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Applications Note

Systems biology

IntelliPy: a GUI for analyzing IntelliCage data

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Abstract

Summary: The IntelliCage systems offer the possibility to conduct long-term behavioral experiments on mice in social groups without human intervention. Although this setup provides new findings, only about 150 studies with the IntelliCage system have been published in the last two decades, which is also caused by the challenging problems of processing and handling the large and heterogeneous amounts of captured data. This application note introduces the Python-GUI IntelliPy, especially designed for users not very experienced in using programming languages. IntelliPy allows users to quickly analyze the IntelliCage output in a user-friendly way, thus making the systems more accessible to a broader audience.

Availability and implementation: https://github.com/NiRuff/IntelliPy.

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Supplementary information: Supplementary data are available at *Bioinformatics* online.

1 Introduction

Behavioral experiments in which animals are tested at a single time point and then classified into a particular category are increasingly being replaced by longitudinal studies in which animals are observed over a longer period of time (Wendelmuth *et al.*, 2020). The IntelliCage (IC) system (TSE systems) (for a recent review see Kiryk *et al.* (2020)) is designed for conducting fully automated high-throughput behavioral and learning experiments for mice living in social groups while ensuring minimal human intervention (Bohannon, 2002a,b; Knapska *et al.*, 2006). The animals can be observed for extended time periods up to several weeks, providing new insights into mouse behavior that might not be detectable in short-term observations with human intervention (Knapska *et al.*, 2006). However, even though ICs offer unprecedented opportunities for studying many complex behavioral paradigms and were used in more than 150 studies, the system still lacks broad attention (Kiryk *et al.*, 2020).

This lack of acceptance could have several reasons. There are still some limitations to the IC systems, such as the fact that they can only record the positions and behavioral parameters of the animals in the corners of the cage where the RFID detectors are located. This could be a limitation for some experimental designs. In addition, the experimental design itself, and especially the analysis of the huge amounts of data, may cause difficulties for researchers. This may be partly because they are overwhelmed with the design of the IC experiments, and partly because the GUI (Graphical User Interface) analysis options provided by the integrated TSE analyzer are very limited for the large amounts of data generated. To address this last drawback, the open-source Python library PyMICE (RRID: nlx_158570) for analyzing IC data in Python (Dzik *et al.*, 2018) as well as the proprietary FlowR IntelliCage Suite (XBehavior, Voikar *et al.*, 2018) were developed. The former project simplified data analysis for IC experiments for users being routine in programming with the Python Programming Language.

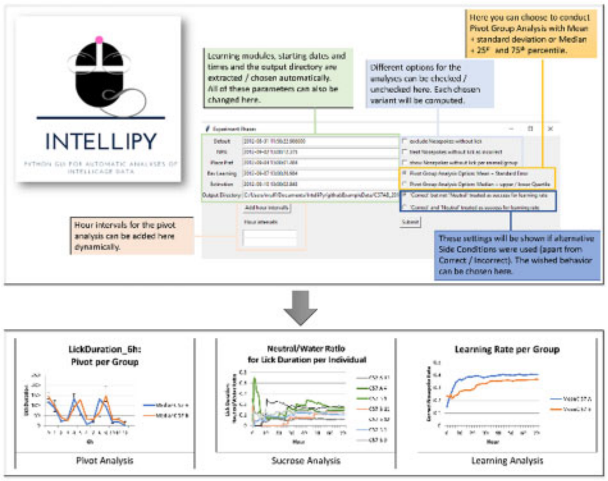
However, the typical users of ICs, namely the behavioral scientists, are in the majority of cases not versed with programming languages at all. Therefore, these scientists are still left with the limited data analysis capabilities included in the TSE Analyzer or the proprietary FlowR IntelliCage Suites.

The here introduced IntelliPy aims to provide a free open-source graphical user interface, that expands some limited possibilities of the TSE Analyzer and accelerates the whole analysis, by providing a user-friendly yet powerful GUI. The GUI simplifies and automizes many aspects of the analysis, such as acquiring data per group, creating learning curves over time or pivoting parameters in different timeframes. All plots are automatically created, and the final tables for statistical tests are stored separately for the user. Installing, launching and running IntelliPy can be done within several minutes, and all chosen options are stored in a log file to make all settings traceable and thus ensure reproducibility. Being open source, an extension of the included analysis options is possible and desired.

2 Materials and methods

2.1 Installation and dependencies

IntelliPy is distributed using the Python Packaging Index (PyPI) and can be installed using pip with the command pip install intellipy. For



Here you can choose to conduct Pivot Group Analysis with Mean + standard deviation or Median + 25st and 75th percentile.

Learning modules, starting dates and times and the output directory are extracted / chosen automatically. All of these parameters can also be changed here.

Different options for the analyses can be checked / unchecked here. Each chosen variant will be computed.

Hour intervals for the pivot analysis can be added here dynamically.

These settings will be shown if alternative Side Conditions were used (apart from Correct / Incorrect). The wished behavior can be chosen here.

