Compound Screening via AI-Based Zebra Fish Behavioral Tracking

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Overview

Screening compounds for a drug development campaign may yield initial hits, getting signals for the downstream effectiveness of the compounds is still challenging, especially for psychiatric disorder related indications. The group of Prof. Takashi Kawashima has developed a potential solution via a high-resolution tracking method used to analyze zebrafish behavior. Established to overcome limitations of confined environments of standard multi-well plates, this method employs machine learning analysis of body movements to categorize different behavioral states. The Kawashima group has tested the system using psychedelic compounds to understand their effects by observing changes in zebrafish larvae behavior.

Background and Unmet Need

Traditional methods for studying drug effects on zebrafish larvae primarily rely on small, confined chambers such as those found in multi-well plates. These environments can induce stress and restrict natural behaviors (e.g. exploration), hindering accurate assessments of a drugs impact. Therefore, a significant limitation exists in understanding how drugs influence zebrafish behavior in more natural settings.

The Solution

Prof. Kawashima and his team addressed this need by developing a cutting-edge method for tracking zebrafish behavior in a large, unconfined environment (90 mm) compared to the standard multi-well plate (~4 mm). Their system integrates a high-resolution camera to capture detailed movements of individual fish within the open environment. Then the video is evaluated by a machine learning algorithm to ***track behavioral states, including anxiety and the anxiolytic effects of drugs.***

Technology Essence

The system uses a machine learning algorithm trained to recognize subtle differences in zebrafish movement patterns, extracting features such as:

- ***Body curvature:*** Turning, exploration, and resting postures.
- ***Tail fin movement:*** Reveals swimming speed and intensity.
- ***Overall velocity and displacement:*** Measures exploration range and activity level.

Analysis of these features can classify distinct behavioral states with high accuracy, enabling objective assessment of drug-induced changes.

Applications and Advantages

- ***Studying natural behaviors:*** Enables observation of how drugs impact exploration, stress responses, and other behaviors in an unconfined setting, providing a more realistic picture of their effects.
- ***Evaluating novel therapeutic agents:*** A tool for screening and assessing the behavioral effects of potential drugs for mood disorders and other neurological conditions.
- ***Understanding neural mechanisms:*** Correlating behavioral changes with neural activity data, deeper insights into the mechanisms underlying drug action in the brain.

Development Status

The researchers have built and established their zebrafish larvae tracking system. Along with successfully validating their method by studying the effects of psilocybin, ketamine, and fluoxetine on zebrafish behavior. Their findings demonstrate the method's sensitivity in detecting significant changes in exploration and stress-related behaviors following psychedelic modality administration. Further application and expansion of the system to screen multiple fish simultaneously is being considered and other types compounds for modalities could be potentially screened.

References

Braun, D., Rosenberg, A.M., Rabaniam, E. et al. High-resolution tracking of unconfined zebrafish behavior reveals stimulatory and anxiolytic effects of psilocybin. Mol Psychiatry (2024). https://doi.org/10.1038/s41380-023-02391-7 [1]