Running Wheel Metric

Continuously Monitor Animal Wheel Running Activity

INTRODUCTION

The Vium Digital Vivarium Platform offers two different types of activity metrics, which allow researchers to dissociate overall physical activity and voluntary activity: the Vium Motion metric and the Vium Percentage (%) Time Running on Wheel metric. The Vium Motion metric measures overall activity, which is comprised of both voluntary and involuntary motor movements, including wheel running, asa well as a wide range of complex behaviors, such as eating drinking and grooming. These behaviors contribute to background activity levels, especially during the light cycle when animals are less active. In contrast, the Vium % Time Running on Wheel metric specifically captures free running on the wheel, which accounts for voluntary activity. A number of factors are known to differentially alter overall physical activity and voluntary wheel running activity (1,2).

Running wheels are commonly employed in rodent research not only to provide animal enrichment, but to measure physical activity and circadian rhythm pattens (1). Wheel running provides valuable information on many aspects of an animal's well-being and physiology, including motor function, energy balance, cognition, as well as stress-, anxiety, and depression-like behaviors (2,3). Wheel running activity has also been reliably used as a gold standard for measuring circadian rhythm patterns, therefore becoming an invaluable tool for phenotyping and investigating a number of disease models, including aging, metabolic, psychiatric, and neurological diseases (4-6).

Preclinical Researchers Use This Metric to:

- **Continuously and automatically monitor percentage time animal spent running on wheel with both low and high resolution time bins**
- **Complement overall and spontaneous physical activity (Vium Motion Metric)**
- **Measure short- and long-term changes in animal behavior, physiology, and well-being**
- **Assess circadian rhythm patterns**
- **Evaluate therapeutic interventions in animal models of disease**

PERCENTAGE TIME RUNNING ON WHEEL METRIC

This metric determines whether a mouse is running on the wheel on a frame-by-frame basis and reports the percentage (%) of time spent running on the wheel. To derive this metric, computer vision algorithms locate animals in the wheel zone of the home cage and determine if they are running on the wheel (Fig. 1). The result is reported as a binary output: 1 for animal running on the wheel and 0 for animal not running on the wheel. These outputs are then aggregated into time bins (ex. 60-sec, 600-sec, or 3600-sec bins), wherein each bin represents the percentage time the animal spent running on the wheel (total number of instances running / total number of frames * 100).

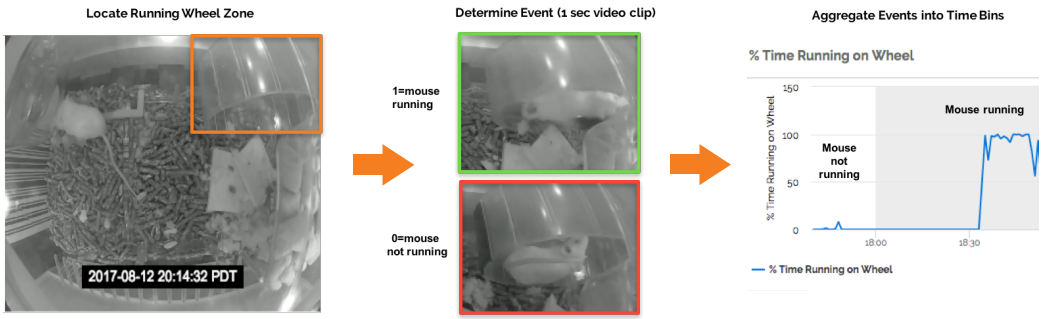

Figure 1. Schematic depicting generation of percentage (%) time running on wheel metric.
Computer vision algorithms locate running wheel zone then detect binary event (1=mouse is running on wheel for full 1-sec video clip, 0=mouse is not running on the wheel for full 1-sec video clip). Events are aggregated into time bins and can be visualized for individual subjects or as group averages in the online Research Suite.

METRIC VALIDATION

Metric development and validation were conducted by sampling >24,000 1-sec video clips from six independent studies of black and white mouse strains (n=3 studies each). Clips were manually annotated with the following labels: "mouse running on the wheel" or "mouse not running on the wheel." Animals coming in and out of the wheel zone or running only during a portion of the 1-sec video clip were classified as "not running on the wheel." Metric performance was compared to manual performance and validated for accuracy.

RESULTS

Performance of the digital metric was compared to manual annotations for black (Fig. 2A) and white mice (Fig. 2B), respectively. For majority of cases, the Vium metric correctly classified whether an animal was running or not running on the wheel. The balanced accuracies for black and white mice were 96.81% and 98.53%, respectively.