INTELLIPY
PYTHON GUI FOR AUTOMATIC ANALYSES OF INTELLICAGE DATA
Experiment Phases
Default
NPS
Place Pref
Rev Learning
Extinction
Output Directory
Add hour intervals
Hour intervals
□ exclude Nosepokes without lick
□ treat Nosepokes without lick as incorrect
□ show Nosepokes without lick per animal/group
● Pivot Group Analysis Option: Mean + Standard Error
○ Pivot Group Analysis Option: Median + upper / lower Quartile
● 'Correct' but not 'Neutral' treated as success for learning rate
○ 'Correct' and 'Neutral' treated as success for learning rate
Submit
LickDuration_6h: Pivot per Group
6h
Pivot Analysis
Neutral/Water Ratio for Lick Duration per Individual
Hour
Sucrose Analysis
Learning Rate per Group
Hour
Learning Analysis

Fig. 1. Settings in the IntelliPy GUI. The experimental phases are extracted automatically. Furthermore, additional hour intervals for the pivot analysis can be added dynamically. Further options can be chosen in the top right corner of the GUI before starting the analysis using the 'Submit' button. At the bottom, some of the automatically created plots for the analyses are exemplified

users not familiar with pip, a Windows exe, created using py2exe (0.10.1.0) is provided on the github page and can be used immediately after the download without having Python or any packages installed.

2.2 Usage

IntelliPy utilizes three .txt files of an IC experiment that can be extracted using the TSE Analyzer. Additionally, suppose new groups should be assigned that are not included in the *Animal.txt* file. In that case, a group assignment file can be created in order to conduct further groupwise analyses, assign one animal to multiple groups or to specify the used alternative label for experiments using more states than 'Correct' and 'Incorrect' for the learning rate (e.g. sucrose preference experiments). Details about the creation of this tab-separated text file and about running IntelliPy are given on the github page. An overview of the settings is given in Figure 1.

2.3 Pivot analyses

For the parameters measured by the IC systems, such as *LickDuration* or *NosepokeNumber*, pivot tables are created for each module by *IntelliPy*. By default, these timeframes are created per day, but others, e.g. 12-h timeframes can be added in the IntelliPy GUI settings. Each pivot analysis is conducted for the individual animals as well as for the defined groups. The analysis of the latter can be performed with mean or median including plots showing the standard deviation or quartiles of the groups' individuals. Resulting tables and plots are stored as xlsx files to show a broad overview immediately while enabling the user to utilize the data for further statistical tests.

2.4 Learning rates

As the experiments made with the IC systems can be conducted as learning experiments with different setups per phase, each individual's learning rate, and each group can be of high interest. Rather than only the final rate of correct attempts, the cumulative learning rate per hour and per visit is computed and plotted by *IntelliPy*. Herewith, the user can utilize longitudinal learning information for each individual and group per learning phase. It is even possible for those learning rates to choose whether to include all nosepoke (NP) occurrences or remove those not followed by a lick for the automated analysis. It can be argued about whether a NP not followed by a lick should or should not be accounted for as a correct attempt, so this decision is up to the user. Furthermore, there is the possibility of excluding all NPs not followed by a lick or treating them as incorrect attempts.

2.5 Alternative label analyses

If alternative labels as *SideCondition* were used in the experiment, e.g. when using two different liquids in the IC, this alternative label can be passed to IntelliPy in order to show more options for possible analyses. New output files will be created, treating the alternative label as wished and showing the ratio of *LickDuration* spent with each of the liquids per animal and group.

3 Discussion

The IC systems allow the research community to conduct long-term behavioral experiments of mice in social groups without human intervention. The here introduced GUI IntelliPy significantly expands the current analysis repertoire of the built-in TSE Analyzer by providing additional options for longitudinal analysis, such as treating NPs not followed by a lick in different ways or the computation of the current learning rate as a time—and trial-wise analysis. Additionally, the whole analysis is strongly accelerated by automatically extracting all used learning modules and automatically creating the analysis output. In comparison to the proprietary FlowR IntelliCage Suites, IntelliPy is simpler and lacks some analysis, such as anxiety and autism test or included statistical analyses but can still be expanded regarding modules that are important to the community as it is free and open source. IntelliPy was tested successfully using five public datasets of the PyMICE library (Dzik *et al.*, 2018) in IntelliCage Plus 3 format, with the most extensive dataset containing data of 21 mice over a period of two weeks. Newer formats did not introduce any changes that constrain the functionality of IntelliPy. The whole system aims to make the analyses as user-friendly as possible by e.g. automatically extracting all modules, start times and groups derived from the analyzed data. Overall, IntelliPy helps to simplify analyses of extensive IntelliCage data, which has so far been overwhelming for many users, thus making the application of these systems possible for a broader base of researchers.

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Author contributions

N.R. wrote the manuscript, designed, implemented and tested the GUI. M.M. and U.S. edited the manuscript and contributed to designing the research idea. S.G. supervised the research, edited the manuscript and contributed to writing. All authors read and approved the final manuscript.

Conflict of Interest: none declared.

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