos. Previously reported algorithms involve image segmentation to identify the nose in IR videos and extract breathing-relevant pixels which is particularly challenging if the videos have low contrast or suffer from suboptimal focusing.

New method: To address this challenge, we developed a novel algorithm, which extracts respiration signals based on pixel time series, removing the need for nose-tracking and image segmentation.

Results & comparison with existing methods: We validated the algorithm by performing respiration measurements in head-restrained mice and in humans with IR thermography in parallel with established standard techniques. We find the algorithm reliably detects inhalation onsets with high temporal precision.

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Conclusions: The new algorithm facilitates the application of IR thermography for measuring respiration in biomedical research and in clinical settings.

1. Introduction

All mammals rely on the active ventilation of their lungs for pulmonary gas exchange. Coordinated muscle contractions control a suction-pump process which eventually delivers oxygen to and removes carbondioxide from the bloodstream during inhalation and exhalation, respectively. Inhalation also mediates the transport of airborne odorant molecules to the olfactory receptors in the nasal epithelium, which is the first step in olfactory perception. During odorant sampling in the environment, inhalations are commonly structured into one or more brief pulses, also referred to as sniffing. Sniffing is an active sensing process which has a major influence on olfactory perception (Bensafi et al., 2003; Mainland and Sobel, 2006) and which is modulated in response to environmental factors and by emotional states (Bensafi et al., 2002; Ferdenzi et al., 2015, 2014). Olfactory dysfunction is also one of the earliest pathological symptoms in various neurodegenerative diseases (Godoy et al., 2015; Sobel et al., 2001). Respiration and sniffing behavior thus not only reflect a critical vital function, but are also crucial for assessing the physiological and psychological state of an organism.

A wide variety of methodologies have been established for monitoring respiration in biomedical research and in clinical settings. A particularly attractive approach involves the use of infrared cameras to enable non-contact, distant measurement. In this measurement modality, respiration rate is obtained based on imaging temperature differences related to inhalation and exhalation at the intranasal surface. Proof-of-principle demonstrations of nasal thermography have been performed in neonates and adult humans (Abbas et al., 2011; Chauvin et al., 2016; Cho et al., 2017; Fei and Pavlidis, 2010; Lewis et al., 2011; Pereira et al., 2015) Furthermore, we have recently adapted IR thermography for respiration monitoring in the most common preclinical experimental animal model, the mouse *mus musculus.* Specifically, we have established thermography for use in head-restrained animals (Esquivelzeta Rabell et al., 2017). This experimental approach facilitates combining precise stimulus control with monitoring neural activity and is widely used by researchers studying sensory systems including vision (Andermann et al., 2010), somatosensation (O'Connor et al., 2010) and olfaction (Rokni et al., 2014), as well as reward-based learning (Cohen et al., 2012) and decision-making (Allen et al., 2017) in rodents.

While the non-invasive nature of IR thermography undoubtedly offers advantages, it also bears the complication of extracting respiration signals from complex video data. Previously reported algorithms, including our own first-generation algorithm (Esquivelzeta Rabell et al., 2017), involve image segmentation to identify the nose in IR videos in order to extract breathing-relevant pixels. This step can be particularly challenging if the videos have low contrast or suffer from suboptimal focusing, compromising the overall robustness of the approach.

In this work, we have developed a novel algorithm to address this limitation. Signal extraction is based on the analysis of temporal pixel properties, rather than using image segmentation. We validated our approach by comparison to the invasive standard method in mice, which is based on monitoring respiration-related pressure changes in the nasal cavity. Compared to the previously published algorithm (Esquivelzeta Rabell et al., 2017), the new algorithm provides major improvements; a) it does not require manual parameter setting, b) it is about 10 times faster and c) it detects inhalation onsets with fewer errors. We have further applied the new algorithm to IR videos from freely breathing humans, taken while the subject was performing small head movements. Validation was performed by comparison to signals obtained from a piezo-electric belt.

2. Materials and methods

2.1. Mice

Experiments were performed in accordance with standards and rules of KU Leuven and national regulations, implementing European policies, including the EEC Council Directive 2010/63/UE. We used C57BL/6 males at postnatal ages of 2–6 months. Mice were housed on a 12 h dark/12 h light cycle (dark from 07:00 to 19:00).

2.2. Surgery

All surgeries were performed under aseptic conditions with animals under ketamine/medetomidine (60 mg kg^{-1}, and 0.5 mg kg^{-1}, intraperitoneal, respectively) anesthesia. Analgesia (ketoprofen, 5 mg kg^{-1} intraperitoneally; buprenorphine, 0.1 mg kg^{-1}, intraperitoneally) was administered post-operatively.

2.3. Intranasal cannula implantation

To monitor intranasal pressure, a 7 mm long, 0.8 mm inner diameter ×1.6 mm outer diameter PTFE cannula (PTFE Tubing, item # EW-06407-41; Cole-Parmer) was implanted into the left nostril. An incision was made along the midline from the fur transitional area at the tip of the nose to caudal of the eyes using a scalpel. Then, a small hole was drilled with a carbide bur (Neoburr FG 1/4; Microcopy) in the bone overlying the nostril. The cannula was put on the bone such that it covers the hole, stabilized with luting agent (RelyX Luting Cement; 3 M) and mounted using dental cement (Jet Denture Repair; Lang Dental). The cannula was capped using a steel plunger. The length of the plunger was chosen such that when inserted into the cannula, the distal end of the plunger would protrude ∼200 μm from the distal end of the cannula.

2.4. Head plate implantation

Mice were implanted with a head plate for head fixation as described previously (Cohen et al., 2012). The scalp and fascia were removed, and a metal head plate was stabilized over the midline with luting agent (RelyX Luting Cement; 3 M) and mounted using dental cement (Jet Denture Repair; Lang Dental).

2.5. Olfactometry

Animals were head-restrained inside a sound and light isolated box (75 cm3) with constant exhaust to ensure rapid clearance of odorants and to prevent distraction of the animal. To test the performance of our method during sniffing, we presented novel and familiar odors to the mouse, as described previously (Esquivelzeta Rabell et al., 2017). Briefly, odors were delivered using a custom-made olfactometer. The flow rate was fixed to 500 ml min^{-1}. The olfactometer was controlled using custom-written scripts in LabVIEW (National Instruments).