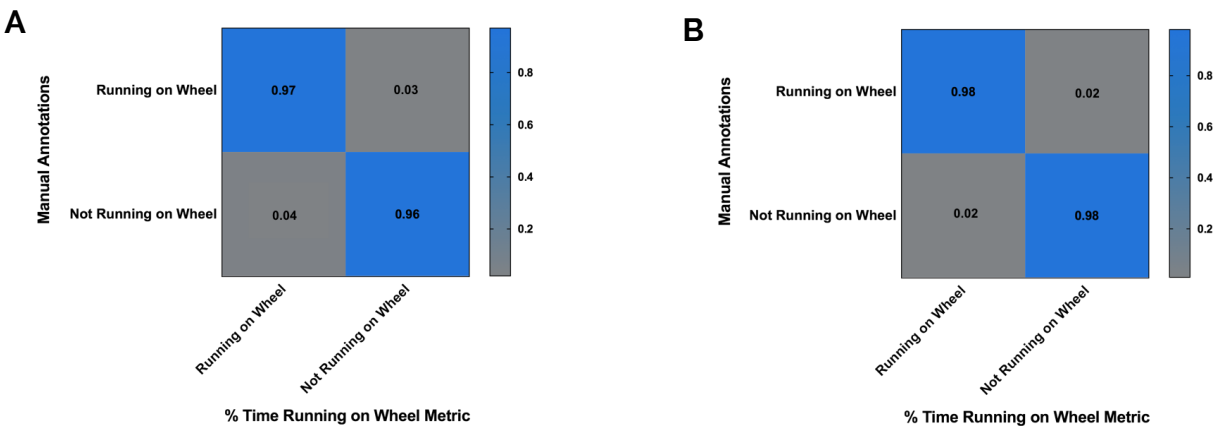

Figure 2. Confusion matrices of metric model performance.
Metric model performance using video clips from black (n=3020) **(A)** and white (n=2788) **(B)** mice. Color bar indicates percentage of agreement between digital metric and manual annotations with intense shades of gray and blue indicating close to 0 or 100% agreement, respectively.

This validated metric provides continuous information on the % time a mouse spent running on the wheel during specified time bins. Figure 3 shows representative charts of the metric aggregated into 5-min (Fig. 3A) and 20-min (Fig. 3B) time bins from an individual subject in a curprizone mouse model of multiple sclerosis (MS) study. When fed with 0.2% cuprizone in chow, this subject showed periods of attenuated wheel running activity.

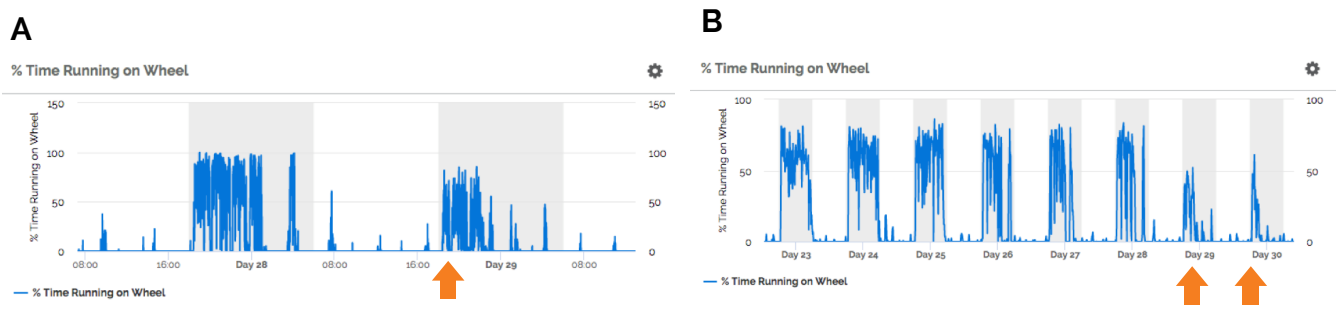

Figure 3. Sample data of percentage (%) time running on wheel metric.
The percentage (%) time running on wheel metric aggregated into 5-min **(A)** or 20-min **(B)** time bins for an individual subject on the online Research Suite. In a mouse model of multiple sclerosis (MS), a representative subject showed periods of attenuated wheel running activity, which may indicate presence of disease (orange arrows). Gray shaded areas depict time in dark cycle.

DISCUSSION

Here we show that the Vium Percentage (%) Time Running on Wheel metric provides automated, continuous, and accurate determination whether an animal is running on the wheel. Depending on the goals of the experiment, low and high-resolution time bins can be investigated for individual subjects or as group averages on the online Research Suite.

We also demonstrate the capability of this digital metric to investigate mouse models of disease. In a cuprizone mouse model of Multiple Sclerosis (MS), a representative subject showed periods of attenuated wheel running activity, which may indicate periods of decreased gross motor function resulting from demyelination (7). In conjunction with spontaneous physical activity, wheel running can be used not only to detect changes in overall activity, energy homeostasis, cognition, and social behaviors, but also to acquire more sensitive measurements of circadian rhythm patterns over short and long-term periods of time (2-5). The Vium % Time Running on Wheel metric can be used as a direct readout for the evaluation of compound therapeutic efficacy and investigation of animal models of aging and disease (5,6).

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