DANISH TECHNOLOGICAL INSTITUTE

Project proposal – Danish Technological Institute (DTI)

Progression of clinical symptoms and humane endpoint in experimental mice

Organisation

The Danish Technological Institute is a workplace and research-based organization that helps companies develop new products, technologies, and processes. The institute works with innovation, consultancy, testing, and certification across a wide range of technical fields. It is characterized by an interdisciplinary environment focused on professional development, collaboration, and applied research closely connected to industry.

Challenge outline

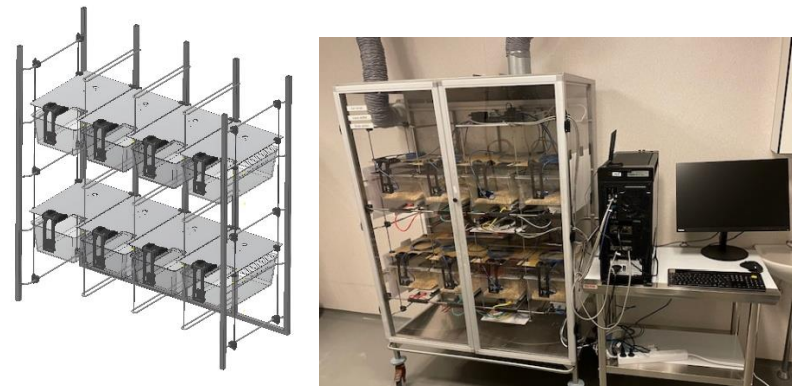
The welfare of laboratory mouse is critical for accuracy and reproducibility in research. Mouse behaviour is a reliable indicator of its well-being. Traditional methods for monitoring welfare can disturb the mice and are resource-intensive tasks. The approach is to monitor mice that are group-housed in cages with shelters and environmental enrichment in accordance with current housing regulations. Environmental enrichment and the use of computer vision are typically incompatible, and in many studies where AI is used, the mice are therefore housed without enrichment. The idea here is to use AI while the mouse remains housed in the "complex" environment. With this monitoring, the aim is to identify behavioral parameters that can distinguish between healthy and sick mice, and to detect early signs that a mouse is approaching the Humane Endpoint (HE) (if/when the mice are so affected that, for animal welfare reasons, they must be removed and euthanized), without needing to take the mouse out of the cage for assessment.

In the project that has been carried out, various correlations between behavior and disease progression have already been demonstrated, including that behavior can, with fairly high precision, be used to characterize the course of disease comparably to current manual assessment of the mice. Where more knowledge is needed—and there is a need for better precision—is in the final stage of the disease course. This concerns better identification of when a mouse is approaching the Humane Endpoint (HE).

Experimental setup

The experiment included 18 mice from the EAE model and 6 control mice. There are 4 weeks of video from 8 cages, with 2 cameras in each cage, 3 tail-marked mice per cage, and daily manual EAE scoring of the mice.

The EAE model is a widely used animal model for assessing therapeutic agents targeting autoimmune-mediated central nervous system (CNS) disease, such as multiple sclerosis. In experimental mice the disease course initiates paresis beginning in the tail, followed by retrograde impairment of the legs. The progression is monitored daily using a standardized scale from 0 (healthy) to 5 (HE), where mice are taken out of the cage and evaluated. This categorization can be used to track progression and compare with what is observable in the recordings from the cage at each stage.



8 cages, with 2 cameras in each cage (front and top)

Top view pictures, tracking and tail-mark

Desired project outcome

To describe clinical symptoms of progression of the EAE model with special focus on late symptoms and/or human end points at the end of the disease course.

Possible solution strategies

Perhaps a classic supervised keypoint model, which is subsequently used to classify known EAE symptoms, e.g. sideways movement or reduced tail curl. Alternative testing of general foundation models that can be appropriately "calibrated" for the task.

Relevant literature

A systematic review of the development and application of home cage monitoring in laboratory mice and rats https://bmcbiol.biomedcentral.com/articles/10.1186/s12915-023-01751-7

A systematic review of methods typically used, https://arxiv.org/abs/2301.06187

Note: **This project will require a confidential agreement to access data.**

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